External expert opinions for morphological pathology (histology and cytopathology)

August 2014

MSAC Application no.

1332

Assessment report

Assessment 1332 - External expert opinions for morphological pathology (histology and cytopathology) – Final Report, August 2014

Electronic copies of the report can be obtained from the Medical Service Advisory Committee's Internet site at http://www.msac.gov.au/

Enquiries about the content of the report should be directed to the above address.

This report is a contracted technical report for use by the Medical Services Advisory Committee (MSAC) to inform its deliberations. MSAC is an independent committee which has been established to provide advice to the Minister for Health on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC's advice does not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared for MSAC by Ms Kate Applegarth, Dr Suzanne Campbell, Dr Lisa Fodero and Mr Joe Scuteri from HealthConsult Pty Ltd with the assistance of members of the MSAC Health Expert Standing Panel (Appendix 1). The economic evaluation was undertaken by Mr Paul Mernagh (subcontractor for HealthConsult Pty Ltd). The report was commissioned by the Department of Health on behalf of MSAC.

This report should be referenced as follows:
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Abbreviations

APA	Approved Pathology Authority
APP	Approved Pathology Practitioners
CAP	College of American Pathologists
EEO	external expert opinion
EMSN	Extended Medicare Safety Net
HESP	Health Expert Standing Panel
HTA	Health Technology Assessment
ICC	immunocytochemistry
ICER	incremental cost-effectiveness ratio
IHC	immunohistochemistry
LSG	labial salivary gland
MBS	Medicare Benefits Schedule
MSAC	Medical Services Advisory Committee
NATA	National Association of Testing Authorities
NCSP	National Cervical Screening Program
NHS	National Health Service
PASC	Protocol Advisory Sub-Committee
PICO	population, intervention, comparator, outcomes
QALY	quality-adjusted life year
RCPA	The Royal College of Pathologists Australasia
SO	second opinion
UK	United Kingdom

Executive summary

Assessment of external expert opinions for morphological pathology (histology and cytopathology)

Purpose of application

In September 2012, the Department of Health and Ageing received an application from The Royal College of Pathologists of Australasia (RCPA) requesting Medicare Benefits Schedule (MBS) reimbursement of external expert opinions for morphological pathology (histology, cytopathology, haematology, microbiology and genetic pathology). The application was initially considered in August 2013 by the Protocol Advisory Sub-Committee (PASC) of the Medical Services Advisory Committee (MSAC), and was reconsidered by PASC in April 2014. The Final Protocol, dated May 2014, restricted the scope of the assessment to external expert opinions for bone marrow specimens (included in Group P1), all tissue pathology (which includes Group P5 items) and all cytopathology (which includes Group P6 items).

PASC advised that public funding for the proposed service should only apply in circumstances where:

Scenario 1 – the initial pathologist communicates with the clinician in charge of patient management, and suggests referral to an external expert pathologist, due to a rare, unusual or complex case where a primary or definitive diagnosis cannot be confidently made. It would then be at the discretion of the treating clinician to decide whether expert opinion is necessary (i.e. the service is not pathologist determinable).

Scenario 2 – the clinician in charge of patient management wants the initial pathology opinion verified or refined by a second, expert pathologist or by their preferred pathologist, irrespective of whether the initial pathologist cited uncertainty in their initial diagnosis or not.

Clinician-initiated expert opinion (*Scenario 2*) typically occurs at a tertiary centre to which a patient (most often an oncology patient) has been referred for further management. The initial pathology report may provide insufficient information to effectively manage the patient and the clinician may request an expert opinion from a pathologist who would normally provide the service to the treatment centre. In this case, the requesting clinician and the expert pathologist may be co-located; nevertheless, the expert pathologist would still need to provide a comprehensive written report in order for the service to be eligible for MBS funding.

PASC advised that second, expert opinions requested by a treating clinician should only be considered for public funding when there is insufficient information or uncertainty in the diagnosis. The intention of the proposed MBS items is not to provide funding for mandatory or routine review of all cases referred to treatment centres.

Furthermore, it is not intended that expert opinion provided within the original pathologist's laboratory (i.e. intra-departmental or intra-institutional) is funded under the proposed items.

Current arrangement for public reimbursement

Currently, public reimbursement of pathology opinions only applies to the initial pathology report. In circumstances where an expert pathology opinion is considered necessary for patient management, it is requested and provided though approved laboratories but this extra service is not eligible for MBS reimbursement.

Expert opinions are becoming a large component of specialist pathologists' workload and the introduction of MBS items will provide an avenue for reimbursement for complicated work that is both time- and resource-consuming.

Proposed MBS listing sought

There is not necessarily a correlation between the complexity level of the initial MBS item and the complexity level (and therefore the appropriate reimbursement) for a second morphological opinion. The Applicant has therefore suggested a simple, two-tier fee structure with different rebates for 'non-complex' and 'complex' expert opinions. It would be up to the expert pathologist to determine the workload involved in providing the second opinion and bill the service accordingly (similar to the situation where a clinician is allowed to determine whether they bill for a short or long consultation).

The proposed Schedule fee for the 'non-complex' expert opinion item (Table ES-1) is approximately equal to the fee for initial examination of a complexity level 4 biopsy with at least 12 separately identified specimens; the proposed fee for 'complex' expert opinion (and Table ES-2) is approximately equal to the average of the initial fees for examination of complexity level 5 and 7 biopsy materials. Section A.2.5 of the Assessment Report provides a full list of the existing services and fees for morphological pathology and a list of the complexity levels assigned to tissue types from different anatomic sites.

Rather than differentiate the two proposed items on the basis of complexity, the Department has worded the item descriptors to reflect the amount of time taken to process and examine the specimen and prepare a full written report (either ≤30 minutes or >30 minutes).

It is possible that some patients may receive a second, expert pathology opinion as an inpatient; however, the majority of services are expected to be provided in an outpatient setting. Explanatory notes are needed to limit second, expert opinion to tissue pathology, cytology and bone marrow items.

Table ES-1 Proposed MBS item descriptor for non-complex, second, expert opinion on a patient sample

Category 6 - Pathology
MBS item number (*assigned by the Department if listed*)
A no more than 30 minute limit, expert opinion and detailed written report on a patient sample, requested by a treating clinician, where further information is needed for accurate diagnosis and appropriate patient management.
Fee: $180.00
The service will be initiated upon the request of the referring clinician where there is uncertainty in the initial morphological diagnosis, or when the clinician involved in the care of the patient requests a second opinion. The item is applicable to cases where the expert pathologist is able to examine and/or re-process case material and produce a full written report in ≤30 minutes. The fee will not be payable if the service is provided within the same Approved Pathology Laboratory.

Abbreviations: MBS, Medicare Benefits Schedule
Source: Final Protocol May 2014

Table ES-2 Proposed MBS item descriptor for complex, second, expert opinion on a patient sample

Category 6 - Pathology
MBS item number (*assigned by the Department if listed*)
A greater than 30 minute, second, expert opinion and detailed written report on a patient sample, requested by a treating clinician, where further information is needed for accurate diagnosis and appropriate patient management.
Fee: $370.00
The service will be initiated upon the request of the referring clinician where there is uncertainty in the initial morphological diagnosis, or when the clinician involved in the care of the patient requests a second opinion. The item is applicable to cases that are not obvious or straightforward, where the examination and/or re-processing of case material and the production of a full written report takes more than 30 minutes. The fee will not be payable if the service is provided within the same Approved Pathology Laboratory.

Abbreviations: MBS, Medicare Benefits Schedule
Source: Final Protocol May 2014

Background

The intended purpose of a benefit payable for second opinion is to assist the initial pathologist and/or the clinician in charge of patient management to arrive at a definitive diagnosis in difficult cases with the help of an external expert pathologist. Morphological diagnosis and staging is integral to the management of many diseases. Once a definitive diagnosis has been made, appropriate management of the disease process can proceed.

There are a number of reasons why a pathologist may not be able to provide a primary or definitive diagnosis or why a clinician may lack confidence in the initial pathologist's diagnosis: the rare or esoteric nature of the lesion; complexity of, or lack of familiarity with, a particular cancer classification scheme; the type, quantity or quality of the diagnostic biopsy specimen; or the requirement for special ancillary stains or tests to aid interpretation.

Second, expert opinions for morphological pathology are undertaken using the specimens/samples/slides used to inform the initial opinion/diagnosis from the initial pathologist. However, where necessary, the expert pathologist may repeat or conduct 'ancillary' tests (such as immunohistochemistry, immunocytochemistry or molecular testing) to provide a more refined diagnosis. It is anticipated that any ancillary services undertaken in conjunction with a second, expert opinion could be reimbursed through the MBS in the normal way, as the fee for these additional services reflects the cost of performing and interpreting the tests. The need to repeat or conduct ancillary tests will vary according to the clinical condition under review.

The provision of external expert opinion is also associated with administrative and handling costs relating to transferring the original specimens/slides to and from an external expert pathologist. The 'specimen referred fee' (MBS Group 11, item 73940) may be appropriate to cover some of these costs, but can only be claimed by the second laboratory. PASC suggested that handling costs require separate consideration, similar to MSAC Application 1331[1].

It would be expected that a second, expert opinion on any specific pathology service episode would only be requested once. However, it is possible that a third opinion may

[1] MSAC Application 1331: Retrieval of tissue for further diagnostic testing specifically genetic testing for diagnostic/prognostic purposes.

be sought if the expert pathologist was unable to provide a definitive diagnosis, or if the clinician had concerns regarding the diagnosis provided by the expert pathologist.

Second, expert opinions for morphological pathology would be provided by pathologists and laboratories operating under the same regulatory requirements as those for initial pathology opinions; that is, Approved Pathology Practitioners (APP) operating in National Association of Testing Authorities (NATA) and RCPA accredited laboratories (Approved Pathology Laboratory; APL) within Australia.

Under the proposed funding arrangements, an expert pathology opinion could be sought from within the same Approved Pathology Authority (APA), but must be conducted by a pathologist from a different APL. This requirement has been proposed by the Applicant to avoid any concern that inappropriate internal pathologist referrals might be made to generate revenue. Consideration should be given as to whether there could also be inappropriate referrals between a clinician and an expert pathologist who are co-located at a tertiary treatment centre.

Clinical need

It is anticipated that second, expert opinion requests will cover a range of conditions, including cancer-related diagnoses, dermatopathology (such as inflammatory skin), difficult liver biopsies, and difficult transplant biopsies, such as surveillance biopsies on heart or liver transplants. The rate of referral for expert opinion will depend on the expertise of the original pathology staff and the case mix of the institution.

The proposed MBS items are intended to cover second, expert opinion on bone marrow specimens (bone marrow aspirates and sections of bone marrow trephine biopsies), tissue pathology specimens (primarily biopsy material) and cytology specimens (including smears from the skin, lip, mouth, nose, vagina, cervix or anus, or liquid discharges such as sputum, urine or discharge from the nipple).

In many instances, cytology is undertaken as a screening or preliminary test. Difficult cases are usually reported as suspicious or indeterminate and a formal histological biopsy suggested. It would be rare that a second, expert opinion would be required on a cytology item, except where it is difficult to re-biopsy sites (such as the pancreas).

There is an argument for excluding gynaecological cytology from the proposed MBS listing as most cases are for screening rather than diagnostic purposes, and it is relatively cheap ($19.45) to repeat the initial smear. However, given the inconvenience and discomfort of obtaining a smear, repeat sampling can be problematic, particularly for women in rural and remote areas.

Currently, approximately three-quarters of all initial cytopathology claims relate to MBS item 73053 for routine Pap smear screening, which is promoted through the National Cervical Screening Program (NCSP). However, this is likely to change substantially from 2016, when changes to the NCSP, recently recommended by MSAC, are anticipated to come into effect.

Clinical claim

Incorrect or incomplete diagnoses may lead to delayed or sub-optimal care, adversely affecting clinical outcomes and resulting in inefficient use of resources. The purpose of seeking MBS funding for expert opinions for morphological pathology is therefore to

facilitate access to expert pathologists for review of rare, unusual or complex cases, thereby decreasing the frequency of incorrect, missing or incomplete pathology opinions.

Expert pathologists often have to prioritise routine work over unfunded expert opinions and therefore the introduction of MBS items could result in more timely and optimal diagnosis and treatment of patients. There is also anecdotal evidence that second, expert opinions are not sought as frequently as they should be (particularly from isolated regional or remote pathologists) due to the cost, lack of funding, and/or perceived impost on colleagues. This can lead to a sub-optimal diagnosis or report being provided to the treating clinician, or in some cases, referral without a diagnosis.

Thus, the ability for clinicians to obtain a funded second, expert opinion has the potential to positively impact on patient care via the more accurate classification of disease and thus more appropriate planning and selection of therapy; and more rapid diagnosis of rare and diagnostically challenging cases.

Comparator

The comparator is the standard management which currently applies. Under current arrangements, the MBS does not provide reimbursement for second, expert opinions for pathology. However, there are circumstances where the primary pathologist or the treating clinician may require an expert opinion to optimise patient management. In those instances, a number of alternative pathways may be followed:

1) The original pathologist may request an expert opinion from an external pathologist who provides the opinion at no cost (but may be obliged to place low priority on the request), or the second pathology laboratory charges the initial laboratory privately. It is very difficult in these circumstances to charge the patient, as they would not have consented to pay for a second opinion; or
2) The treating clinician requests an expert opinion from a pathology provider, and this is provided either at no cost (gratis) or at cost to the patient (privately) or the clinical unit.

The Applicant claims that in some cases, an expert opinion would be desirable but the costs associated with providing a second opinion and the lack of funding means that an expert opinion is not sought.

Scientific basis of comparison

Although there is a relatively large body of evidence that relates to second pathology opinion in cases where routine review is mandated by institutional policies, this evidence was excluded from the assessment due to inherent differences in the type and complexity of cases referred for second opinion. In studies where expert opinions are exclusively requested due to pathologist or clinician uncertainty or a clinical need for diagnostic refinement, a larger proportion of cases will have no initial diagnostic opinion or be missing pertinent clinical information that is required to effectively manage the patient. In contrast, studies assessing the value of routine review of all pathology cases may report lower discrepancy rates because they include a higher proportion of cases where the specimen types are unlikely to be misdiagnosed or the initial pathologist was confident in their diagnostic opinion. Thus, the findings of studies relating to routine review of all pathology cases are not applicable to the proposed scenarios for public funding.

No studies were identified that compared publicly funded second, expert opinion with unfunded second, expert opinion. However, 14 studies (prospective and retrospective) were identified that compared second, expert opinion with initial pathology opinion (i.e. no second, expert opinion). The 14 studies were heterogeneous, with sample sizes that ranged from 60 cases to 2,686 cases. Many of the studies reported a single institution's experience of second, expert opinion, and as such, there is considerable variation across the studies, depending on factors such as the case mix of patients encountered by the initial pathologist, the complexity of the tissue being studied, the availability of intra-institutional consultation prior to referral, and the experience and qualifications of the expert pathologist who reviewed the case. The availability of funding for expert opinions may also alter referral patterns. None of the studies were conducted in Australia.

There were 10 studies that met the inclusion criteria for *Scenario 1* – i.e. cases in which an external expert opinion was sought by the initial pathologist due to diagnostic uncertainty. Two studies included all surgical pathology cases while the remaining eight focussed on subspecialty areas (dermatology, sarcoma, lung biopsies, oral and maxillofacial pathology, and urothelial lesions). Four additional studies were identified that met the inclusion criteria for *Scenario 2* – i.e. cases where an initial pathology opinion may have been provided, but where uncertainty or insufficient detail regarding the diagnosis remains. One of the four studies examined all surgical pathology cases while the remaining three focussed on prostate biopsies, brain and spinal cord specimens, and labial salivary gland biopsies. The 10 studies that met the inclusion criteria for *Scenario 1* are also relevant to *Scenario 2*, as an ambiguous or equivocal report from the initial pathologist would be likely to result in clinician uncertainty.

The gold standard in diagnostic morphological pathology is good clinical correlation and adequate follow-up. In the majority of included studies there was an underlying assumption that the opinion of the expert pathologist was 100% accurate and that any discordance was due to misdiagnosis on the part of the initial pathologist. Follow-up data was rarely available to confirm the assumption that, in discrepant cases, the second, expert opinion was accurate. Numerous studies have reported a high degree of discordance between expert pathologists when diagnosing difficult lesions, and this has been substantiated in studies that have undertaken patient follow-up. Thus, studies that report discrepancy rates without patient follow-up or, at the very least, consensus pathology opinion, should be interpreted with caution.

Diagnostic accuracy

All studies assessed diagnostic accuracy by comparing the initial pathology diagnosis (usually undertaken by a general, non-expert pathologist) with that of an expert pathologist. While the nature of the initial pathology opinion is not an outcome explicitly evaluated in the Assessment Report, the interpretation of diagnostic accuracy requires consideration of whether or not a provisional diagnosis was provided by the initial pathologist. In particular, in circumstances where the initial pathologist does not provide a diagnosis, the expert opinion would not usually be regarded as a true diagnostic discrepancy, as it would technically be the first diagnosis upon which patient management decisions could be based. The proportion of cases referred for expert opinion with no initial diagnosis varied substantially between the included studies, from 0.3% (in a study that included pathology specimens from any anatomical site) to 46.8% (in a study that included soft tissue lesions only).

Rates of discordance between the initial and expert pathologist varied across the studies from 31% (in a study of all histopathology from any organ system) to 88% (in a study of granulomatous or giant cell reactions in the lung). While misdiagnosis by the initial pathologist was often cited as the cause of discordance, some studies also reported discordance related to the different reporting styles or classification systems used by the initial and expert pathologists. Thus, the different definitions of what constitutes discordance limits interpretation and comparisons across studies.

Change in management

The majority of the included studies used the terminology 'major discrepancy' to refer to clinically relevant changes in diagnosis that would result in a change in patient management. It could therefore be argued that the rate of major discrepancies represents the best available evidence from the body of literature to determine the value of second, expert opinions.

The highest major discrepancy rates (23-27% of cases) were reported in studies of skin lesions and soft tissue sarcoma. In contrast, studies of all surgical pathology (from any organ system) found major discrepancy rates of 12-18%, indicating that major discrepancies between initial and expert pathologists are uncommon in some tissue types. Due to heterogeneity across studies, no conclusions could be drawn regarding major discrepancy rates from pathologist-initiated compared with clinician-initiated second, expert opinions.

It is important to acknowledge that there are major limitations associated with using major discrepancies as a surrogate for change in management. In most cases of diagnostic uncertainty, treatment is withheld until after an expert diagnosis is received. Thus, a major discrepancy between the initial and expert pathologist does not necessarily translate into a change in management, but rather the potential for more accurate classification of disease. This, in turn, could lead to more appropriate planning and selection of therapy, which should translate into better health outcomes and more effective utilisation of resources. However, due to lack of reliable follow-up data, this claim was not substantiated on the basis of the existing evidence.

Nonetheless, the high proportion of major discrepancies across some tissue types provides a compelling clinical argument for second, expert opinions when there is diagnostic uncertainty or a rare or complex case that warrants verification.

Safety

Only two of the included studies provided any patient follow-up information upon which an assessment of the safety (i.e. accuracy) of the expert pathologist's diagnosis could be made. However, in both cases, follow-up was inadequate and the results were therefore uninterpretable or unreliable. While several of the included studies provided information regarding turnaround time, none of the studies attempted to quantify harms due to a delay in diagnosis.

Effectiveness

None of the included studies reported relevant effectiveness outcomes such as mortality, morbidity or quality of life.

Pre-modelling studies

In lieu of reliable published data, anticipated rates of second, expert opinion were obtained from an Expert Opinion Survey (detailed in Appendix 5). The survey was developed to obtain quantitative estimates from large public and private pathology laboratories about the number and nature of tissue pathology and non-gynaecological cytology cases that are currently referred for second, expert opinion in Australia, and any potential changes that would result from MBS funding of second, expert opinions.

The survey captured information relating to the two circumstances for funding (*Scenario 1* and *Scenario 2*), the two proposed complexity levels (≤30 mins and >30 mins) and the use of ancillary tests. The survey results are shown in Section C.4 and were used in the economic evaluation and the financial impact analysis.

Economic evaluation

The economic model is based upon the Decision Analytic structure presented in the Final Protocol, with structural changes (discussed in Section D.1) due to limitations in the evidence base. Health outcomes are derived from the rate of major discrepancies between the initial (provisional) diagnosis and the expert pathologist diagnosis, from studies that included all surgical pathology from any organ system. Such cases are representative of those that could potentially result in a change in clinical management due to second, expert opinion. These cases are often those in which diagnosis is modified from benign to malignant or vice versa and can, therefore, be thought of as 'significant'.

The most notable simplification of the structure is that there is no explicit consideration of either improved or inferior treatment outcomes. Instead, on the basis of available data, the economic evaluation estimates the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. The focus is therefore on the attainment of a definitive diagnosis and, as a consequence, the economic evaluation does not extrapolate to final health outcomes. While it may be argued that comprehensive modelling beyond this point would be warranted, there are several reasons why this is unlikely to be informative:

- *The general nature of the requested listings render it very difficult to accurately assess the cost-effectiveness beyond the point of definitive diagnosis.* It is not feasible to comprehensively consider the differential impacts of significant changes in diagnosis on all conditions to which the listing would apply; the range of conditions means that the range of different treatments, natural histories and subsequent mortality/morbidity implications is enormous. As such, a pragmatic approach was taken. To do otherwise would introduce unreasonable uncertainty to the model, rendering it misleading and/or impossible to interpret.
- *The paucity of data imposes very real limitations on the ability to extrapolate beyond diagnosis.* Long term data describing the transition from final diagnosis to mortality (and intermediate morbidity) do not exist for the research questions at hand.

Rather than attempting complex downstream modelling of a wide range of illnesses, the evaluation focusses on providing decision-makers with the most informative assessment of cost-effectiveness. Specifically, the evaluation provides an assessment of how much it will cost, on average, to provide information to trigger a change in diagnosis where required if second, expert opinions are funded by the MBS.

Cases in which no diagnosis is offered by the initial pathologist are excluded from the model as no data are available to inform how such patients may be managed, or how clinical management may change in the event of a second, expert opinion.

The economic evaluation considers tissue pathology and cytopathology independently, appropriately applying data relevant to each analysis. Due to data limitations, cytopathology is considered in a sensitivity analysis while tissue pathology forms the base case analysis.

In addition to claiming reimbursement for the second opinion, expert pathologists would have the ability to recharge for ancillary items in conjunction with one of the proposed new items. These costs are also factored into the evaluation.

The incremental cost-effectiveness is shown in Table ES-3. The economic evaluation demonstrates that if second, expert opinions were to be funded by the MBS as per the requested listing, it would cost an additional $3,838 to generate one significant change in diagnosis in the case of tissue pathology.

Table ES-3 Incremental cost per significant (clinically relevant) change in diagnosis or interpretation

	Proposed funding arrangements	Current funding arrangements	Incremental
Average cost per patient	$4.19	$0.15	$4.04
Average rate of significant change in diagnosis per patient	0.0018	0.0007	0.0011
Incremental cost per significant (clinically relevant) change in diagnosis or interpretation	-	-	$3,838.26

Note: Figures may not sum due to rounding

Importantly, in the absence of information otherwise, this analysis assumes that there is a zero cost associated with second, expert opinions under the current funding arrangements. As such, it represents a worst-case scenario in that sense.

A series of sensitivity analyses were conducted to highlight potential areas of uncertainty with regards to the base case. Key sensitivity analyses are shown in Table ES-4 (see Section D.5 for all a full list and discussion).

Table ES-4 Incremental cost per significant (clinically relevant) change in diagnosis or interpretation: Sensitivity analyses

Description	Incremental cost	Incremental outcome	Incremental cost per significant change in diagnosis
Base case	*$4.04*	*0.0011*	*$3838.26*
Cytopathology	$2.58	0.0011	$2460.01
Scenario 1 alone	$4.21	0.0011	$4000.26
Scenario 2 alone	$3.53	0.0011	$3353.95
'Complex' second, expert opinions alone	$5.55	0.0011	$5278.96
'Non-complex' second, expert opinions alone	$2.66	0.0011	$2531.19
Soft tissue/sarcoma	$4.04	0.0013	$3193.34
Dermatology	$4.04	0.0018	$2208.92
Average cost of second, expert opinion in the comparator arm set to unit cost of 'non-complex' second, expert opinion	$1.49	0.0011	$1420.59

Estimated utilisation and financial implications

The number of second, expert opinion services that would be expected to occur under the current and proposed funding arrangements was calculated by applying estimates from the Expert Opinion Survey to the predicted number of 'core' pathology items (based on historical data from Medicare Australia).

For simplicity, the financial estimates assume that 100% of cases are outpatients, bulk-billed using the 85% benefit. Any use of the proposed service for private inpatients would reduce the financial impact to the MBS.

The estimated number of MBS services for the proposed items is shown in Table ES-5.

Table ES-5 Estimated number of MBS services for second, expert opinions, over the first five years of the proposed MBS listing – Proposed funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	32,994	34,190	35,385	36,580	37,776
Complex	17,734	18,377	19,019	19,662	20,305
Non-complex	15,260	15,813	16,366	16,918	17,471
Non-gynaecological cytology	1820	1872	1925	1978	2031
Complex	338	348	358	367	377
Non-complex	1482	1525	1568	1611	1654
All cytology	14,475	14,633	14,791	14,949	15,107
Complex	2,688	2,718	2,747	2,776	2,806
Non-complex	11,787	11,915	12,044	12,173	12,302
Sub-total (excluding gynaecological cytology)	*34,814*	*36,062*	*37,310*	*38,558*	*39,807*
Sub-total (including all cytology)	*47,469*	*48,822*	*50,176*	*51,530*	*52,883*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	11,368	11,780	12,191	12,603	13,015
Complex	3,410	3,534	3,657	3,781	3,905
Non-complex	7,957	8,246	8,534	8,822	9,111
Non-gynaecological cytology	1,239	1,275	1,310	1,346	1,382
Complex	227	234	240	247	253
Non-complex	1,012	1,041	1,070	1,100	1,129
All cytology	9,853	9,960	10,068	10,176	10,283
Complex	1,806	1,826	1,846	1,866	1,885
Non-complex	8,046	8,134	8,222	8,310	8,398
Sub-total (excluding gynaecological cytology)	*12,606*	*13,054*	*13,502*	*13,950*	*14,398*
Sub-total (including all cytology)	*21,220*	*21,740*	*22,259*	*22,779*	*23,298*
TOTAL (*S1* and *S2* – excluding gynaecological cytology)	47,420	49,116	50,812	52,508	54,204
TOTAL (*S1* and *S2* – all cytology)	68,689	70,562	72,436	74,309	76,182

Source: Section E.2

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table ES-6 presents a summary of the total cost to the MBS of the proposed listing, including associated costs related to ancillary tests, specimen referral and bulk billing.

Table ES-6 Estimated total cost to the MBS of second, expert opinion and associated services, over the first five years of the proposed MBS listing

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	$9,213,248	$9,547,064	$9,880,889	$10,214,714	$10,548,537
Second, expert opinion	$7,912,188	$8,198,864	$8,485,547	$8,772,231	$9,058,912
Ancillary tests	$908,430	$941,345	$974,260	$1,007,175	$1,040,090
Specimen referred fee[b]	$288,698	$299,158	$309,619	$320,079	$330,540
Bulk billing incentive[c]	$103,931	$107,697	$111,463	$115,229	$118,994
Non-gynaecological cytology	$368,113	$378,792	$389,471	$400,150	$410,830
Second, expert opinion	$332,981	$342,641	$352,300	$361,960	$371,621
Ancillary tests	$13,479	$13,870	$14,261	$14,652	$15,043
Specimen referred fee[b]	$15,922	$16,384	$16,846	$17,308	$17,769
Bulk billing incentive[c]	$5,732	$5,898	$6,064	$6,231	$6,397
All cytology	$2,928,249	$2,960,250	$2,992,248	$3,024,246	$3,056,246
Second, expert opinion	$2,648,780	$2,677,727	$2,706,671	$2,735,615	$2,764,561
Ancillary tests	$107,219	$108,391	$109,563	$110,734	$111,906
Specimen referred fee[b]	$126,654	$128,038	$129,422	$130,806	$132,190
Bulk billing incentive[c]	$45,596	$46,094	$46,592	$47,090	$47,589
Sub-total (excluding gynaecological cytology)	*$9,581,360*	*$9,925,856*	*$10,270,360*	*$10,614,865*	*$10,959,366*
Sub-total (including all cytology)	*$12,141,497*	*$12,507,314*	*$12,873,137*	*$13,238,960*	*$13,604,783*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	$2,673,673	$2,770,546	$2,867,422	$2,964,298	$3,061,172
Second, expert opinion	$2,290,025	$2,372,998	$2,455,973	$2,538,948	$2,621,922
Ancillary tests	$248,372	$257,371	$266,371	$275,370	$284,369
Specimen referred fee[b]	$99,467	$103,071	$106,675	$110,279	$113,883
Bulk billing incentive[c]	$35,808	$37,106	$38,403	$39,701	$40,998
Non-gynaecological cytology	$250,059	$257,313	$264,567	$271,822	$279,076
Second, expert opinion	$226,174	$232,736	$239,297	$245,859	$252,420
Ancillary tests	$9,145	$9,411	$9,676	$9,941	$10,207
Specimen referred fee[b]	$10,838	$11,152	$11,466	$11,781	$12,095
Bulk billing incentive[c]	$3,902	$4,015	$4,128	$4,241	$4,354
All cytology	$1,989,157	$2,010,895	$2,032,631	$2,054,368	$2,076,106
Second, expert opinion	$1,799,163	$1,818,824	$1,838,484	$1,858,144	$1,877,806
Ancillary tests	$72,749	$73,544	$74,339	$75,134	$75,929
Specimen referred fee[b]	$86,210	$87,152	$88,094	$89,036	$89,978
Bulk billing incentive[c]	$31,036	$31,375	$31,714	$32,053	$32,392
Sub-total (excluding gynaecological cytology)	*$2,923,732*	*$3,027,860*	*$3,131,989*	*$3,236,119*	*$3,340,249*
Sub-total (including all cytology)	*$4,662,830*	*$4,781,442*	*$4,900,053*	*$5,018,665*	*$5,137,278*
TOTAL (*S1* and *S2* – excluding gynaecological cytology)	$12,505,092	$12,953,716	$13,402,349	$13,850,984	$14,299,615
TOTAL (*S1* and *S2* – all cytology)	$16,804,327	$17,288,756	$17,773,190	$18,257,625	$18,742,061

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

The estimated costs also represent the total incremental cost of the proposed and associated services to the MBS, given that under current funding arrangements the relevant services are provided either without MBS reimbursement or not at all (i.e. specimen referred fee and bulk billing incentive).

For the same reasons cited for the economic evaluation, the financial analysis does not attempt to capture the use and cost of resources that are downstream of the provision of second, expert opinion. The proposed MBS listing may result in a subsequent increase or decrease in the use of other services (e.g. biopsy, imaging, treatment, monitoring).

The results of key sensitivity analyses are shown in Table ES-7 (see Section E.6 for the full list of analyses).

Table ES-7 Estimated total incremental costs of the proposed and associated services over the first five years of the proposed MBS listing: Results of key sensitivity analyses

Assumption	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Base case – excluding gynaecological cytology	$12,505,092	$12,953,716	$13,402,349	$13,850,984	$14,299,615
Expert opinion survey results summarised using the median.	$8,976,757	$9,300,238	$9,623,726	$9,947,215	$10,270,701
Expert Opinion Survey responses from a HESP member.	$2,545,984	$2,637,846	$2,729,710	$2,821,575	$2,913,439
Higher second, expert opinion rate than the base case.	$17,886,453	$18,526,898	$19,167,356	$19,807,817	$20,448,273
Assume a one-tier fee structure – Schedule fee $200	$9,805,126	$10,156,207	$10,507,295	$10,858,386	$11,209,473
Assume that all *Scenario 1* tissue pathology cases are 'complex' – involving more than 30 minutes of expert pathologist's time.	$15,334,763	$15,885,912	$16,437,073	$16,988,236	$17,539,394
Assume that second, expert opinion is not requested for complexity 2 or 3 items (MBS items 72813-72818).	$5,984,984	$6,267,373	$6,549,767	$6,832,168	$7,114,561
Base case – including gynaecological cytology	$16,804,327	$17,288,756	$17,773,190	$18,257,625	$18,742,061
Assume that proposed changes to the NCSP come into effect in 2016, with an immediate 86% decrease in use of MBS items 73053 and 73055.	$14,983,693	$13,614,312	$14,065,575	$14,516,839	$14,968,101

Source: Section E.6

Additional relevant information

There is an argument that a lack of funding for a second, expert opinion disproportionately affects patients, clinicians and laboratory staff in rural and remote areas. Unlike their metropolitan counterparts, pathologists in remote areas have less opportunity to approach colleagues for intra-institutional second and/or expert opinion. In addition, there may be a financial disincentive to seek a second, expert opinion because the patient or their laboratory/hospital are likely to be charged for the service, plus any associated transportation costs. This contributes to inequities in the care of patients outside metropolitan areas.

Background

In September 2012, the Department of Health and Ageing received an application from The Royal College of Pathologists of Australasia (RCPA) requesting MBS reimbursement of external expert opinions for morphological pathology (histology, cytopathology, haematology, microbiology and genetic pathology). The application was initially considered in August 2013 by the Protocol Advisory Sub-Committee (PASC) of the Medical Services Advisory Committee (MSAC) who restricted the scope of the Protocol to assessment of external expert opinions for tissue pathology (which includes Group P5 items) and cytopathology (which includes Group P6 items). Although the Applicant proposed two circumstances in which expert opinion should be considered for public funding, PASC agreed with only one of these circumstances:

- where the pathologist communicates with the clinician in charge of patient management, and suggests referral to an external expert pathologist, due to a rare, unusual or complex case where a primary or definitive diagnosis cannot be confidently made by the reporting pathologist.

Due to inconsistencies within the Final Protocol and concerns raised by the Applicant regarding the intended circumstances for use of the service, the Department of Health requested that PASC reconsider the Protocol for MSAC Application 1332 at the April 2014 PASC meeting. At this meeting, the scope of the assessment was broadened to include:

- second, expert pathologist opinion on bone marrow specimens (included in Group P1); and
- second, expert pathologist opinion where the clinician in charge of patient management wants the initial pathology opinion verified or refined by a second, expert pathologist or by their preferred pathologist, in cases where there is uncertainty in the diagnosis or insufficient information to effectively manage the patient.

PASC also agreed in principle to the Applicant's simple two-tiered fee structure for second, expert opinion, which reflects the amount of work undertaken by the expert pathologist rather than linkage to the original pathology items.

The Final Protocol was revised to reflect all of these changes in May 2014 and was ratified out of session by the PASC Chair in June 2014.

HealthConsult Pty Ltd was contracted to conduct an assessment of the safety, effectiveness and cost-effectiveness of second, expert opinions for morphological pathology in order to inform a decision as to whether this service should be reimbursed through the Medicare Benefits Schedule (MBS).

Section A. Details of the proposed medical service and its intended use

A.1. Address all items in the Protocol

This Assessment Report reflects the circumstances for funded second, expert opinions agreed to by PASC and the Applicant in the PASC meeting on 17th April 2014 and outlined in the revised Final Protocol, dated May 2014. Table A.1-1 shows that the Assessment Report follows the framework that was provided in the Final Protocol. However, it is noted in the Final Protocol that the main outcome of interest for the economic evaluation is cost per clinically relevant change in diagnosis/interpretation but PASC also decided that "a small number of examples of cost-utility analysis, restricted to specific clinical areas where expert opinions are known to be sought, and where sufficient comparative evidence regarding health outcomes is available, and modelling is feasible, would be informative". Due to limitations in the existing data sources, example cost-utility analyses were not undertaken (see Section D.3 for a detailed explanation).

Table A.1-1 Items addressed in the revised Final Protocol and Assessment Report

Items in the revised Final Protocol	Location in Assessment Report	Concurs with Protocol	Change and justification
Proposed MBS listing	Section A.3	Yes	The proposed MBS listing is consistent with the advice from PASC in terms of restricting second, expert opinion to: • Bone marrow (Group P1), tissue pathology (Group P5) and cytopathology (Group P6) items only; and • Only those circumstances where a treating clinician needs further information for accurate diagnosis and appropriate patient management (i.e. not for routine review of all cases). The MBS fees for second, expert opinion are consistent with the simple two-tiered fee structure proposed in the revised Final Protocol.
Comparator	Section A.4	Yes	The comparator is consistent with the revised Final Protocol.
Clinical management algorithm	Section A.5, Figure A-1, Figure A-2, Figure A-3	Yes	The three clinical management algorithms (one current and two proposed) are consistent with the revised Final Protocol. There are different algorithms reflecting the two proposed scenarios where second, expert opinion is either: • desired by the initial pathologist but requested by the treating clinician (*Scenario 1*), or • desired and requested by the treating clinician (*Scenario 2*).
Clinical outcomes assessed	Section A.8; Section B.5	Yes	The evidence was reviewed for the clinical outcomes outlined in the PICO criteria in the Final Protocol. However, the available evidence does not address all of the specified outcomes.
Healthcare resources	Section D.3.1, Section E.1.4	Partly	The economic evaluation considered the costs associated with the expert opinion item and ancillary tests. The financial estimates apply the resources outlined in the Final Protocol, with the exception of an additional consultation item.

Items in the revised Final Protocol	Location in Assessment Report	Concurs with Protocol	Change and justification
Economic evaluation structure	Section D.2.2, Section D.3, Figure D-1	Partly	The economic evaluation is based on the structure of the Decision Analytic proposed in the Final Protocol, with simplifications due to limitations in the available clinical evidence. The economic evaluation estimates the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. There is no extrapolation to final health outcomes. Instead, the focus is on the attainment of a definitive diagnosis upon which patients can be effectively managed. Example CUAs were not feasible or credible with existing data sources.

Abbreviations: CUAs, cost-utility analyses; MBS, Medicare Benefits Schedule; PASC, Protocol Advisory Sub-Committee

A.2. Proposed medical service

The proposed service involves the provision of a morphological second opinion on a patient sample by an expert pathologist. Currently, public reimbursement of pathology opinions only applies to the initial pathology report.

PASC has advised that public funding for the proposed service should only apply in the following circumstances where:

Scenario 1 – the initial pathologist communicates with the clinician in charge of patient management, and suggests referral to an external expert pathologist, due to a rare, unusual or complex case where a primary or definitive diagnosis cannot be confidently made. It would then be at the discretion of the treating clinician to decide whether expert opinion is necessary (i.e. the service is not pathologist determinable).

Scenario 2 – the clinician in charge of patient management wants the initial pathology opinion verified or refined by a second, expert pathologist or by their preferred pathologist, irrespective of whether the initial pathologist cited uncertainty in their initial diagnosis or not.

There are a number of reasons why a pathologist may not be able to provide a primary or definitive diagnosis or why a clinician may lack confidence in the initial pathologist's diagnosis:

- the rare or esoteric nature of the lesion;
- complexity of, or lack of familiarity with, a particular cancer classification scheme;
- the type, quantity or quality of the diagnostic biopsy specimen; or
- the requirement for special ancillary stains or tests to aid interpretation.

In such cases, the initial pathologist would communicate an initial opinion to the treating clinician, together with a recommendation that the case is referred for expert opinion. The initial pathology opinion could include:

- no diagnostic interpretation;
- a differential diagnosis (i.e. a written list of alternative diagnoses, provided due to diagnostic uncertainty, which may or may not indicate the preferred or primary diagnosis); or
- a provisional/preliminary/tentative diagnosis, issued with the intent of following up with supplemental information or a final diagnosis after expert consultation.

Alternatively, the clinician may have concerns about the initial opinion, regardless of whether a confident diagnosis was provided, and decide that a second, expert opinion is necessary.

In both circumstances, the decision to obtain a second, expert opinion is ultimately at the discretion of the clinician who is aiming for an authoritative final diagnosis upon which treatment decisions could be made (i.e. 'definitive' diagnosis).

In cases where external expert second opinion is sought due to pathologist uncertainty, usual practice is to provide the expert pathologist with the same specimens/slides and case material as that reviewed by the initial pathologist. The expert pathologist then provides a diagnosis and a comprehensive written report back to the primary (initial) pathologist, who retains the medico-legal responsibility for the diagnosis. The primary pathologist is responsible for synthesising the information and refining the diagnosis as required.

Clinician-initiated expert opinions would also involve review of the original pathology case material by an expert pathologist. This type of expert opinion typically occurs at a tertiary centre to which a patient (most often an oncology patient) has been referred for further management. The initial pathology report may provide insufficient information to effectively manage the patient and the clinician may request an expert opinion from a pathologist who would normally provide the service to the treatment centre (i.e. the requesting clinician and the expert pathologist may be co-located). Nevertheless, the expert pathologist would still need to provide a comprehensive written report in order for the service to be eligible for MBS funding.

PASC has advised that second, expert opinions requested by a treating clinician (such as in a referral centre) should only be considered for public funding when there is uncertainty in the diagnosis or insufficient information to effectively manage the patient. The intention of the proposed MBS item is not to provide funding for mandatory or routine review of all cases referred to treatment centres.

A.2.1. Clinical need

Incorrect or incomplete diagnoses may lead to delayed or sub-optimal care, adversely affecting clinical outcomes and resulting in inefficient use of resources. The purpose of seeking MBS funding for expert opinions for morphological pathology is therefore to facilitate access to expert pathologists for review of rare, unusual or complex cases, thereby decreasing the frequency of incorrect or incomplete diagnoses. Expert pathologists often have to prioritise routine work over unfunded expert opinions and therefore the introduction of an MBS item (or items) could result in more timely and optimal treatment of patients (see Section A.7 for the clinical claim).

Second opinions for morphological pathology have received a great deal of attention as a result of efforts to enhance institutional performance plans as well as reduce medical errors. Many studies have explored the value of second morphological opinions in terms of identifying discrepancies between the diagnoses made by the primary and secondary pathologist (Ray-Coquard et al, 2012; Renshaw and Gould, 2005; Veenhuizen et al, 1997). The studies often evaluate whether diagnostic errors made by the primary pathologist are clinically important; that is, whether discrepancies have major or minor therapeutic significance. Diagnostic discrepancies can result in over- or under-diagnosis of a particular condition or changes in status (e.g. tumour grade, subtype, resection

margin, etc.), all of which can have a significant impact on prognosis, clinical management, quality of life and cost.

However, the mechanism by which a second opinion is obtained greatly influences discrepancy rates. Relatively low discrepancy rates have been cited when all surgical pathology specimens are reviewed by a second (intramural) pathologist. In contrast, second opinions performed by another institution or a specialty panel at the time of patient referral produce higher discrepancy rates because of the bias towards complicated case material and/or the use of different pathology classification systems between institutions. Within general surgical pathology, reported discrepancy rates range from approximately 30% to 65%, with approximately 12-18% having major therapeutic significance (Ahmed et al, 2004; Cook et al, 2001; Hsu et al, 2010).

More recently, there has been interest in evaluating the value of second opinions within subspecialty areas because of the assumption that certain areas in anatomic pathology present difficult or unique diagnostic challenges. For example, diagnostic discrepancies occur with a high frequency in soft tissue sarcomas, which is likely attributable to the relative paucity of these malignancies in conjunction with their vast heterogeneity and complex classification schemes. Major discrepancy rates for expert opinion on skin biopsies is approximately 25% across several studies (Arbiser et al, 2001; Gaudi et al, 2013; van Dijk et al, 2008; Veenhuizen et al, 1997). However, that rate could vary quite substantially depending on the case mix of patients that the initial pathologist ordinarily encounters, the availability of intra-institutional or intra-departmental consultation prior to referral, and also the precise experience and qualifications of the expert pathologist who reviews the case.

A.2.2. Regulatory status and prerequisites

Second, expert opinions for morphological pathology would be provided by pathologists and laboratories operating under the same regulatory requirements as those for initial pathology opinions; that is, Approved Pathology Practitioners (APP) operating in National Association of Testing Authorities (NATA) and RCPA accredited laboratories (Approved Pathology Laboratory; APL) within Australia.

To be eligible for public funding, the service would be required to be undertaken in NATA/RCPA accredited laboratories within Australia. Furthermore, the Anatomical Pathologists, and General Pathologists, who provide the morphological interpretive assessment would be required to have Fellowship of the RCPA, or equivalent.

Under the proposed funding arrangement, an expert pathology opinion could be sought from within the same Approved Pathology Authority (APA), but must be conducted by a pathologist from a different APL. This requirement has been proposed by the Applicant to avoid any concern that inappropriate internal pathologist referrals might be made to generate revenue. However, the requirement that the two pathologists are from different APLs would also apply in circumstances where the expert opinion was clinician-initiated. Consideration should be given as to whether there could also be inappropriate referrals between a clinician and an expert pathologist who are co-located at a tertiary treatment centre.

Experts advise that within any given laboratory there are many referrals for second opinion between pathologists during the course of a day's work.[2] It is not the intent of the application to provide funding for this activity. As such, the proposed MBS items require that expert opinion can only be sought from a pathologist at a different APL to that of the initial pathologist, upon the request of the treating clinician. It is argued that if the initial pathologist defers to expert opinion too often, it is quite likely that the clinician will refrain from using them for diagnosis in the future.

A.2.3. Co-administered and associated services

Second, expert opinions for morphological pathology are undertaken using the specimens/samples/slides used to inform the initial opinion/diagnosis from the initial pathologist. However, where necessary, the expert pathologist may repeat or conduct additional tests, such as immunohistochemistry (IHC), immunocytochemistry (ICC) or molecular testing (collectively referred to as 'ancillary services' or 'ancillary tests'), to provide a more refined diagnosis. It is anticipated that any ancillary services undertaken in conjunction with a second, expert opinion could be reimbursed through the MBS in the normal way, as the fee for these additional services reflects the cost of performing and interpreting the tests. Thus, expert pathologists would be able to charge for additional ancillary tests required to provide a definitive diagnosis, irrespective of whether or not the test had already been conducted to inform the original pathology opinion.

Examination of patient material using IHC, ICC or electron microscopy is subject to Rule 13 of the Pathology Services Table, which states that if multiple services are delivered in a single patient episode, a Medicare benefit is payable only for the item performed that has the highest scheduled fee (see Appendix 2). The Applicant has advised that current MBS 'cones' provide a significant disincentive to unnecessary ordering of ancillary tests.

The need to repeat or conduct ancillary tests will vary according to the clinical condition under review. For example, additional IHC stains are often required to confirm, refute or modify a lymphoma diagnosis whereas it would be rare to repeat stains for breast or colon cancer review[3].

Likewise, it would rarely be the case that an expert pathologist would need to conduct additional electron microscopy or enzyme histochemistry as part of their review. In cases where electron microscopy is required, it would most likely have been conducted by the initial reporting pathologist and the relevant images or grids would be sent to the expert pathologist. Nevertheless, it is anticipated that, if required, these additional services would be claimed through the existing scheduled item in the normal way, in conjunction with one of the proposed expert opinion items.

The provision of external expert opinion is also associated with administrative and handling costs relating to transferring the original specimens/slides to and from an external expert pathologist. It is unclear whether utilisation of the 'specimen referred fee' (MBS Group 11, item 73940) would be appropriate to cover these costs. The current wording of MBS item 73940 is restricted to being claimed by the second laboratory; however, there are costs involved with both laboratories. Laboratory 1 may incur costs of

[2] Expert pathologist opinion (Prof A Morey, HESP), email 5/7/2013.
[3] Expert pathologist opinion (Prof J Dahlstrom, HESP), email 17/3/2014

retrieving the slides from the archives, and would incur the cost of collating the case, sending the slides and refining the original diagnosis and for re-filing the case material upon return. Laboratory 2 would incur costs in receiving the case material and accessioning the case; and packaging and returning the case material to Laboratory 1 at the end of the episode.[4] In the Final Protocol (p14), PASC suggested that these costs require separate consideration, similar to MSAC Application 1331 (Retrieval of tissue for further diagnostic testing specifically genetic testing for diagnostic/prognostic purposes).

A.2.4. Current reimbursement arrangements

Currently, the public reimbursement of pathology opinions only applies to the initial pathology report (see Section A.2.5 for details of the existing pathology services relevant to this application). As discussed in Section A.2.1, morphological diagnosis and staging is integral to the management of many diseases, particularly cancers. Providing a definitive diagnosis can be difficult in rare or complex diseases and so a second opinion from another pathologist with a particular expertise in the condition, or type of disease, is sometimes required. In circumstances where an expert pathology opinion is considered necessary for patient management, it is requested and provided though approved laboratories but this extra service is not eligible for MBS reimbursement. Therefore, the second pathologist opinion is currently provided either: (i) without payment; (ii) at the expense of the patient; (iii) at the expense of the requesting hospital/unit (which may be publicly funded through other health budgets); or (iv) at the expense of the initial pathology laboratory, if this was the source of the referral.

There is anecdotal evidence that second, expert opinions are not sought as frequently as they should be (particularly from isolated regional or remote pathologists) if there is a charge levied on the service (or to the patient) by the referring laboratory or if it is seen as an impost on colleagues.[5]

A.2.5. Existing pathology services for morphological pathology

Under current arrangements, pathologists are reimbursed for initial pathology opinions using items under Category 6 (Pathology Services) of the MBS. Haematology, histology and cytopathology services that are relevant to this assessment are covered in Group P1 (Haematology), Group P5 (Tissue pathology) and Group P6 (Cytology) of Category 6 (see Appendix 2 for the full MBS item descriptors and fees).

Many of these services involve the examination of tissue or cells under a microscope and are usually conducted when the presence of a disease or health condition is suspected in order to provide a definitive diagnosis.

[4] Royal College of Pathologists response to draft PROTOCOL, 9th August 2013
[5] Expert pathologist opinion (Prof A Morey, HESP), email 5/7/2013.

Haematology (bone marrow) items

Examination of bone marrow specimens is included in Group P1 (items 65084-65087). The pathology opinion may involve examination of aspirated material and histopathological sections of bone marrow trephine biopsies. The MBS Schedule fee for bone marrow items is inclusive of any ancillary test described in items 65060, 65066 and 65070. In addition to those ancillary services included in the Schedule fee, the expert pathologists may undertake other relevant ancillary tests that are not necessarily in Group P1, such as immunoperoxidase stains on bone marrow trephines (claimed under Group P5, item 72846).

Table A.2-1 Relevant Medicare items in Group P1 (Haematology)

MBS item	Brief descriptor	Schedule fee
'Core' items	-	-
65084	Bone marrow trephine biopsy – examination of sections and aspirated material	$165.85
65087	Bone marrow – examination of aspirated material	$83.10

Source: Final Protocol May 2014, p28

Tissue pathology items

The majority of the tissue pathology services in Group P5 (items 72813-72838) involve the examination of biopsy material, often a stained histologic specimen, under a light microscope. The various item numbers differentiate the service provided based on the number of separate specimens examined and the complexity of the material (see Table A.2-2 for a summary of Group P5 items). Table A.2-3 provides a list of the complexity levels assigned to tissue types from different anatomical sites.

Other items in Group P5 (items 72844-72852) relate to IHC examination of biopsy material, enzyme histochemistry of skeletal muscle and electron microscopic examination. These are not 'core' items and are always claimed in conjunction with one of the 'core' items outlined above. Items relating to intraoperative consultation and examination of biopsy material by frozen section or tissue imprint or smear (items 72855-72857) are not applicable to second, expert opinion in the Australian setting. In practice, where a definitive diagnosis cannot be made intraoperatively, the diagnosis is deferred to permanent section and the 'core' tissue pathology items apply.

Table A.2-2 Medicare items in Group P5 (Tissue pathology)

MBS item	Brief descriptor	Schedule fee
'Core' items	-	-
72813	Complexity level 2 biopsy material – ≥1 specimens	$71.50
72816	Complexity level 3 biopsy material – 1 specimen	$86.35
72817	Complexity level 3 biopsy material – 2-4 specimens	$96.80
72818	Complexity level 3 biopsy material – ≥5 specimens	$107.05
72823	Complexity level 4 biopsy material – 1 specimen	$97.15
72824	Complexity level 4 biopsy material – 2-4 specimens	$141.35
72825	Complexity level 4 biopsy material – 5-7 specimens	$180.25
72826	Complexity level 4 biopsy material – 8-11 specimens	$194.60
72827	Complexity level 4 biopsy material – 12-17 specimens	$208.95
72828	Complexity level 4 biopsy material – ≥18 specimens	$233.30
72830	Complexity level 5 biopsy material – ≥1 specimens	$274.15
72836	Complexity level 6 biopsy material – ≥1 specimens	$417.20
72838	Complexity level 7 biopsy material – ≥1 specimens	$466.85
'Non-core' ancillary items	-	-
72844	Enzyme histochemistry of skeletal muscle – ≥1 tests	$30.75
72846	IHC examination of biopsy material – 1-3 antibodies	$59.60
72848	IHC examination of biopsy material – 1-3 of the following antibodies: oestrogen, progesterone, c-erb-B2	$74.50
72847	IHC examination of biopsy material – 4-6 antibodies	$89.40
72849	IHC examination of biopsy material – 7-10 antibodies	$104.30
72850	IHC examination of biopsy material – ≥11 antibodies	$119.20
72851	Electron microscope examination of biopsy material – 1 specimen	$184.35
72852	Electron microscope examination of biopsy material – ≥2 specimens	$245.80
72855	Intraoperative consultation and examination of biopsy material – 1 specimen	$184.35
72856	Intraoperative consultation and examination of biopsy material – 2-4 specimens	$245.80
72857	Intraoperative consultation and examination of biopsy material – ≥5 specimens	$286.75

Source: Final Protocol May 2014, p28-31
Abbreviations: IHC, immunohistochemistry

Table A.2-3 Complexity levels for histopathology items

Complexity level 2	Complexity level 3	Complexity level 4	Complexity level 5	Complexity level 6	Complexity level 7
• Digits, amputation – traumatic • Fallopian tube, sterilization • Foreskin - new born • Hernia sac • Hydrocele sac • Testis and adjacent structures, castration • Testis and adjacent structures, vas deferens sterilization • Tonsil or adenoids or both	• Anus, all specimens not otherwise specified • Appendix • Artery, all specimens not otherwise specified • Bartholin's gland – cyst • Cholesteatoma • Eye, conjunctiva - biopsy or pterygium • Foreskin - not new born • Gallbladder • Ganglion cyst, all sites • Joint and periarticular tissue, without bone - all specimens • Large bowel, colostomy – stoma • Lip, biopsy - all specimens not otherwise specified • Nerve - not otherwise specified • Nose or sinuses, polyps • Oesophagus, diverticulum • Products of conception, termination of pregnancy • Salivary gland, Mucocele • Skin - all specimens not otherwise specified including all neoplasms and cysts • Small bowel, diverticulum • Soft tissue, lipoma and variants • Tendon or tendon sheath - not otherwise specified • Testis and adjacent structures - not otherwise specified • Tissue or organ not otherwise specified, abscess • Tissue or organ not otherwise specified, haematoma	• Adrenal resection, not neoplasm • Anus, neoplasm, biopsy • Artery, biopsy • Bone, femoral head • Bone marrow, biopsy • Bone - all specimens not otherwise specified • Brain neoplasm, resection - cerebello-pontine angle • Brain or meninges, resection - not neoplasm • Branchial cleft, cyst • Breast, incision biopsy or needle biopsy, malignant neoplasm - all specimen types • Breast tissue - all specimens not otherwise specified • Bronchus, biopsy • Digits, amputation - not traumatic • Ear, middle and inner - not cholesteatoma • Extremity, amputation - not otherwise specified • Eye, cornea • Eye - not otherwise specified • Fallopian tube, biopsy • Fallopian tube, ectopic pregnancy • Gum or oral mucosa, biopsy • Heart valve • Joint tissue, including bone - all specimens • Kidney, partial or total nephrectomy - not neoplasm • Large bowel (including rectum), biopsy - all sites • Large bowel (including rectum),	• Adrenal resection, neoplasm • Anus, submucosal resection – neoplasm • Bone, biopsy, curettings or fragments – lesion • Brain or meninges, biopsy - all lesions • Brain or meninges, resection - neoplasm (intracranial) • Carotid body – neoplasm • Endocrine neoplasm - not otherwise specified • Heart - not otherwise specified • Kidney, biopsy including transplant • Kidney, nephrectomy transplant • Large bowel (including rectum), biopsy, for confirmation or exclusion of Hirschsprung's Disease • Large bowel, segmental resection - colon, not neoplasm • Large bowel (including rectum), submucosal resection – neoplasm • Larynx, partial or total resection • Liver - all specimens not otherwise specified • Lung, wedge biopsy • Lymph node, biopsy – for lymphoma or lymphoproliferative disorder • Lymph nodes, regional resection - all sites • Mediastinum mass • Nerve, biopsy neuropathy • Odontogenic neoplasm • Oesophagus, submucosal	• Anus, neoplasm, radical resection • Bile duct, resection - all specimens • Bone, biopsy or curettings quantitation - metabolic disease • Bone, resection, neoplasm - all sites and types • Brain or meninges, not neoplasm - temporal lobe • Breast, excision biopsy, guidewire localisation - non-palpable lesion • Breast, excision biopsy, or radical resection, malignant neoplasm or atypical proliferative disease - all specimen types • Breast – microdochectomy • Extremity, amputation or disarticulation – neoplasm • Eye, enucleation or exenteration - all lesions • Fetus with dissection • Gallbladder and porta hepatis-radical resection • Jaw, upper or lower, including bone, radical resection for neoplasm • Kidney, partial or total nephrectomy or nephroureterectomy – neoplasm • Large bowel (including rectum), segmental resection, neoplasm • Larynx, resection with nodes or pharynx or both	• Breast, orientated wide local excision for carcinoma, with margin assessment • Prostate, radical prostatectomy or cystoprostatectomy for carcinoma

Complexity level 2	Complexity level 3	Complexity level 4	Complexity level 5	Complexity level 6	Complexity level 7
	• Tissue or organ not otherwise specified, pilonidal cyst or sinus • Tissue or organ not otherwise specified, thrombus or embolus • Tissue or organ not otherwise specified, veins varicosity • Tissue or organ - all specimens not otherwise specified • Uterus, endocervix, polyp • Uterus, endometrium, polyp • Vaginal mucosa, incidental	polyp • Larynx, biopsy • Lip, wedge resection or local excision with orientation • Liver, hydatid cyst or resection for trauma • Lung, needle or transbronchial biopsy • Lymph node, biopsy - all sites • Nasopharynx or oropharynx, biopsy • Nerve, neurectomy or removal of neoplasm • Nose, mucosal biopsy • Odontogenic or dental cyst • Oesophagus, biopsy • Omentum, biopsy • Ovary with or without tube - not neoplasm • Pancreas, cyst • Parathyroid gland(s) • Penisectomy – simple • Peritoneum, biopsy • Pituitary neoplasm • Placenta - not third trimester • Placenta - third trimester, abnormal pregnancy or delivery • Pleura or pericardium, biopsy or tissue • Products of conception, spontaneous or missed abortion • Prostate - all types of specimen not otherwise specified • Salivary gland - all specimens not otherwise specified • Sinus, paranasal, biopsy • Skin, biopsy - blistering skin diseases • Skin, biopsy - inflammatory	resection – neoplasm • Ovary with or without tube – neoplasm • Pancreas, biopsy • Penisectomy with node dissection • Retroperitoneum, neoplasm • Salivary gland, neoplasm - all sites • Skin biopsy - for investigation of alopecia other than for male pattern baldness, where serial horizontal sections are taken • Skin, biopsy - for investigation of lymphoproliferative disorder • Skin, resection of malignant melanoma or melanoma in situ • Small bowel – resection, all specimens • Small bowel, submucosal resection – neoplasm • Soft tissue, neoplasm, not lipoma - all specimens • Spleen • Stomach, submucosal resection – neoplasm • Testis, biopsy • Testis and adjacent structures, neoplasm with or without nodes • Thymus - not otherwise specified • Thyroid - all specimens • Tongue or tonsil, neoplasm local • Ureter, resection • Urethra, resection • Urinary bladder, transurethral resection of neoplasm • Uterus, cervix cone, biopsy	• Liver, total or sub-total hepatectomy – neoplasm • Lung, resection – neoplasm • Lung segment, lobar or total resection • Muscle, biopsy • Oesophagus, partial or total resection • Pancreas, sub-total or total with or without splenectomy • Prostate, radical resection • Sinus, paranasal, resection – neoplasm • Small bowel, resection – neoplasm • Soft tissue, infiltrative lesion, extensive resections at least 5cm in maximal dimension • Stomach, resection, neoplasm - all specimens • Tissue or organ not otherwise specified, malignant neoplasm with regional nodes • Tongue or tonsil, neoplasm with nodes • Urinary bladder, partial or total with or without prostatectomy • Uterus with or without adnexa, malignant neoplasm - all specimen types not otherwise specified • Uterus with or without adnexa, neoplasm, Wertheim's or pelvic clearance • Vagina, radical resection • Vulval, sub-total or total with or without nodes	

Complexity level 2	Complexity level 3	Complexity level 4	Complexity level 5	Complexity level 6	Complexity level 7
		dermatosis • Skin,eyelid, wedge resection • Skin, local resection – orientation • Small bowel - biopsy, all sites • Soft tissue - not otherwise specified • Stomach, endoscopic biopsy or endoscopic polypectomy • Stomach - all specimens not otherwise specified • Tendon or tendon sheath, giant cell neoplasm • Thyroglossal duct - all lesions • Tissue or organ not otherwise specified, neoplasm local • Tongue, biopsy • Tonsil, biopsy - excluding resection of whole organ • Trachea, biopsy • Ureter, biopsy • Urethra, biopsy • Urinary bladder - all specimens not otherwise specified • Uterus, cervix, curettings or biopsy • Uterus and/or cervix - all specimens not otherwise specified • Vagina, biopsy • Vulva or labia, biopsy	(including LLETZ or LEEP biopsy)		

Source: Australian Government Department of Health. Medicare Benefits Schedule Book, Category 6. Operating from 01 April 2014

Cytology items

Cytopathology (Group P6, items 73043-73057, 73062-73063 and 73066-73067) refers to the microscopic examination of stained preparations of free cells (i.e. not whole tissues) separated naturally or artificially. It includes the examination of smears from the skin, lip, mouth, nose, vagina or anus, or liquid discharges such as sputum, urine or discharge from the nipple (see Appendix 2). A very common cytopathology service is the examination of cervical smears (or Pap smears). Other items in Group P6 (items 73059-73061 and 73064-73065) relate to ICC examination of material obtained by procedures described in the 'core' items outlined at the top of Table A.2-4.

Table A.2-4 Medicare items in Group P6 (Cytology)

MBS item	Brief descriptor	Schedule fee
'Core' items	-	-
73043	Cytology of nipple discharge or smears from skin, lip, mouth, nose or anus for detection of precancerous or cancerous changes - ≥1 tests	$22.85
73045	Cytology for malignancy performed on washings or brushings from sites not specified in 73043, a single specimen of sputum or urine, or one or more specimens of other body fluids	$48.60
73047	Cytology of 3 sputum or urine specimens for malignant cells	$94.70
73049	Cytology of material obtained at 1 site by fine needle aspiration of solid tissue	$68.15
73062	Cytology of material obtained at 2 or more sites by fine needle aspiration of solid tissue	$89.00
73063	Cytology of material obtained at 1 site by fine needle aspiration of solid tissue, if an APA employee attends the aspiration	$99.35
73067	Cytology of material obtained at 2 or more sites by fine needle aspiration of solid tissue, if an APA employee attends the aspiration	$129.15
73051	Cytology of material obtained at 1 site by fine needle aspiration of solid tissue, if a recognised pathologist performs or attends the aspiration	$170.35
73066	Cytology of material obtained at 2 or more sites by fine needle aspiration of solid tissue, if a recognised pathologist performs or attends the aspiration	$221.45
73053	Cytology of a smear from the cervix for the detection of precancerous or cancerous changes in women with no symptoms or signs of cervical neoplasia	$19.45
73055	Cytology of a smear from the cervix for the management of previously detected abnormalities or symptoms or signs of cervical neoplasia	$19.45
73057	Cytology of a smear from the vagina	$19.45
'Non-core' ancillary items	-	-
73059	ICC examination of material obtained in 73045-73063 – 1-3 antibodies	$43.00
73061	ICC examination of material obtained in 73045-73063 – 1-3 of the following antibodies: oestrogen, progesterone, c-erb-B2	$51.20
73060	ICC examination of material obtained in 73045-73063 – 4-6 antibodies	$57.35
73064	ICC examination of material obtained in 73045-73063 – 7-10 antibodies	$71.70
73065	ICC examination of material obtained in 73045-73063 – ≥11 antibodies	$86.00

Source: Final Protocol May 2014, p31-33
Abbreviations: APA, Approved Pathology Authority; ICC, immunocytochemistry

In many instances, cytology is undertaken as a screening or preliminary test. It would be rare that a second, expert opinion would be required, except where it is difficult to re-biopsy sites (such as the pancreas). Difficult cases are usually reported as suspicious or indeterminate and a formal histological biopsy suggested.

In the public consultation process, the possibility of excluding gynaecological cytology cases (items 73053-73057) from the proposed second, expert opinion item(s) was discussed. The rationale behind excluding those services was that the majority of current services relate to screening rather than diagnosis and that it is relatively cheap ($19.45) to repeat the initial smear. It was subsequently argued that excluding gynaecological cytology items, particularly MBS item 73053, could be problematic given that the inconvenience and discomfort of obtaining a smear could be a deterrent against repeating the test and that a lack of funding for a second, expert opinion would disproportionately affect women, clinicians and laboratory staff in rural and remote areas.

MSAC therefore need to consider whether the inclusion of gynaecological cytology cases in the second, expert opinion service is appropriate. As explained in the Final Protocol, approximately 75% of all initial cytopathology claims currently relate to MBS item 73053 for routine Pap smear screening (i.e. cytology of a smear from the cervix in women with no symptoms, signs or recent history suggestive of cervical neoplasia), which is promoted through the National Cervical Screening Program (NCSP). Despite the high usage of MBS item 73053, it may be that a second opinion for this and other gynaecological cytology items would rarely be required.

Furthermore, the current widespread use of MBS item 73053 is likely to change substantially from 2016, when changes to the NCSP, recently recommended by MSAC, are anticipated to come into effect. The renewed screening pathway is based on five-yearly screening with human papillomavirus (HPV) testing in place of cytology as the primary screening tool. According to the Public Summary Document from the April 2014 MSAC meeting[6], the estimated use of cytology is expected to decrease from 2.4 million per year in 2016 to 0.34 million per year, and conventional cytology will be replaced with liquid based cytology.

A.3. Proposed MBS listing sought

As discussed in Section A.2, the intended purpose of a benefit payable for second opinion is to assist the initial pathologist and the clinician in charge of patient management to arrive at a definitive diagnosis in difficult cases with the help of an external expert pathologist. Once a definitive diagnosis has been made, appropriate management of the disease process can proceed.

Expert opinions are becoming a large component of specialist pathologists' workload and the introduction of an MBS item(s) will provide an avenue for reimbursement for complicated work that is both time- and resource-consuming.

It is anticipated that second, expert opinion requests will cover a range of conditions, including cancer-related diagnoses, dermatopathology (such as inflammatory skin), difficult liver biopsies, and difficult transplant biopsies, such as surveillance biopsies on heart or liver transplants. The rate of referral for expert opinion will depend on the expertise of the original pathology staff and the case mix of the institution.

As discussed in Section A.2.2, the fee is only payable if the expert opinion is sought from a different APL to that of the initial pathology opinion. It is not intended that expert

[6] MSAC 61st Meeting (3-4 April 2014) Outcomes for Application No. 1276 – Renewal of the National Cervical Screening Program [available at http://www.msac.gov.au/]

opinion provided within the original pathologist's laboratory (i.e. intra-departmental or intra-institutional) is funded under the proposed items.

In the Consultation Protocol and the original Final Protocol, PASC stated that it would be administratively easier if there were only a small number (three or four) expert opinion items, rather than having a second, expert opinion item mirror every bone marrow, tissue pathology and cytology item currently on the MBS. The Applicant was asked to draft the wording of the relevant items and to suggest appropriate fees. PASC also asked the Applicant to specify which current pathology services would fall under each of the proposed second, expert opinion items.

In their response to the Consultation Protocol, the Applicant suggested a simplified, tiered approach with two different rebates reflecting the time and work involved. In subsequent communications, the Applicant has added that the complexity level of the initial MBS item cannot always predict the difficulty of the expert review. For example, a blistering inflammatory skin biopsy (complexity level 4) may take a considerable time to review, whereas a breast biopsy (complexity level 6 or 7) may be relatively simple for an expert to review if the issue requiring clarification relates to classification and the opinion does not involve a full review of margins[7].

Health Expert Standing Panel (HESP) members have supported a simplified approach, also arguing that there is not necessarily a correlation between the complexity level of the initial MBS item and the appropriate level of reimbursement for a second morphological opinion[8]. It would be up to the expert pathologist to determine the workload involved in providing the second opinion and bill the item accordingly as 'non-complex' or 'complex' (similar to the situation where a clinician is allowed to determine whether they bill for a short or long consultation). When the Final Protocol for MSAC Application 1332 was reconsidered by PASC in April 2014, PASC agreed that this approach was appropriate.

Table A.3-1 and Table A.3-2 reflect the proposed two-tier fee structure for 'non-complex' and 'complex' expert opinions, respectively, as per the revised Final Protocol. The proposed Schedule fee for the 'non-complex' expert opinion item is approximately equal to the fee for initial examination of a complexity level 4 biopsy with at least 12 separately identified specimens; the proposed fee for 'complex' expert opinion is approximately equal to the average of the initial fees for examination of complexity level 5 and 7 biopsy materials. Rather than differentiate the two proposed items on the basis of complexity, the Department has worded the item descriptors to reflect the amount of time taken to process and examine the specimen and prepare a full written report (either ≤30 minutes or >30 minutes).

Explanatory notes will need to be included to explicitly limit second, expert opinion to tissue pathology, cytology and bone marrow items.

According to the Final Protocol, the application of a Patient Episode Initiation fee is considered inappropriate in the provision of an external expert pathology opinion.

[7] Advice from the Applicant (Dr Bronwen Ross, Deputy CEO, RCPA), email 17 March 2014
[8] Expert pathologist opinion (Prof A Morey and Prof J Dahlstrom), email 17 March 2014

Table A.3-1 Proposed MBS item descriptor for a non-complex, second, expert opinion on a patient sample

Category 6 - Pathology
MBS item number (*assigned by the Department if listed*)
A no more than 30 minute limit, expert opinion and detailed written report on a patient sample, requested by a treating clinician, where further information is needed for accurate diagnosis and appropriate patient management.
Fee: $180.00
The service will be initiated upon the request of the referring clinician where there is uncertainty in the initial morphological diagnosis, or when the clinician involved in the care of the patient requests a second opinion. The item is applicable to cases where the expert pathologist is able to examine and/or re-process case material and produce a full written report in ≤30 minutes. The fee will not be payable if the service is provided within the same Approved Pathology Laboratory.

Abbreviations: MBS, Medicare Benefits Schedule
Source: Final Protocol May 2014

Table A.3-2 Proposed MBS item descriptor for a complex, second, expert opinion on a patient sample

Category 6 - Pathology
MBS item number (*assigned by the Department if listed*)
A greater than 30 minute, second, expert opinion and detailed written report on a patient sample, requested by a treating clinician, where further information is needed for accurate diagnosis and appropriate patient management.
Fee: $370.00
The service will be initiated upon the request of the referring clinician where there is uncertainty in the initial morphological diagnosis, or when the clinician involved in the care of the patient requests a second opinion. The item is applicable to cases that are not obvious or straightforward, where the examination and/or re-processing of case material and the production of a full written report takes more than 30 minutes. The fee will not be payable if the service is provided within the same Approved Pathology Laboratory.

Abbreviations: MBS, Medicare Benefits Schedule
Source: Final Protocol May 2014

It would be expected that a second, expert opinion on any specific pathology service episode would only be requested once. The pathologist reporting the case initially may suggest an appropriate expert to whom the case would be referred for the second opinion. Alternatively, the referring clinician may seek expert opinion from their preferred pathologist or a pathologist who normally provides the service to their institution. It is considered highly unlikely that a third opinion would be requested.[9]

Although the need for a second, expert opinion for morphological diagnosis on a patient sample is not anticipated to occur often, it is not possible to define or limit how many times a second opinion on different pathology services might be required for an individual patient. As noted in the Final Protocol, this would depend entirely on how many initial pathology services are requested for them, and the complexity of their illness(es) and future illness(es). It would be rare that someone would need to utilise an expert pathology opinion more than once for a particular disease episode; however it is possible.

[9] Expert pathologist opinion (Prof A Morey), email 05 July 2013.

A.4. Comparator details

As discussed in Section A.2.4, under current arrangements, the MBS does not provide reimbursement for second, expert opinions for pathology. However, there are circumstances where the primary pathologist or the treating clinician may require an expert opinion to optimise patient management. In those instances, a number of alternative pathways may be followed:

1) The original pathologist may request an expert opinion from an external pathologist who provides the opinion at no cost (but may be obliged to place low priority on the request), or the second pathology laboratory charges the initial laboratory privately. It is very difficult in these circumstances to charge the patient, as they would not have consented to pay for a second opinion; or
2) The treating clinician requests an expert opinion from a pathology provider, and this is provided either at no cost (gratis) or at cost to the patient (privately) or the clinical unit.

The Applicant suggests that, in some cases, an expert opinion would be desirable (e.g. by the original pathologist who considers it a difficult case) but the costs associated with providing a second opinion and the lack of funding often means that an expert opinion is not sought. This can result in a sub-optimal diagnosis or report being provided to the treating clinician. This is identified as a potential problem, particularly with remote isolated pathologists. Thus, this issue is potentially contributing to inequities in the care of patients in remote areas (see Section F). The Applicant further describes, in general terms, the associated risks of incomplete or incorrect diagnoses and subsequent inappropriate patient management, i.e. negative health outcomes, increased healthcare costs, and the potential for litigation (see Section A.7).

The comparator, as defined by the Applicant, is the standard management which currently applies, which is described as a scenario where there is "an absence of funding for morphological second opinions. Such opinions are therefore not sought as often as they should be for optimal patient care".

A.5. Clinical management algorithms

The current clinical management algorithm for patients having a morphology-based pathology test is shown in Figure A-1. The proposed clinical management algorithms, with the addition of MBS funding for pathologist- and clinician-initiated second, expert opinion are shown in Figure A-2 (*Scenario 1*) and Figure A-3 (*Scenario 2*), respectively. All of the algorithms refer to cases in which the primary pathologist cannot provide a definitive diagnosis and an expert opinion is considered desirable.

Under the current treatment algorithm, second, expert opinion is either provided: (i) without payment (ex gratis); (ii) at the expense of the patient; (iii) at the expense of the requesting hospital/unit (which may be publicly funded through other health budgets); or (iv) at the expense of the initial pathology laboratory, if this was the source of the referral. Alternatively, the expert opinion, although desirable, may not be requested due to lack of funding.

In the proposed treatment algorithms (Figure A-2 and Figure A-3) the patient pathway is similar to the current situation. However, expert pathologists are able to claim a fee for their opinion using one of the new MBS items. Theoretically, in the proposed scenario all

cases in which the initial pathologist was unable to confidently provide a definitive diagnosis would have the opportunity to be reviewed by an expert pathologist, provided that: (i) the initial pathologist and treating clinician agree that uncertainty remains in the diagnosis (*Scenario 1*); or (ii) the treating clinician requires verification or further information to effectively manage the patient (*Scenario 2*).

Figure A-1 Clinical management algorithm depicting current scenario (no second opinion funded)

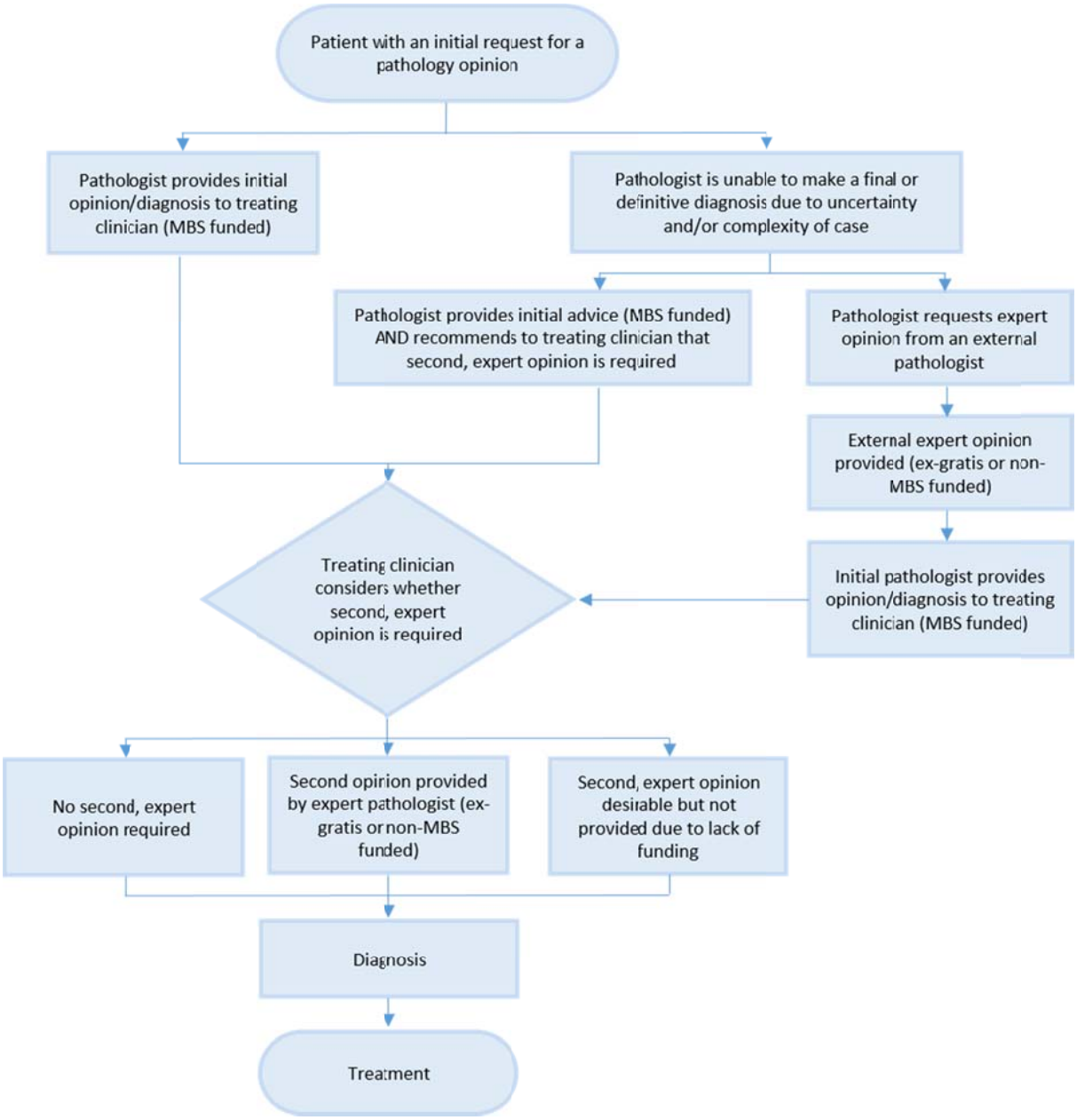


Figure A-2 Clinical management algorithm including proposed MBS item for second pathology opinion (*Scenario 1*)

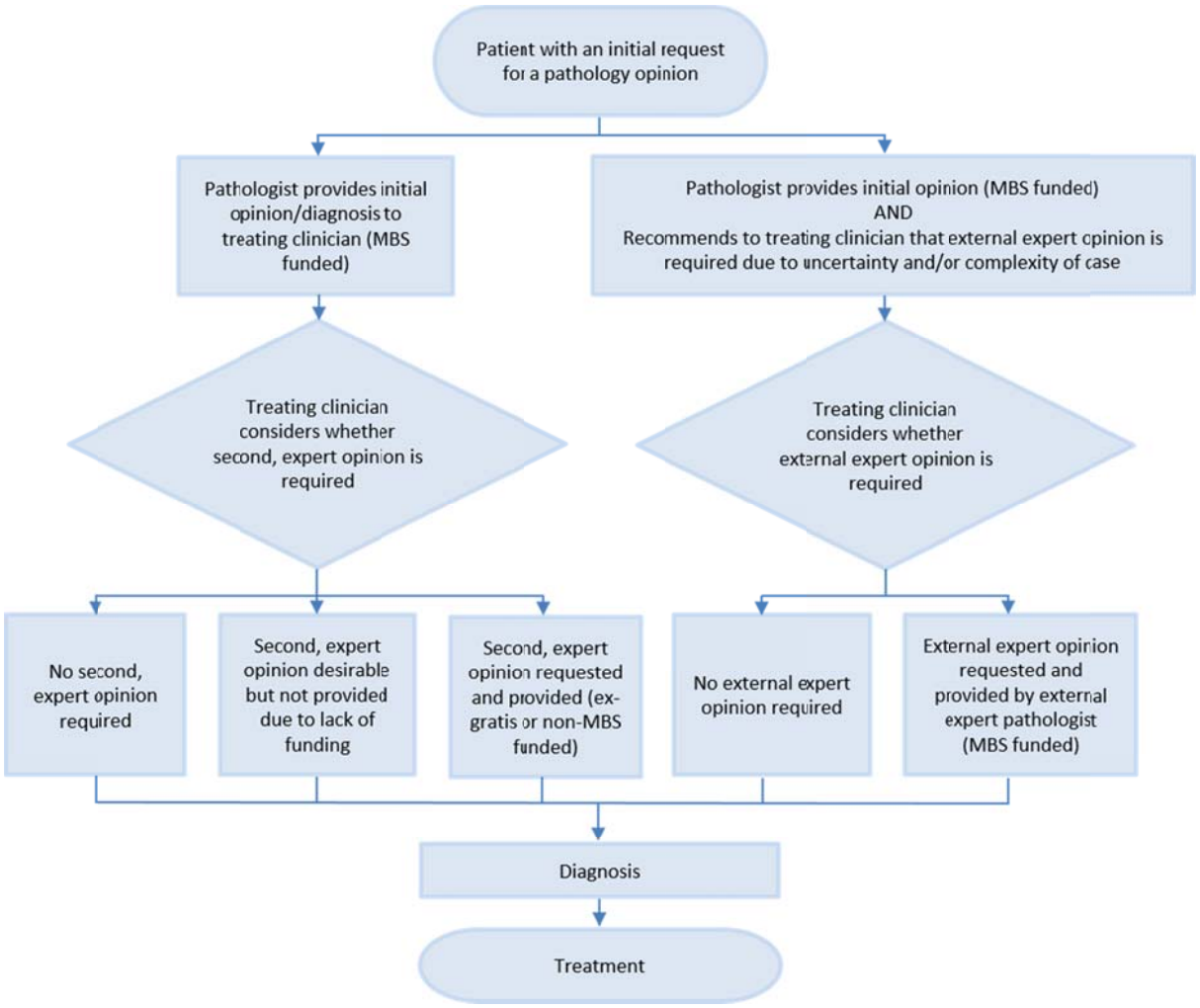
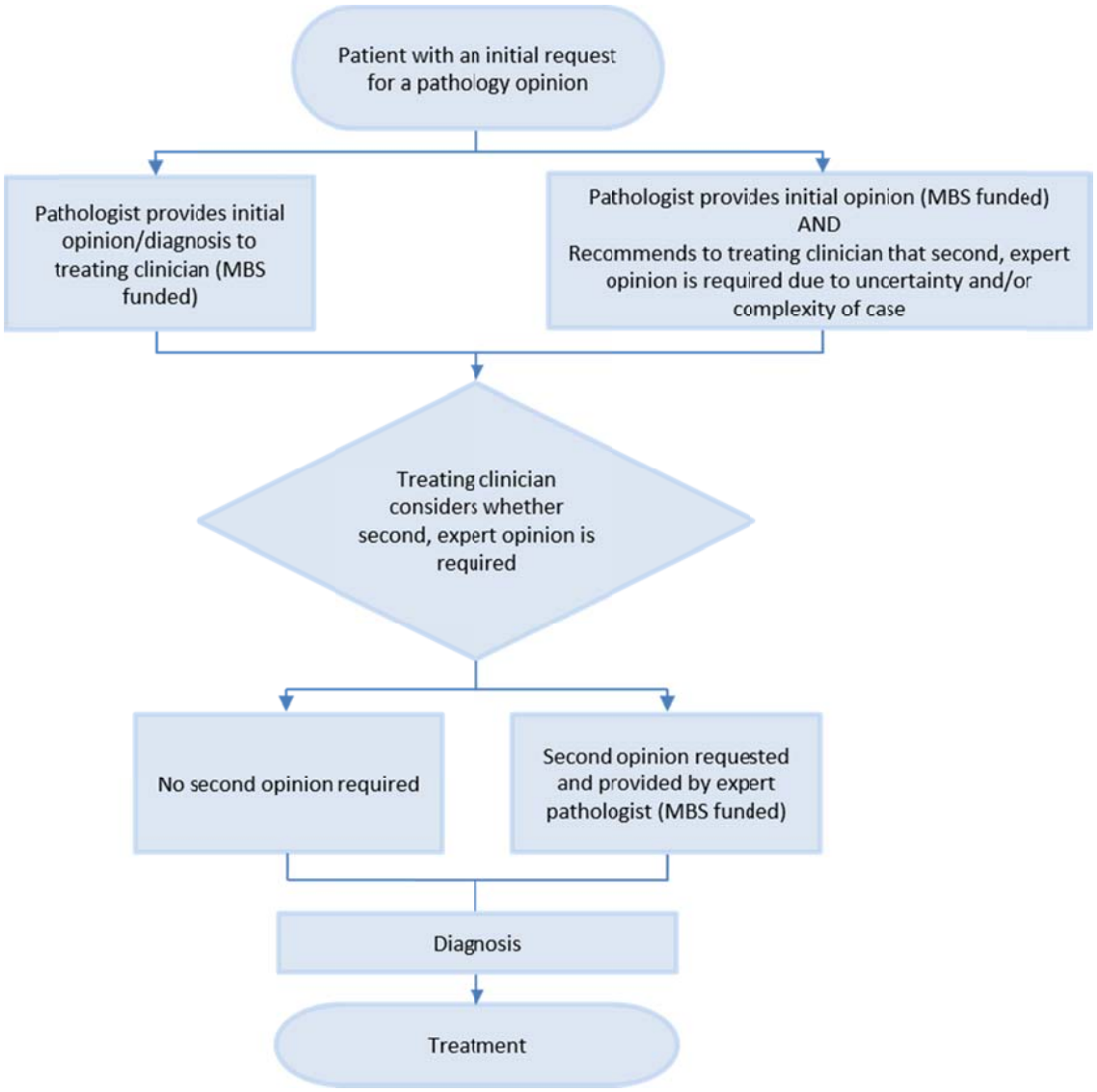


Figure A-3 Clinical management algorithm including proposed MBS item for second pathology opinion (*Scenario 2*)



A.6. Differences between the proposed medical service and the main comparator

As described in Section A.5, the difference between the proposed medical service and the main comparator is the provision of public funding for a service that is often already undertaken. Alternatively, in the proposed scenario, a second, expert opinion is provided in instances where it might not otherwise have been due to a lack of public funding. Thus, with MBS funding, a higher rate of requests for expert opinions would be expected than is currently the case.

A.7. Clinical claim

There is anecdotal evidence that second, expert opinions are not sought as frequently as they should be (particularly from isolated regional or remote pathologists) due to the cost, lack of funding, and perceived impost on colleagues. This can lead to a sub-optimal diagnosis or report being provided to the treating clinician, or in some cases, referral without a diagnosis. Without appropriate reimbursement, second opinion requests may

not be prioritised, leading to delays in diagnosis and therefore treatment. Thus, the ability for clinicians to obtain a funded second, expert opinion (in circumstances where the initial pathologist is unable to provide a final or definitive diagnosis or where the clinician lacks confidence in the initial pathologist's diagnosis) has the potential to positively impact on patient care via:

- the more accurate classification of disease and thus more accurate planning and selection of therapy; and
- more rapid diagnosis of rare and diagnostically challenging cases.

In cases where the initial pathologist is unable to provide a diagnosis, expert opinion may be necessary before therapy can be initiated. Where the expert pathologist is able to confirm a diagnosis that was in doubt by the initial pathologist or clinician, the expert may also add significant information that could support either the initiation or withholding of specific therapy. In cases where the expert pathologist makes a major change to the submitted diagnosis (such as a change from neoplastic to non-neoplastic, from non-neoplastic to neoplastic, from malignant to benign, or from benign to malignant), there may be an immediate alteration in the choice and timing of therapy, leading to reduced costs in terms of quality of life and effective utilisation of resources.

Additional information or changes relating to the type or grade of a tumour, as a result of expert opinion, may affect the choice of treatment, prognosis and therefore quality of life of the patient.

Importantly, changes in pathological diagnoses for gynaecological oncology cases are unlikely to affect treatment decisions, as most malignancies are surgically staged and graded (Chan et al, 1999). As such, second, expert opinions on cervical and vaginal smears and cervical biopsy specimens in patients with gross tumours are unlikely to impact on treatment decisions or prognosis. However, it may still be important to review cervical biopsy specimens in those patients without gross tumours.

A.8. Primary elements of the decision analysis

Evidence-based assessments of health technologies and procedures are underpinned by a research question or several research questions, which are formulated to ensure the appropriate identification and application of the evidence. Research questions are usually based around the PICO criteria, in which the key components are the target population (P), the intervention (I), comparator (C) and target outcomes (O). In the case of diagnostic tests, it is also important to consider what prior tests are performed to further define the tested population and spectrum of disease. As such, research questions for diagnostics tests are generally underpinned by the PPICO criteria, where the additional 'P' refers to prior tests.

The research questions that underpin this assessment were formulated in order to:

1) define the question for public funding;
2) select the evidence to assess the safety and effectiveness of second, expert pathology opinions in circumstances where:
    a) the initial pathologist could not confidently provide a final or definitive diagnosis and recommends that external expert opinion is sought *(Scenario 1),*

b) an initial pathology opinion may have been provided, but where uncertainty or insufficient detail regarding the diagnosis remains *(Scenario 2)*; and

3) provide the evidence-based inputs for determining the cost-impact of the proposed service.

The specific components of the PPICO criteria (shown in Table A.8-1) are used to inform the literature search strategy and the economic evaluation. According to the revised Final Protocol, the research questions that are addressed in this review are:

Scenario 1:

What is the safety, effectiveness, and cost-effectiveness of clinicians sourcing an external expert, tissue pathology (including bone marrow) or cytology second opinion on a patient sample, upon the recommendation of the initial reporting pathologist, compared with no publicly funded external expert opinion?

Scenario 2:

What is the safety, effectiveness, and cost-effectiveness of clinicians sourcing a second, expert, tissue pathology (including bone marrow) or cytology opinion on a patient sample, where there is a need to obtain, verify or refine a diagnosis, compared with no publicly funded second opinion?

For the purposes of this assessment, the main economic outcome of interest is cost per clinically relevant change in diagnosis or interpretation. The Final Protocol explains that while transformation of economic outcomes into quality-adjusted life-years (QALYs) may be possible for some patient subgroups where data are available, a whole of pathology patient population analysis predicting QALY outcomes is unlikely to be feasible or credible with existing data sources. Section D.2.2 provides rationale for the economic model undertaken, based on very limited clinical data.

Table A.8-1 Summary of PPICO for the assessment of second, expert pathology opinion

PPICO element	Description
Patients	All patients having a morphology-based pathology test Subgroups: by suspected disease or indication
Prior tests	Initial pathology examination and opinion
Interventions	*Scenario 1* External expert tissue pathology (including bone marrow) or cytology opinion sourced upon the suggestion of the initial reporting pathologist, due to uncertainty and/or complexity of the case. *Scenario 2* Second, expert tissue pathology (including bone marrow) or cytology opinion sourced due to uncertainty and/or complexity of the case or a need to obtain, verify or refine a pathology diagnosis.
Comparators	No publicly funded second, expert opinion (i.e. ex gratis second opinion or alternatively funded second opinion); or No second, expert opinion.
Evidentiary standards	Long term clinical diagnosis; Follow-up pathology on subsequent sample; or Consensus pathology opinion.

PPICO element	Description
Outcomes to be assessed	Safety Harms (physical and psychological) due to delay in diagnosis, incorrect diagnosis/ interpretation, incorrect treatment, incorrect revision of diagnosis/interpretation Diagnostic accuracy Sensitivity, specificity, positive predictive value, negative predictive value, concordance data Change in management Rate of clinically relevant revisions of initial pathology opinions, change in clinical management (e.g. biopsy rates, additional test ordering, change in treatment options) Effectiveness Morbidity, mortality, quality of life Cost-effectiveness Cost per clinically relevant change in diagnosis/interpretation

Although the overall body of evidence regarding second, expert opinions is large, there is only limited evidence about the clinical value of expert opinions that are requested due to pathologist or treating clinician uncertainty or a clinical need for diagnostic refinement. In such cases, input is actively sought to arrive at a definitive diagnosis; treatment will often be postponed until the expert opinion is received. Therefore, the rate of discrepancies between the initial opinion and the expert opinion does not have the same impact on patient care as discrepancies that are noted after cases have been finalised. Where the pathologist actively seeks expert opinion, discrepancies should not be viewed as errors but as a reflection of the acknowledged need for assistance. Furthermore, as a large proportion of cases are referred without a diagnosis, a true discrepancy rate cannot be ascertained.

Similarly, discrepancy rates in clinician-initiated second, expert opinions should be interpreted with caution, as such discrepancies would often be identified when a clinician has actively sought expert opinion for verification or refinement of complex cases in order to assist management. Discrepancies would therefore be discovered prior to treatment and would not be associated with a change in management.

Table A.8-2 provides a list of the terms used in the literature to describe the different types of second opinion for morphological pathology. Identification and classification of the evidence is not straightforward due to the differences in terminology and intention of seeking a second opinion. The majority of studies deal with intra-departmental review (which is undertaken primarily as part of quality assurance to find correctable errors) or mandatory/routine inter-institutional or extra-departmental second opinions or case reviews. Although important for appropriate patient management, there are relatively few studies that explicitly state the purpose of seeking second, expert opinion according to the circumstances (scenarios) described above (see Section B.2 for the included evidence base).

Table A.8-2 Definitions of second opinion terms used in the literature

Definitions:
Initial (primary) pathologist: The pathologist who first received the histopathology or cytopathology case for morphological interpretation.
Expert pathologist: a pathologist whose diagnostic acumen in a particular field (subspecialty) is recognised by his/her peers by virtue of his/her experience. An expert pathologist may be locally or nationally known.
External expert opinion: a histopathology or cytopathology case sent to a specific expert pathologist or pathology department at a different institution, upon the recommendation of an initial pathologist who could not confidently provide a primary or definitive diagnosis. The case may have been sent by the initial pathologist or

Definitions:
by the treating clinician at the request of the initial pathologist.
Voluntary/self-referred opinion: a histopathology or cytopathology case sent to a specific pathologist or pathology department by a pathologist who recognises their own limitations and/or seeks guidance from an expert pathologist due to uncertainty.
Personal (expert) consultation/referral: a histopathology or cytopathology case sent for a second opinion to a specific pathologist or pathology department, typically sought to resolve diagnostic uncertainty or to obtain input on a case from an expert. The pathologist, the clinician, or the patient may seek this consultation.
Intra-departmental consultation: Second opinions on a histopathology or cytopathology case that is sought (often informally) from a particular pathologist(s) within the same department.
Intra-institutional consultation/referral: a histopathology or cytopathology case that is sent to a pathologist within the same institution. This type of consultation is typically sought when a patient has been referred to the institution from a different hospital or clinic and a case review (including a review of the histopathology/cytopathology diagnosis) is undertaken at the new institution. At some institutions this is standard (or mandatory) practice.
Extra-departmental consultation/referral: a histopathology or cytopathology case that is sent out to a pathologist within a different department or to another institution.
Inter-institutional consultation/referral: a histopathology or cytopathology case that is sent out to a pathologist in another institution.

Source: Adapted from Azam et al. 2002.

Finally, it is generally assumed that a second opinion sought from an expert is correct; however, second, expert opinion is not the gold standard in diagnostic morphological pathology. Second, expert opinion provides an assessment of precision (consensus of opinion), where precision is regarded as a surrogate for determining the accurate diagnosis (Lueck et al, 2009). Precision may reflect consensus between the initial and expert pathologists or, on some occasions, between a panel of experts at a laboratory or consultation service, or both. However, numerous studies have reported a high degree of discordance between expert pathologists when diagnosing difficult lesions, suggesting that expert opinion diagnoses are not always accurate/correct (Cook et al, 2001). This has been substantiated in studies that have undertaken patient follow-up. Diagnoses in anatomical pathology are essentially judgements dependent on the available tissue and clinical information about the patient's condition. As such, the gold standard of diagnostic accuracy is good clinical correlation and adequate follow-up. Studies that report discrepancy rates without patient follow-up or consensus pathology opinion should be interpreted with caution.

Section B. Clinical evaluation for the main indication

B.1. Description of search strategies

A comprehensive search of the scientific literature was undertaken to locate all relevant studies that assessed the value of expert opinions for morphological pathology. Electronic searches of EMBASE.com and the Cochrane Library were conducted using the search terms outlined in Appendix 3. The search terms were broad enough to ensure that economic studies relating to second, expert opinion would also be captured, see Section D.2.1. The search of EMBASE.com (which concurrently searches Medline and EMBASE) was conducted on 21 March, 2014. The Cochrane Library (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effect, Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, Economic Evaluation Database) was searched on 15 April, 2014.

In addition, reference lists of relevant reviews and primary articles were hand-searched to identify additional studies. Databases maintained by health technology assessment (HTA) agencies were also reviewed for relevant reports.

B.1.1. Selection criteria

To be eligible for inclusion in this Assessment Report, studies had to fulfil the PPICO criteria as presented in Table A.8-1. Only studies that reported diagnostic accuracy, change in management, safety, effectiveness or cost-effectiveness outcomes were included and only if the expert opinion had been sought upon the suggestion of the initial reporting pathologist or a clinician in charge of patient management. Studies that included a combination of expert opinion types (e.g. pathologist-initiated, patient-requested, and/or routine review of all cases) were included, provided that some cases were referred due to pathologist or clinician uncertainty. However, if outcomes were not provided separately according to reason for referral (i.e. patient, pathologist or clinician-initiated) or type of referral (i.e. personal consultation vs routine review) the study was later excluded (see Section B.2).

Although there is a relatively large body of evidence that relates to second pathology opinion in cases where routine review is mandated by institutional policies, this evidence was excluded from the assessment due to inherent differences in the type and complexity of cases referred for second opinion. In studies where expert opinions are exclusively requested due to pathologist or clinician uncertainty or a clinical need for diagnostic refinement, a larger proportion of cases will have no initial diagnostic opinion or be missing pertinent clinical information that is required to effectively manage the patient. In contrast, studies assessing the value of routine review of all pathology cases may report lower discrepancy rates because they include a higher proportion of cases where the specimen types are unlikely to be misdiagnosed or the initial pathologist was confident in their diagnostic opinion. Thus, the findings of studies relating to routine review of all pathology cases are not applicable to the scenarios for public funding proposed in this Assessment Report.

A number of studies that examined diagnostic accuracy and/or the value of second opinion in pathology using virtual microscopy or telepathology were also excluded, as

this assessment focusses specifically on circumstances in which the expert pathologist is sent actual patient samples (e.g. glass slides, specimens) for second, expert opinion.

In addition, literature reviews, case reports, non-human and in vitro studies were excluded. Studies not published in English or articles not fully published and peer-reviewed (e.g. editorials, letters, conference proceedings, abstracts) were also excluded.

In summary, studies were excluded for the following reasons:

- Wrong publication type – literature reviews, case reports, non-human and in vitro studies, studies not fully published or peer-reviewed (editorials, letters, conference proceedings, abstracts).
- Wrong indication – not morphological pathology relating to tissue pathology, cytology or bone marrow.
- Wrong intervention – not external second opinion on a pathology sample (including telepathology and in-house/intra-institutional review), not expert opinion resulting from pathologist or clinician uncertainty (including studies that examine mandatory/routine review of all cases).
- Wrong outcomes (exclusion criteria for full text review only).
- Insufficient sample size – second, expert opinion involving less than 50 cases.
- Article not published in English.

B.1.2. Search results

The search of EMBASE.com yielded 4,174 potentially relevant publications, excluding seven duplicate citations. All titles and abstracts were screened using the selection criteria outlined in Section B.1.1.

A total of 4,065 studies were excluded, leaving 109 publications for which the full texts were retrieved. Using the selection criteria outlined in Section B.1.1, each publication was assessed for inclusion/exclusion. Eighty-five of the studies were subsequently excluded, leaving 24 included studies. None of the 141 potentially relevant citations identified through the Cochrane Library were included in the Assessment Report.

No additional relevant studies were identified through the search of HTA databases or hand-searching of reference lists.

A summary of the literature review process is presented in Table B.1-1.

Table B.1-1 Summary of the process used to identify relevant studies

	Embase.com	Cochrane library
Number of citations retrieved by search	4,181	141
Number of duplicate citations removed	7	0
Number of citations screened by title and abstract review	4,174	141
Number of citations excluded after title/abstract review:	-	-
• Wrong publication type	2,956	7
• Wrong indication: not morphological pathology	506	104
• Wrong intervention: not external second opinion on a pathology sample	481	15
• Wrong intervention: not expert opinion from pathologist or clinician uncertainty	37	13
• Wrong intervention: mandatory or routine review of all cases or review of a random sample of cases not associated with uncertainty	76	0
• Sample size <50	2	0
• Not published in English	8	1
Total excluded	4,066	140
Number of citations screened by full text review	108	1
Number of citations excluded after full text review:	-	-
• Wrong publication type	23	0
• Wrong indication: not morphological pathology	0	0
• Wrong intervention: not external second opinion on a pathology sample	8	0
• Wrong intervention: not expert opinion from pathologist or clinician uncertainty	25	0
• Wrong intervention: mandatory or routine review of all cases or review of a random sample of cases not associated with uncertainty	14	1
• Wrong outcomes	7	0
• Sample size <50	1	0
• Not published in English	6	0
Total excluded	84	1
Total number of citations included from each database	24	0

B.2. Listing of all studies

In total, 10 studies were identified that met the inclusion criteria for *Scenario 1* – i.e. cases in which an external expert opinion was sought by the initial pathologist due to diagnostic uncertainty. Studies were included in *Scenario 1* regardless of whether it was the initial pathologist or a treating clinician that actually referred the case, provided that pathologist uncertainty was the underlying reason for referral. Of the 10 included studies, two included all surgical pathology cases (Cook et al, 2001; Hsu et al, 2010). As well as presenting overall results, Hsu et al (2010) also presented some results (e.g. discordance and major discrepancies) according to subspecialty areas such as dermatology and bone/soft tissue. The remaining included studies focussed on the effectiveness of second, expert opinions within one subspecialty area, including dermatology (Gaudi et al, 2013; van Dijk et al, 2008; Veenhuizen et al, 1997); sarcoma (Arbiser et al, 2001; Ray-Coquard et al, 2012); lung biopsies (Hutton Klein et al, 2010); oral and maxillofacial pathology (Jones and Jordan, 2010); and urothelial lesions (Tavora et al, 2009).

As per the PPICO criteria outlined in Section A.8, the 10 studies that met the inclusion criteria for *Scenario 1* are also relevant to *Scenario 2* – i.e. cases where an initial pathology opinion may have been provided, but where uncertainty or insufficient detail regarding

the diagnosis remains. *Scenario 2* allows for clinicians to refer cases that have not been identified by the pathologist as diagnostically challenging; however, in practice, *Scenario 2* would also include the *Scenario 1* evidence, as an ambiguous or equivocal report from the initial pathologist would be likely to result in clinician uncertainty.

One of the aforementioned studies (Hutton Klein et al, 2010) contained additional information that was relevant to *Scenario 2*, as twenty (20%) of the cases in that study were clinician-initiated (see Table B.4-2). Four additional studies were identified that met the inclusion criteria for *Scenario 2* only, including one study that examined all surgical pathology cases (Ahmed et al, 2004). The other three studies focussed on prostate biopsies (Chan and Epstein, 2005); brain and spinal cord specimens (Bruner et al, 1997); and labial salivary gland biopsies (Vivino et al, 2002).

Table B.2-1 provides the citation details for all included studies. The characteristics of included studies are summarised in Section B.4. None of the studies were conducted in Australia.

Table B.2-1 Citations details and study characteristics for all included studies

Study ID	Citation details	Study characteristics
Scenario 1	-	-
Arbiser 2001	Arbiser ZK, Folpe AL & Weiss SW (2001). Consultative (expert) second opinions in soft tissue pathology: Analysis of problem-prone diagnostic situations. American Journal of Clinical Pathology, 116(4):473-476.	Retrospective review of 500 consecutive cases referred to a soft tissue consultation practice for EEO in a 2-month period in 1998. *United States*
Cook 2001	Cook IS, McCormick D & Poller DN (2001). Referrals for second opinion in surgical pathology: Implications for management of cancer patients in the UK. *European Journal of Surgical Oncology,* 27(6):589-594.	Retrospective review of all cases sent for SO during 1998, compared to 1990, from two large district general hospitals histopathology laboratories. *United Kingdom*
Gaudi 2013	Gaudi S, Zarandona JM, Raab SS, English JC & Jukic DM (2013). Discrepancies in dermatopathology diagnoses: The role of second review policies and dermatopathology fellowship training. *Journal of the American Academy of Dermatology,* 68(1):119-128.	Retrospective review of all outside cases referred to a dermatopathology unit for expert consultation or mandatory second review during one calendar year. *United States*
Hsu 2010	Hsu CY, Su IJ, Lin MC, Kuo TT, Jung SM & Ho DMT (2010). Extra-departmental anatomic pathology expert consultation in Taiwan: A research grant supported 4-year experience. *Journal of Surgical Oncology,* 101(5):430-435.	Retrospective multi-institutional review of consecutive cases sent for extra-departmental anatomic pathology consultation by Taiwan Society of Pathology (TSP) members from 2003 to 2006. TSP received research funding for EEO provided. Study does not include cases sent directly to Taiwan-based or overseas consultants. *Taiwan*
Hutton Klein 2010	Hutton Klein JR, Tazelaar HD, Leslie KO & Colby TV (2010). One hundred consecutive granulomas in a pulmonary pathology consultation practice. *The American journal of surgical pathology,* 34(10):1456-1464.	Prospective study of 100 consecutive lung biopsies referred to a pulmonary pathology consultation service by a pathologist or clinician over a 7-week period in 2008. *United States*
Jones 2010	Jones K & Jordan RCK (2010). Patterns of second-opinion diagnosis in oral and maxillofacial pathology. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology,* 109(6):865-869.	Retrospective review of consecutive cases referred to an oral and maxillofacial pathology consultation practice in a 24-month period in 2007-2008. Excluded intra-institutional referrals and referrals from oral and maxillofacial pathologists (OMPs). *United States*
Ray-Coquard 2012	Ray-coquard I, Montesco MC, Coindre JM, Dei tos AP, Lurkin A, Ranchere-vince D, et al. (2012). Sarcoma: Concordance between initial diagnosis and centralized expert review in a population-based study within three European regions. Annals of Oncology, 23(9):2442-2449.	Prospective review of 1463 cases of soft tissue or visceral sarcoma reviewed by expert pathologists between 2005 and 2008. The study included cases referred for expert SO at the request of the initial 'non-expert' pathologist and also cases in which the initial 'non-expert' pathologist did not request confirmation of diagnosis and whose findings were reviewed in the context of the study. *France*

Study ID	Citation details	Study characteristics
Tavora 2009	Tavora F, Fajardo DA, Lee TK, Lotan T, Miller JS, Miyamoto H, et al. (2009). Small endoscopic biopsies of the ureter and renal pelvis: Pathologic pitfalls. *American Journal of Surgical Pathology,* 33(10):1540-1546.	Retrospective review of 76 consecutive biopsies of the mid-upper ureter and renal pelvis submitted for expert consultation at The John Hopkins Hospital from 2004 to 2009. *United States*
van Dijk 2008	Van Dijk MCRF, Aben KKH, Van Hees F, Klaasen A, Blokx WAM, Kiemeney LALM, et al. (2008). Expert review remains important in the histopathological diagnosis of cutaneous melanocytic lesions. *Histopathology,* 52(2):139-146.	Retrospective review of 1887 lesions sent to the pathology panel of the Dutch Melanoma Working Group for voluntary expert review between 1991 and 2004. Fifty lesions were not diagnosed as cutaneous melanocytic lesions and were subsequently excluded from the study. *The Netherlands*
Veenhuizen 1997	Veenhuizen KCW, De Wit PEJ, Mooi WJ, Scheffer E, Verbeek ALM & Ruiter DJ (1997). Quality assessment by expert opinion in melanoma pathology: Experience of the Pathology Panel of the Dutch Melanoma Working Party. *Journal of Pathology,* 182(3):266-272.	Retrospective review of 1069 consecutive lesions sent to the pathology panel of the Dutch Melanoma Working Group for expert review between 1992 and 1994. Cases were referred from hospitals and institutes throughout The Netherlands and from some pathologists abroad. *The Netherlands*
Scenario 2	-	-
Ahmed 2004	Ahmed Z, Yaqoob N, Muzaffar S, Kayani N, Pervez S & Hasan SH (2004). Diagnostic surgical pathology: The importance of second opinion in a developing country. *Journal of the Pakistan Medical Association,* 54(6):306-311.	Retrospective study of all consecutive cases referred to a major referral centre for EEO in a 9-month period 2001 to 2002. Cases excluded if no initial diagnosis provided. *Pakistan*
Bruner 1997	Bruner JM, Inouye L, Fuller GN & Langford LA (1997). Diagnostic discrepancies and their clinical impact in a neuropathology referral practice. *Cancer,* 79(4):796-803.	Retrospective review of 500 consecutive brain and spinal cord biopsies referred to a neuropathology consultation service for review (referred patient cases) or EEO in 1995. *United States*
Chan 2005	Chan TY & Epstein JI (2005). Patient and urologist driven second opinion of prostate needle biopsies. *Journal of Urology,* 174(4 I):1390-1394.	Retrospective review of all prostate needle biopsies sent for expert consultation at the request of a patient or urologist over a 6-month period in 2001. *United States*
Vivino 2002	Vivino FB, Gala I & Hermann GA (2002). Change in final diagnosis on second evaluation of labial minor salivary gland biopsies. *Journal of Rheumatology,* 29(5):938-944.	Review of cases received for SO consultation for the classification of Sjögren's syndrome (SS), an autoimmune exocrinopathy, between 1994 and 2000. Cases were submitted by institutions that largely lacked xerostomia clinics. *United States*

Abbreviations: EEO, external expert opinion; OMP, oral and maxillofacial pathologist; SO, second opinion; SS, Sjögren's syndrome; TSP, Taiwan Society of Pathology.

Importantly, some further studies met the inclusion criteria and were later excluded for a variety of reasons. Five studies included evidence for second, expert opinions that came from patient-initiated referrals, as well as other patients who received a second, expert opinion due to pathologist and/or clinician uncertainty (Azam and Nakhleh, 2002; Fajardo et al, 2011; Kronz et al, 2003; Renshaw and Gould, 2013; Renshaw et al, 2009). While those studies did include patients whose case material was reviewed at the request of a pathologist or clinician, it was not possible to extract any outcome data from those studies, as the results were not presented separately according to the source of referral.

Similarly, some studies included a combination of cases that were referred due to uncertainty, as well as cases that underwent expert review due to institutional policies mandating second pathology opinion for all patients referred for treatment (Hamady et al, 2005; Zembowicz et al, 2011). One study was not applicable to an Australian setting, as the evidence came from an International Outreach Program in low- to middle-income countries (Santiago et al, 2012). Finally, one study was excluded because it only included a subset of cases in which the initial pathologist suspected malignancy and an expert pathologist diagnosed the case as benign (Herawi et al, 2005).

The characteristics of the aforementioned excluded studies are presented in Table B.2-2 and more detail regarding the specific reasons for exclusion are provided in Table B.2-3. The excluded studies will not be discussed beyond Section B.2 of this Assessment Report.

Table B.2-2 Comparative summary of characteristics of clinical studies relating to second, expert opinion: excluded studies

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
Azam 2002	Prospective multi-institutional study of cases sent for extra-departmental personal (expert) consultation in 1999. Study concluded when 20 extra-departmental cases were documented or 4 months had passed, whichever came first. Participants included 180 institutions enrolled in the College of American Pathologists (CAP) voluntary Q-Probes quality improvement program. Cases excluded if no diagnostic impression was rendered in the primary laboratory. Cases resulting from a patient's referral to a different institution were excluded. *United States (95.6%), Canada and Australia*	Surgical pathology (any organ system) and haematopathology (lymph node and bone marrow) cases N=2746 cases	Initial diagnosis. Most participating institutions (59.9%) did not have an expert in a branch of surgical pathology in their pathology group	EEO, requested by the pathologist, clinician or patient. Additional special histopathologic studies conducted as required.	Initial diagnosis	• Diagnostic accuracy • Characteristics of participating laboratories • Extra-departmental consultation rate • Turnaround time • Satisfaction rate • Reason for selecting the consultant pathologist • Nature of the specimen • Type of specimen provided • Communication characteristics • Institutional protocol characteristics • Factors contributing to delays
Fajardo 2011	Prospective study of consecutive cases of prostatic needle core biopsies in which the EEO was Gleason pattern 5. The final diagnosis was then compared to the Gleason score assigned by the initiating pathologist. *United States*	Prostatic needle core biopsies N=59 (138 biopsy parts)	Initial diagnosis	EEO provided by an expert pathologist at The John Hopkins Medical Institution. EEO was sought by clinicians or patients and not because the initial pathologist was seeking a second opinion.	Initial diagnosis	• Diagnostic accuracy (correlation of initial and expert Gleason score) • Morphologic pattern of Gleason pattern 5 and its relationship to its under-diagnosis

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
Hamady 2004	Retrospective review of all patients referred to endocrine multidisciplinary meetings at a teaching hospital for further management of thyroid malignancy or for expert thyroid surgical pathology opinion from Jan 2001 to March 2003. *United Kingdom*	All patients with an initial diagnosis of thyroid cancer N=66 cases (n=49 for routine review of referred cases, n=17 sent for EEO)	Initial diagnosis	EEO provided by an expert pathologist at the Institute of Pathology at Leeds Teaching Hospitals, and was confirmed by a second expert pathologist if diagnosis was discrepant from initial diagnosis. EEO requested by general pathologists from district hospitals.	Initial diagnosis	• Reason for referral • Nature of disagreement • Effect on therapy and prognosis
Herawi 2005	Prospective study of all prostate needle biopsies sent for expert consultation over a 7-month period in 2004. Only included cases referred for suspected malignancy, where a review of the entire case diagnosed the case to be benign. *United States*	All prostate needle biopsy cases where diagnosis was changed from malignant to benign. N=345 cases (567 lesions of concern)	Initial diagnosis of suspected malignancy	EEO provided by an expert pathologist at Johns Hopkins School of Medicine. EEO requested by pathologists from 183 centres in 35 states in the US.	Initial diagnosis of suspected malignancy	• Incidence of benign lesions causing diagnostic difficulty • IHC results
Kronz 2003	Prospective study of all prostate needle biopsy cases referred to a urological pathology consult service over a 10-month period in 1999-2000. *United States*	Prostate needle biopsy N=3251 cases	Initial diagnosis	EEO at John Hopkins Hospital. All cases were previewed by uropathology fellows or anatomic pathology residents and then reviewed for final diagnosis by the faculty expert in urological pathology.	Initial diagnosis	• Outside preliminary diagnosis • Expert review diagnosis • Number of missed lesions (including details of cases with missed lesions such as age and type of outside institution) • Type of missed lesion • Whether the missed lesion(s) were on the slide(s) of concern

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
Renshaw 2005	Review of inter-departmental consultations (incoming from outside institutions, pathologist-generated outgoing, patient- or clinician-generated outgoing) during a 2-year period from 2003 to 2005. *United States*	Pathology cases; any organ system Incoming: N=328 Outgoing: N=928 pathologist-generated, N=227 patient- or clinician-generated	Initial diagnosis	Incoming: SO provided by outside institutions. SO requested by pathologists from Department of Pathology Baptist Hospital of Miami. Outgoing: SO provided by Department of Pathology, Baptist Hospital of Miami. SO requested from outside the department (but may include requests from within the institution).	Initial diagnosis	• Diagnostic accuracy (disagreement rate) • Nature of consultations with follow-up (additional consultation, additional biopsy, additional testing)
Renshaw 2009	A retrospective review of inter-laboratory SOs requested by patients or clinicians from 2004 to 2009. The aim of the study was to compare disagreement rates based on whether the initial pathologist sent all or only selected slides. *United States*	All routine slides (excluding frozen section slides and IHC slides, unless the IHC stains were necessary to make a diagnosis) N=596	Initial diagnosis	Original material rather than recuts were sent for review, unless there were known legal reasons for retaining the originals, which occurred in less than 1% of cases.	Initial diagnosis	• Diagnostic accuracy (disagreement rate, error rates at first and second laboratories) • Disagreement rate according to whether all or selected slides were reviewed • Whether outside institution attempted to contact original institution regarding discrepant cases
Renshaw 2013	A review of patient/clinician-initiated consultations (incoming and outgoing) handled by the Baptist Hospital of Miami from 2006 to 2012. *United States*	All anatomic pathology (including surgical pathology and cytology) Incoming: N=1966 Outgoing: N=1532	Initial diagnosis	EEO requested or provided by the Baptist Hospital of Miami. All discrepant cases were reviewed by one of the authors.	Initial diagnosis	• Diagnostic accuracy (disagreement rate) • Change in disagreement rate over time • Use of IHC

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
Santiago 2013	Retrospective review of international paediatric cases from low- to middle-income countries submitted to an International Outreach Program for histopathologic EEO during a 3-year period from 2009 to 2011. Excluded cases when EEO was not definitively conclusive, insufficient tissue quality or quantity for diagnosis, or when original primary diagnostic report not available. *Low- to middle-income countries obtaining EEO from United States*	Paediatric malignancy histopathology cases N=705	Initial diagnosis	EEO provided by one or more pathologists (a board-certified anatomic pathologist, a haematopathologist, and/or a neuropathologist) from the Department of Pathology at St. Jude Children's Research Hospital. EEO requested by 184 pathologists from 37 countries (International Outreach Program partner sites).	Initial diagnosis	• Diagnostic accuracy (agreement, minor disagreement, major disagreement) • Diagnostic accuracy by anatomic site • Characteristics of cases sent for review • Nature of IHC used by initial pathologist and EEO pathologist • Correlation between major disagreements and use of IHC
Zembowicz 2011	Review of dermatopathology cases received for SO consultation from within the United States during a 6-month period from February to August, 2009. *United States*	Dermatopathology cases N=1229 cases (average case consisted of 3.4 ± 3 slides)	Initial diagnosis or no diagnosis rendered	EEO provided by a consultant pathologist at a free-standing clinical laboratory with no formal affiliations with large medical institutions. EEO requested by pathologists or clinicians due to diagnostic challenges or specific policies at outside institutions requiring external second opinion.	Initial diagnosis	• Turnaround time • Diagnostic categories of specimens submitted for review

Abbreviations: EEO, external expert opinion; IHC, immunohistochemistry; SO, second opinion.

Table B.2-3 Reasons to exclude each study from further detailed assessment

Study ID	Grounds for seeking exclusion	Details
Azam 2002	Study included EEO sought by the primary pathologist, clinician or patient.	The main reasons for seeking personal (expert) consultation were (Azam et al 2002, Table 2, p407): diagnostic uncertainty of the referring pathologist (46.8%), disagreement of opinion between 2 or more pathologists (6.0%), to seek additional information/ recommendation from an expert (28.2%), clinician's request (13.4%), patient's request (4.2%), other (1.3%). Results were not reported separately for EEO requests by pathologists or clinician only. Cases were excluded from the study if no diagnostic impression was rendered in the primary laboratory. These cases would represent a proportion of cases sent at the recommendation of the clinician or primary pathologist.
Fajardo 2011	Study included EEO sought by patients or clinicians.	In all cases the initial pathologist had provided a 'final' diagnosis and the cases were sent at the behest of clinicians or patients. Gleason pattern 5 was missed in 34 of 59 (57.6%) cases by the initial pathologist; however it is unclear what proportion of those cases were patient- and clinician-initiated. In addition, the study only included cases in which the expert diagnosis was Gleason pattern 5 – the diagnosis of the submitting pathologist was then compared.
Hamady 2005	In most cases second opinion was provided as part of a routine review prior to therapy, not because of any particular uncertainty on the part of the clinician or pathologist.	The study included a total of 66 cases, 49 of which underwent routine review before starting therapy. Only 17 cases were referred by the general pathologist for confirmation of the diagnosis. The relevant cases are therefore less than 50, which is one of the exclusion criteria.
Herawi 2005	Only included cases where referring pathologist suspected malignancy and an expert review of the entire case diagnosed it as benign.	A total of 4,046 prostate needle biopsy cases were sent for consultation and 345 cases (8.5%) were diagnosed on EEO as benign after an initial diagnosis of suspected malignancy (Herawi et al 2005, p874).
Kronz 2003	Study included EEO sought by the initial pathologist, clinician, patient and 'other'.	The study only included expert consultations (i.e. not patients referred for surgery). It was clear that some expert reviews were requested by patients and reasons other than clinician or pathologist uncertainty; however it was unclear what proportion of referrals came from each source.
Renshaw 2005	The reason for obtaining second opinion was not only due to diagnostic uncertainty. It is not clear whether the second opinion was from an expert pathologist.	The study focusses on inter-departmental consultation, but not necessarily expert opinion (particularly for incoming cases). Reason for incoming consults not provided in publication. The discussion section (Renshaw et al, 2005, p881) states that the high rate of pathologist-generated outgoing consultation may be because of litigious environment and the need to have an outside expert's name on the report. The authors claimed that these types of cases were not able to be distinguished in the data set and therefore the impact that these cases had on the rate of disagreement or error could not be directly measured. The publication did not mention cases where no initial opinion could be provided by the primary pathologist.
Renshaw 2009	Study included EEO sought by patients or clinicians.	It is unclear what proportion of cases were patient/clinician-initiated. Of 596 inter-departmental consultations, disagreements were identified in 81 (13.6%); however, the results were not presented separately according to the source of referral.

Study ID	Grounds for seeking exclusion	Details
Renshaw 2013	Study included EEO sought by patients or clinicians.	The study examined whether there has been a change over time in inter-laboratory (incoming and outgoing) anatomic pathology consultation material. Incoming requests were based entirely on patient or clinician desire because there is no mandatory requirement for consultation at the study hospital. For outgoing consultations, only those requested by the patient/clinician were reviewed. In both cases, it is unclear what proportion of cases were patient/clinician-initiated and the results were not presented separately according to the source of the referral.
Santiago 2013	Study not applicable to Australian setting.	Study includes cases for histopathological review of paediatric neoplasms submitted by international pathologists from 37 low- and middle-income countries, where pathology services may be sub-optimal (Santiago et al 2013, p1652).
Zembowicz 2011	Study included EEO sought by (i) the primary pathologist; (ii) the clinician; and (iii) a clinician or pathologist because of a policy at their institution mandating second opinion/external review.	Study includes at least 9% of cases that were referred for reasons other than pathologist or clinician uncertainty. In 9% of cases, the authors found records that indicated the review was requested by a clinician, or was referred because of outside institutional policies. In addition, of the remaining 91% of cases (referred by a pathologist) the authors suspect that some cases may have been referred because of considerations other than just seeking a second opinion on a challenging case. For example, it is possible that some pathology practices used the Web-based service as a means of obtaining a primary diagnosis, due to contractual arrangements with the referral centre, low costs and/or minimal logistical barriers. Some cases may have been sent due to medico-legal considerations, despite the fact that a submitting pathologist had little doubt about a diagnosis. Therefore, the type and number of referrals presented in the study may not reflect usual clinical practice due to the Web-based nature which reduces barriers and cost of referral (e.g. minimises secretarial resources needed for referral).

Abbreviations: EEO, external expert opinion.

B.3. Assessment of the measures taken by investigators to minimise bias

Potential sources of bias in the included studies have been assessed using principles from the QUADAS-2 tool developed by Whiting et al (2011). Important sources of bias may relate to patient selection, the index test, reference standard, and patient flow and timing. For the purposes of the following discussion, the 'index test' refers to an initial pathology opinion and the 'reference standard' refers to a second opinion obtained from one or more expert pathologists as a result of diagnostic uncertainty.

B.3.1. Patient selection

Most of the included studies had a low risk of bias in terms of patient selection. The majority of studies, which were both prospective and retrospective, assessed all consecutive cases sent to, or received by an expert consultation practice over the period of the study (Arbiser et al, 2001; Bruner et al, 1997; Chan and Epstein, 2005; Hsu et al, 2010; Hutton Klein et al, 2010; Jones and Jordan, 2010; Ray-Coquard et al, 2012; Tavora et al, 2009; van Dijk et al, 2008; Veenhuizen et al, 1997; Vivino et al, 2002). The remaining studies had a higher risk of patient selection bias for several different reasons, as discussed below.

Over 20% of cases in the study by Cook et al (2001) had a prior final diagnosis of malignant lymphoma. The 27 cases of malignant lymphoma were referred for further lymphoma classification and grading only. Therefore, those cases were likely to be less diagnostically challenging than cases in which the initial pathologist could not provide a diagnosis or could only provide a differential or provisional diagnosis and were unlikely to result in major diagnostic discrepancies. The inclusion of those cases with a pre-existing final diagnosis is likely to bias the results towards better/overoptimistic estimates of diagnostic accuracy.

The risk of patient selection bias in the study by Gaudi et al (2013) was also relatively low. However, it is important to note that one case (0.2%) underwent expert review due to an institutional policy mandating second review of pathology prior to definitive treatment, rather than acknowledged uncertainty on the part of the initial pathologist or clinician. In that case, the initial pathology opinion had been definitive (the patient had been referred for treatment) and the review was undertaken as a means of error detection rather than to seek assistance or clarification by an expert before a final diagnosis was provided. Therefore, the case was not necessarily difficult to diagnose, which may affect diagnostic accuracy results. However, as this was only one case, it is unlikely that any significant bias was introduced into the study.

The results of the study by Ray-Coquard et al (2012) may have low applicability due to some specific aspects of patient selection. In particular, patients were only included if sarcoma was suspected. This suggests a high likelihood that the patient population was different in terms of the severity of their condition compared with the broader focus of the research question (in which all initial cases would have the opportunity to be reviewed regardless of the suspected diagnosis). In addition, the cases included in Ray-Coquard et al (2012) may have differed substantially from the other studies, as initial pathologists were "systematically offered" external expert opinion on suspected sarcoma cases. As such, there may have been a tendency to refer less complex cases than those that a pathologist would refer without similar encouragement.

Overall, the patient selection of the studies matched the research question of this Assessment Report, with the exception of the studies listed above. The remaining studies have a low risk of patient selection bias, as consecutive patients who are referred due to clinical uncertainty are unlikely to be associated with significant bias.

With the exception of one case in Gaudi et al (2013), the large body of evidence that relates to second, expert opinion in cases where an institutional policy mandates expert review was not included in the assessment due to inherent differences in the complexity of cases that would therefore make up the patient sample.

B.3.2. Index test

In all cases the index test (initial opinion) was conducted prior to the reference standard (second, expert opinion). As such, there is no risk of bias relating to the sequence of the index test and reference standard. Importantly, the majority of studies included some patients that were not provided with a diagnosis by the initial pathologist due to the complexity of the case. In those instances it was not possible to compare the result of the reference standard to the index test. The absence of an index test may introduce bias into study results, depending on how the cases without an initial diagnosis are dealt with in calculations of diagnostic accuracy (e.g. concordance and discordance). In this Assessment Report, the cases without an initial diagnosis were generally excluded from results relating to diagnostic accuracy, including the number of major discrepancies (see Section B.5).

It is difficult to assess the applicability of the index test based on the information provided in the publications. In most cases the expertise of the initial pathologist was not reported, despite the likelihood that a small proportion of cases would be examined by an expert in the first instance. Gaudi et al (2013) reported that their study included 85 pathologists who referred cases to a dermatopathology unit for expert consultation, 16 (18.8%) of whom had completed a dermatopathology fellowship. In contrast, Ray-Coquard et al (2012) stated that cases were initially examined by a 'non-expert' pathologist who requested an external, expert opinion for confirmation. Equivalent information is not available in many studies, nor is it possible to determine the proportion of cases that would be likely to be seen by an expert in the first instance in Australia.

Finally, any studies in which the nature or conduct of the index test varied substantially from that of the review question (e.g. expert opinion provided via telepathology) were specifically excluded.

B.3.3. Reference standard

In many of the included studies there was an underlying assumption that the reference standard (second opinion by an expert pathologist) was 100% accurate and that any discordance (i.e. major or minor discrepancies) resulted from an incorrect initial diagnosis. However, none of the reference standards adopted in the included studies met the evidentiary standard defined in the PPICO criteria (see Section A.8) and it is possible that the reference standard did not correctly diagnose/classify the clinical condition.

Follow-up data was rarely available to confirm the assumption that, in discrepant cases, the second, expert opinion is accurate. Only two of the included studies provided patient follow-up information (Hutton Klein et al, 2010; Tavora et al, 2009); however, Hutton

Klein et al (2010) only obtained follow-up information in cases where the expert opinion was not confident (i.e. a probable or broad differential diagnosis was provided).

Furthermore, in all but one of the included studies (Vivino et al, 2002) the reference standard was conducted with full knowledge of the initial diagnosis (index test). The expert pathologist either had access to the initial pathology report, a letter from the initial pathologist or some insight into the initial pathologist's opinion via the clinician's referral letter. However, this is considered to be appropriate bias in the context of this Assessment Report, as it reflects the way in which second, expert opinions would be conducted in Australia under the current and proposed funding circumstances.

B.3.4. Flow and timing

The QUADAS-2 tool highlights the importance of all patients receiving the same reference standard. In several of the studies, expert opinion was not necessarily carried out in an identical manner across all cases. For example, in several studies the expert pathologist could refer a case to a panel of expert pathologists if they felt uncertain about the diagnosis or certain aspects of classification (Ray-Coquard et al, 2012; van Dijk et al, 2008; Veenhuizen et al, 1997). As such, in some cases the reference standard was expert opinion by one pathologist, while in other cases expert opinion may have been a consensus based on the opinion of two or more expert pathologists. In the study by Ray-Coquard et al (2012), all pathologists involved in the expert review attended training sessions in order to homogenise the review process.

In the study by Jones and Jordan (2010), a third expert was approached for a diagnosis when there was disagreement between the diagnosis of the initial and first expert pathologist.

Importantly, the consensus opinion in the studies listed above differs from consensus pathology opinion as an evidentiary standard, referred to in the PPICO criteria in Table A.8-1.

The concept of bias relating to timing is not relevant to this assessment, as the reference standard is conducted using the same case material as the initial opinion.

B.4. Characteristics of the studies

As outlined in Section B.2, 10 studies were identified that met the inclusion criteria for *Scenario 1*. The characteristics of those studies are summarised in Table B.4-1. The studies were heterogeneous, with sample sizes that ranged from 76 cases to 2,686 cases. Five of the studies were conducted in the United States, two were from the Netherlands, and the remaining three studies were from the United Kingdom, France and Taiwan. All studies reported concordance rate and/or rate of major discrepancies (see Section B.5 for further details).

Two of the *Scenario 1* studies included histopathology cases from any organ system (Cook et al, 2001; Hsu et al, 2010), two studies included soft tissue or sarcoma cases (Arbiser et al, 2001; Ray-Coquard et al, 2012), three studies included dermatology cases (Gaudi et al, 2013; van Dijk et al, 2008; Veenhuizen et al, 1997), one study included cases of granulomatous or giant cell reactions in the lung (Hutton Klein et al, 2010), one study included oral and maxillofacial pathology cases (Jones et al, 2010) and one study included cases of urothelial lesions of the renal pelvis and mid-upper ureter (Tavora et al, 2009).

The two studies of histopathology cases from any organ system included consecutive cases sent out of the institution to an external expert pathologist; the other eight studies included cases received for review by an expert pathologist or expert pathology service.

In addition, a further four studies were identified that met the inclusion criteria for *Scenario 2* only. The characteristics of those studies are presented in Table B.4-2. The study by Hutton Klein fulfils the definition of second, expert opinion in the context of both *Scenario 1* and *Scenario 2*; therefore, the characteristics of this study are repeated for completeness in Table B.4-2.

The *Scenario 2* studies ranged in size from 60 cases to 684 cases. One study from Pakistan included surgical pathology cases from any organ system (Ahmed et al, 2004). The other four studies were from the United States; one study of brain and spinal cord cases (Bruner et al, 1997), one study of prostate needle biopsies (Chan et al, 2005), one study of cases of granulomatous or giant cell reactions in the lung (Hutton Klein et al, 2010), and one study of labial salivary gland biopsy cases (Vivino et al, 2002). All studies reported on cases received for review by an expert pathologist or expert pathology service.

Table B.4-1 Comparative summary of characteristics of clinical studies relating to external expert opinion: *Scenario 1* studies

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
ALL SURGICAL PATHOLOGY	-	-	-	-	-	-
Cook 2001	Retrospective review of all cases sent for SO during 1998, compared to 1990, from two large district general hospitals histopathology laboratories. *United Kingdom*	All histopathology cases; any organ system N=128 cases[a]	Initial diagnosis or no diagnosis rendered	SO provided by "external experts" from other pathology laboratories in the UK. SO was mainly requested by pathologists[b] at Portsmouth Hospitals National Health Service (NHS) Trust.	Initial diagnosis	• SO consultation rate • Specimen anatomical site • Nature of initial pathology opinion (no/differential/provisional diagnosis) • Reason for referral • Diagnostic accuracy (concordance/discordance; major discrepancies) • Turnaround time • Nature of expert diagnosis (no diagnosis/confident diagnosis)
Hsu 2010	Retrospective multi-institutional review of consecutive cases sent for extra-departmental anatomic pathology consultation by Taiwan Society of Pathology (TSP) members from 2003 to 2006. TSP received research funding for EEO provided. Study does not include cases sent directly to Taiwan-based or overseas consultants. *Taiwan*	Anatomic pathology; any organ system N=2686 cases	Initial diagnosis or no diagnosis rendered	EEO provided by 65 pathologists with subspecialty expertise from teaching hospitals across Taiwan. Additional specialised testing performed as required. EEO requested by 224 pathologists from 79 institutes across Taiwan. Reasons for consultation not provided.	Initial diagnosis	• Annual SO consultation rate • Tissue origin of specimens • Nature of initial pathology opinion (no diagnosis, tentative diagnosis) • Diagnostic accuracy (concordance, discordance; major and minor discrepancies) • Turnaround time • Use of special stains • Characteristics of referring pathologists • Characteristics of EEO pathologists

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
SOFT TISSUE/ SARCOMA	-	-	-	-	-	-
Arbiser 2001	Retrospective review of 500 consecutive cases referred to a soft tissue consultation practice for EEO in a 2-month period in 1998. *United States*	Soft tissue lesions. Sample obtained by biopsy or definitive excisions (92.4%), or needle or punch biopsy (7.6%) N=500 cases	Initial diagnosis or no diagnosis rendered	EEO provided by a Soft Tissue Consultation Service, "which serves as an excellent resource to evaluate situations in which pathologists themselves recognise their limitations and/or seek guidance". EEO was 'self-referred' from across the US. Additional IHC conducted as required.	Initial diagnosis	• Nature of initial pathology opinion (no diagnosis, provisional diagnosis) • Diagnostic accuracy (concordance; major and minor disagreements) • Specimen diagnostic category
Ray-Coquard 2012	Prospective review of 1463 cases of soft tissue or visceral sarcoma reviewed by expert pathologists between 2005 and 2008. The study included cases referred for expert SO at the request of the initial 'non-expert' pathologist and also cases in which the initial 'non-expert' pathologist did not request confirmation of diagnosis and whose findings were reviewed in the context of the study. *France*	Soft tissue or visceral sarcoma N=1463 cases[c]	Initial diagnosis	EEO provided by an expert pathologist. In rare cases, the reviewing expert requested that the diagnosis was re-examined by another expert or discussed at panel meetings and a final consensus was reached. All pathologist from the three regions involved in this 'central review' attended training sessions in order to homogenise the review process.	Initial diagnosis	• Patient characteristics • Type of referring laboratory (public/private) • Characteristics of submitted tumours (tumour site, histological subtype, grade, type of sample) • Diagnostic accuracy (full/partial concordance, complete discordance) • Nature of discordance (grade, histological type, subtype)

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
DERMATOLOGY	-	-	-	-	-	-
Gaudi 2013	Retrospective review of all outside cases referred to a dermatopathology unit for expert consultation or mandatory second review during one calendar year. *United States*	Dermatopathology N=405 cases[d]	Initial diagnosis or no diagnosis rendered	Expert review provided by either of two university-based dermatopathologists, from the University of Pittsburgh Dermatopathology Unit. Expert review requested by 85 pathologists – 18.8% were dermatopathology trained.	Initial diagnosis	• Number of cases with no initial diagnosis • Diagnostic accuracy (major and minor discrepancies) • Diagnostic category of major discrepancies • Use of IHC • Training of referring pathologist
van Dijk 2008	Retrospective review of 1887 lesions sent to the pathology panel of the Dutch Melanoma Working Group for voluntary expert review between 1991 and 2004. Fifty lesions were not diagnosed as cutaneous melanocytic lesions and were subsequently excluded from the study. *The Netherlands*	Cutaneous melanocytic lesions N=1837 cases	Initial diagnosis or no diagnosis rendered	EEO provided by the Dutch Melanoma Working Group when a primary pathologist encountered difficulties diagnosing or classifying potential cutaneous melanocytic lesion. Approximately 75% of submitted lesions were reviewed by an individual panel member and discussed at a regular pathology panel meeting[e]; 25% were reviewed by the individual panel member only and were not discussed with other panel members.	Initial diagnosis	• Nature of initial pathology opinion (no/differential/provisional diagnosis) • Characteristics of submitted lesions (Spitz naevus, melanoma, etc) • Diagnostic accuracy (concordance, discordance; over- and under-diagnosis) • Use of IHC • Features of problematic lesions • Changes over time regarding the features of submitted lesions

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
Veenhuizen 1997	Retrospective review of 1069 consecutive lesions sent to the pathology panel of the Dutch Melanoma Working Group for expert review between 1992 and 1994. Cases were referred from hospitals and institutes throughout The Netherlands and from some pathologists abroad. *The Netherlands*	Skin lesions N=1069 cases	Initial diagnosis or no diagnosis rendered	EEO provided by the pathology panel of the Dutch Melanoma Working Group when a primary pathologist encountered difficulties in making an unequivocal diagnosis of a potential cutaneous melanocytic lesion. One of the three members of the pathology panel provided the EEO. Where doubt remained, the case was sent to other panel members and/or reviewed at bi-monthly panel meetings. If panel discussion led to a clinically relevant change in the original expert diagnosis, an additional report was promptly issued.	Initial diagnosis	• SO consultation rate (number of cases referred per institution; size of requesting institutions) • Nature of initial pathology opinion (no/differential/provisional diagnosis) • Patient characteristics of submitted cases (age, gender) • Diagnostic accuracy (concordance; over- and under-diagnosis) • Number of cases in which expert panel made an unequivocal diagnosis
LUNG	-	-	-	-	-	-
Hutton Klein 2010	Prospective study of 100 consecutive lung biopsies referred to a pulmonary pathology consultation service by a pathologist or clinician over a 7-week period in 2008. *United States*	Granulomatous or giant cell reactions in the lung N=80 cases[f]	Initial diagnosis or no diagnosis rendered	EEO provided by one or more of three pulmonary pathologists at the Mayo Clinic Scottsdale Pulmonary Pathology Consult Service, using an algorithmic approach to diagnosis.	Initial diagnosis	• Nature of initial pathology opinion (no diagnosis/provisional diagnosis) • Diagnostic accuracy (agreement/disagreement) • Nature of specimens (not reported separately for requests initiated by pathologist) • Clinical follow-up (not reported separately for requests initiated by pathologist)
ORAL AND MAXILLOFACIAL	-	-	-	-	-	-
Jones 2010	Retrospective review of	Oral and	Initial diagnosis	EEO provided by an OMP	Initial	• Nature of initial pathology opinion

Study ID	Study characteristics *Country*	Population	Prior test	Intervention	Comparator	Outcomes
	consecutive cases referred to an oral and maxillofacial pathology consultation practice in a 24-month period in 2007-2008. Excluded intra-institutional referrals and referrals from oral and maxillofacial pathologists (OMPs). *United States*	maxillofacial pathology N=142 cases	or no diagnosis rendered	located within a tertiary care academic centre in a large metropolitan centre, with disagreements reviewed by at least 2 other OMPs from the same institution for diagnostic confirmation. EEO was requested by 81 physician pathologists from community hospitals (90.8%) or academic medical centres (9.2%).	diagnosis	(no diagnosis/provisional diagnosis) • Diagnostic accuracy (agreement/disagreement) • Nature of diagnostic disagreements (major/minor) • Characteristics of referring pathologists • EEO billing information • Specimen anatomical site • Supplemental imaging studies • Use of ancillary tests
UROTHELIAL	-	-	-	-	-	-
Tavora 2009	Retrospective review of 76 consecutive biopsies of the mid-upper ureter and renal pelvis submitted for expert consultation at The John Hopkins Hospital from 2004 to 2009. *United States*	Urothelial lesions of the renal pelvis and mid-upper ureter N=76 cases (39 biopsies from the ureter and 37 from the renal pelvis)	Initial diagnosis	EEO provided by an expert pathologist at The John Hopkins Hospital. The expert opinions were undertaken in response to a request for expert consultation, presumably from the initial pathologist[g].	Initial diagnosis	• Patient characteristics (age, gender) of submitted cases • Diagnostic accuracy (major discrepancies) • Diagnosis at consultation

Abbreviations: EEO, external expert opinion; IHC, immunohistochemistry; NHS, National Health Service; OMP, oral and maxillofacial pathologists; SO, second opinion; TSP, Taiwan Society of Pathology; UK, United Kingdom.

[a] Details of the initial pathology opinion were available in 116 cases (i.e. cases for which the original referring Consultant's referral letter was found).

[b] The study included three cases that were clinician-referred; however, it has been included in Scenario 1 because three cases is a very low proportion (2.6%) of total cases and because most of the results were reported separately according to source of referral.

[c] The study included a total of 1463 cases: 564 cases were initially examined by a 'non-expert' pathologist who requested a second opinion to confirm the diagnosis; 899 cases were initially examined by a 'non-expert' pathologist who did not request confirmation of the diagnosis. The study referred to the latter group as the 'systematic review' or 'control' group.

[d] 404 out of 405 cases were relevant expert opinion cases, in which an outside pathologist sought an expert opinion. One case was a mandatory second review case, in which an expert opinion was required prior to definitive medical or surgical treatment.

[e] Throughout the duration of the study, the pathology panel of the Dutch Melanoma Working Group consisted of at least three pathologists with at least 5 years' extensive experience in diagnosing melanocytic lesions.

[f] The study included a total of 100 cases. Eighty requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[g] The article did not explicitly state where the request for second opinion originated (i.e. pathologist, clinician or patient); however, the terminology throughout the study implied that it was the initial pathologist (e.g. "submitting pathologist", "expert diagnosis consultation").

Table B.4-2 Comparative summary of characteristics of clinical studies relating to second, expert opinion: *Scenario 2* studies

Study ID	Study characteristics *Country*	Population	Prior test	Index test	Comparator	Outcomes
ALL SURGICAL PATHOLOGY	-	-	-	-	-	-
Ahmed 2004	Retrospective study of all consecutive cases referred to a major referral centre for EEO in a 9-month period 2001 to 2002. Cases excluded if no initial diagnosis provided. *Pakistan*	Surgical pathology; any organ system N=381 cases	Initial diagnosis	EEO provided by Section of Histopathology at the Aga Khan University Hospital. EEO requested by clinicians and in some cases the primary pathologist, across Pakistan. Additional IHC conducted as required.	Initial diagnosis	• Nature of initial pathology opinion (no diagnosis/ provisional diagnosis) • Diagnostic accuracy (agreement, disagreement) • Use of IHC • Specimen anatomical site • Number of cases in which expert could not provide diagnosis
BRAIN AND SPINAL CORD	-	-	-	-	-	-
Bruner 1997	Retrospective review of 500 consecutive brain and spinal cord biopsies referred to a neuropathology consultation service for review (referred patient cases) or EEO in 1995. *United States*	Brain and spinal cord biopsies or resections of tumours or suspected tumours N=500 cases[a]	Initial diagnosis or no diagnosis rendered	EEO provided by 3 faculty neuropathologists after conference review at a multihead microscope, from the Section of Neuropathology, Department of Pathology at the University of Texas M.D. Anderson Cancer Center. EEO requested by "pathologists or other attending physicians, such as surgeons, internists, or radiotherapists" (70.1%) or as part of protocol studies for second opinions with regard to therapy (29.9%). Additional special histopathologic studies conducted as required.	Initial diagnosis	• Nature of initial pathology opinion (no diagnosis/ provisional diagnosis) • Diagnostic accuracy (no discrepancy, minor discrepancy, total discrepancy) • Nature of major diagnostic discrepancies • Initiation of therapy before expert opinion in cases that turned out to be major discrepancies
PROSTATE	-	-	-	-	-	-
Chan 2005	Retrospective review of all prostate needle biopsies	Prostate needle	Initial diagnosis	EEO provided by an expert pathologist at John Hopkins	Initial	• Type of referral (patient or urologist-initiated)

Study ID	Study characteristics *Country*	Population	Prior test	Index test	Comparator	Outcomes
	received for expert consultation at the request of a patient or urologist over a 6-month period in 2001. *United States*	biopsy N=684 cases		Hospital. Additional high molecular weight cytokeratin staining conducted if not previously performed and if it would aid diagnosis.	diagnosis	• Type of referring laboratory (community hospitals, commercial laboratories, academic/teaching hospitals) • Original diagnosis (cancer, atypical HGPIN, benign) • Change in diagnosis • Change in Gleason score
LUNG	-	-	-	-	-	-
Hutton Klein 2010	Prospective study of 100 consecutive lung biopsies referred to a pulmonary pathology consultation service by a pathologist or clinician over a 7-week period in 2008. *United States*	Granulomatous or giant cell reactions in the lung N=100 cases[b]	Initial diagnosis or no diagnosis rendered	EEO provided by one or more of three pulmonary pathologists at the Mayo Clinic Scottsdale Pulmonary Pathology Consult Service, using an algorithmic approach to diagnosis. EEO requested by pathologist (80%) or clinician (20%).	Initial diagnosis	• Nature of initial pathology opinion (no diagnosis/provisional diagnosis) • Diagnostic accuracy (agreement/disagreement) • Nature of specimens (not reported separately for requests initiated by pathologist) • Clinical follow-up (not reported separately for requests initiated by pathologist)

Study ID	Study characteristics *Country*	Population	Prior test	Index test	Comparator	Outcomes
LABIAL SALIVARY GLAND	-	-	-	-	-	-
Vivino 2002	Review of cases received for SO consultation for the classification of Sjögren's syndrome (SS), an autoimmune exocrinopathy, between 1994 and 2000. Cases were submitted by institutions that largely lacked xerostomia clinics. *United States*	Labial salivary gland (LSG) biopsy N=60 cases	Initial diagnosis of (or suspected) SS based on physical, serological and/or histological components	Histopathological EEO provided by one or two pathologists from the Department of Pathology, Albert Einstein Medical Center, Philadelphia. SO was requested by the consulting rheumatologist due to clinical-pathologic discordance[c]. The reviewing pathologist(s) determined a focus score, which was used to categorise LSG biopsies as focal lymphocytic sialadenitis (FLS), characteristic of the salivary component of SS; chronic sialadenitis (CS)[d]; within normal limits (WNL); or indeterminate. Some biopsies had insufficient tissue area for expert review.	Initial diagnosis (histological)	• Diagnostic accuracy (disagreements/revisions) • Reason for misdiagnosis • Diagnostic delay • Technical and diagnostic aspects of biopsies (e.g. slides/case, glands/case, levels/case, glandular area, gross focus number, focus score)

Abbreviations: CS, chronic sialadenitis; EEO, external expert opinion; FLS, focal lymphocytic sialadenitis; HGPIN, high-grade prostatic intraepithelial neoplasia; IHC, immunohistochemistry; LSG, labial salivary gland; SO, second opinion; SS, Sjögren's syndrome; WNL, within normal limits.

[a] The study included a total of 500 cases: 284 "consultation-only" cases were submitted because of some doubt about the original diagnosis on the part of pathologists or other attending physicians (e.g. surgeons, internists, or radiotherapists) at an outside institution; 216 cases were reviewed after the patient was referred to the Texas M. D. Anderson Cancer Center for management.

[b] The study included a total of 100 cases. Eighty requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[c] The request may have originated from (1) diagnostic uncertainty in the cases' histologic description or conclusions, (2) absence of marker autoantibodies, or (3) lack of objective evidence of dry eyes and/or dry mouth.

[d] Biopsy material showing both FLS and CS was classified as FLS.

B.5. Outcome measures and analysis

The PPICO criteria in Section A.8 lists the following outcomes for the assessment of second, expert opinion:

- Diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value, concordance data);
- Change in management (rate of clinically relevant revisions of initial pathology opinions, change in clinical management (e.g. biopsy rates, additional test ordering, change in treatment options);
- Safety (physical and psychological harms due to delay in diagnosis, incorrect diagnosis/interpretation, incorrect treatment, incorrect revision of diagnosis/ interpretation);
- Effectiveness (morbidity, mortality, quality of life); and
- Cost-effectiveness (cost per clinically relevant change in diagnosis/interpretation).

Table B.5-1 (*Scenario 1*) and Table B.5-2 (*Scenario 2*) list the PPICO outcomes reported in each of the included studies. The cost-effectiveness outcome is addressed in Section D. All other outcomes are discussed below.

B.5.1. Diagnostic accuracy

The majority of the studies included in Section B were undertaken to determine the diagnostic accuracy of initial pathology opinions. In particular, the studies focussed on complex pathology cases that are diagnostically challenging for general pathologists or cases in which the clinician has concerns about the accuracy or level of detail provided in the initial diagnosis. Such cases, which exhibit unusual features or come from rare disease types, are therefore more likely to be referred to expert pathologists. As such, the primary aim of the included studies was to quantify the proportion of cases referred to expert pathologists that resulted in a change in diagnosis.

Diagnostic accuracy, which refers to the level of agreement between the initial and expert pathologists' diagnoses, was usually reported as a proportion of concordant and/or discordant cases. At least one measure of diagnostic accuracy was reported in all of the included studies (see Table B.5-1 and Table B.5-2). Most of the studies that reported concordance and/or discordance rates also categorised the discrepant cases into major or minor discrepancies. In general, minor discrepancies referred to differences in diagnosis that would have no or minimal impact on patient management. Cases in which the expert pathologist's diagnosis led to a change in patient management were referred to as major discrepancies.

Table B.5-1 Matrix showing outcomes specified in the PPICO criteria that were reported in the *Scenario 1* studies

Outcome	Arbiser 2001	Cook 2001	Gaudi 2013	Hsu 2010	Hutton Klein 2010	Jones 2010	Ray-Coquard 2012	Tavora 2009	Van Dijk 2008	Veenhuizen 1997
Safety	-	-	-	-	-	-	-	-	-	-
Incorrect diagnosis/interpretation	x	x	x	x	✓	x	x	✓	x	x
Incorrect treatment	x	x	x	x	x	x	x	x	x	x
Turnaround time (i.e. delay in diagnosis)	x	✓	x	✓	x	x	x	x	x	x
Diagnostic accuracy	-	-	-	-	-	-	-	-	-	-
Concordance/discordance/minor discrepancies	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Change in management	-	-	-	-	-	-	-	-	-	-
Rate of clinically relevant revisions of initial pathology opinion (major discrepancy)	✓	✓	✓	✓	x	✓	✓	✓	✓	✓
Change in clinical management (e.g. biopsy rates, additional test ordering, change in treatment options)	x	x	x	x	x	x	x	x	x	x
Effectiveness	-	-	-	-	-	-	-	-	-	-
Morbidity	x	x	x	x	x	x	x	x	x	x
Mortality	x	x	x	x	x	x	x	x	x	x
Quality of life	x	x	x	x	x	x	x	x	x	x
Cost-effectiveness	-	-	-	-	-	-	-	-	-	-
Cost per clinically relevant change in diagnosis/interpretation	x	x	x	x	x	x	x	x	x	x

Table B.5-2 Matrix showing outcomes specified in the PPICO criteria that were reported in the *Scenario 2* studies

Outcome	Ahmed 2004	Bruner 1997	Chan 2005	Hutton Klein 2010	Vivino 2002
Safety	-	-	-	-	-
Incorrect diagnosis/interpretation	x	x	x	✓	✓
Incorrect treatment	x	✓	x	x	x
Turnaround time (i.e. delay in diagnosis)	x	x	x	x	✓
Diagnostic accuracy	-	-	-	-	-
Concordance/discordance/minor discrepancies	✓	✓	✓	✓	✓
Change in management	-	-	-	-	-
Rate of clinically relevant revisions of initial pathology opinion (major discrepancy)	x	✓	x	x	✓
Change in clinical management (e.g. biopsy rates, additional test ordering, change in treatment options)	x	✓	x	x	x
Effectiveness	-	-	-	-	-
Morbidity	x	x	x	x	x
Mortality	x	x	x	x	x
Quality of life	x	x	x	x	x
Cost-effectiveness	-	-	-	-	-
Cost per clinically relevant change in diagnosis/interpretation	x	x	x	x	x

B.5.2. Clinically relevant change in diagnosis or interpretation

For the most part, major discrepancies between the initial opinion and second, expert opinion are defined as being clinically relevant changes that would result in a change in patient management (e.g. biopsy rates, additional test ordering, change in treatment options). Importantly, the reported rate of clinically relevant revisions of initial pathology opinion (major discrepancy) is a surrogate for change in management. In the vast majority of cases within the included studies, input is actively sought to arrive at a definitive diagnosis and treatment is postponed until the expert opinion is received. However, this was not the case in at least one study (Bruner et al, 1997) which reported whether or not the patients had received therapy before the final diagnosis had been received from the expert pathologist (see Table B.5-2).

The rate of major discrepancies is a key outcome for the assessment and forms the basis of the economic evaluation, which is reported as cost per clinically relevant change in diagnosis or interpretation (see Section D.3.2). The definitions of major discrepancies, as reported in the included studies, are shown in Table B.5-3.

Table B.5-3 Definitions of major discrepancies or an equivalent outcome – as reported in the included studies

Study	Definition of major discrepancy
Scenario 1	-
Arbiser 2001	Changes in diagnosis that had a significant impact on therapy, such as distinguishing a reactive process from a sarcoma or significant mis-grading of a sarcoma (i.e. mis-grading by two grades in a three-tiered system).
Cook 2001	Benign-malignant or malignant-benign changes in diagnosis.
Gaudi 2013	Changes that would affect patient treatment and result in an altered report, diagnosis, or both. *Note that a narrower definition of major discrepancy was adopted in most included studies. As such, the number of cases in Gaudi et al (2013) that underwent a benign-malignant or malignant-benign change has also been calculated using information in Table I, pg. 122.*
Hsu 2010	Benign-malignant or malignant-benign changes as well as changes between categories of malignancy.
Jones 2010	Changes in diagnosis that would significantly alter the evaluation plan, treatment and/or prognosis of the patient.
Ray-Coquard 2012	Major discrepancies were referred to as 'zero agreement'. Zero agreement corresponded to cases where the initial diagnosis was benign and final diagnosis was sarcoma, or vice versa; sarcoma versus non-mesenchymal diagnosis (i.e. carcinoma, melanoma, lymphoma) or vice versa; or gastrointestinal stromal cancer (GIST) versus non-GIST.
Tavora 2009	Cases initially diagnosed as an urothelial neoplasm that were found to be non-neoplastic upon review (i.e. malignant-benign changes).
van Dijk 2008	Clinically relevant over-diagnosis or under-diagnosis, defined as cases that underwent a shift from malignant to benign or benign to malignant.
Veenhuizen 1997	The study reported clinically relevant over-diagnosis and under-diagnosis, rather than 'major discrepancies'. Clinically relevant over-diagnosis referred to a change from malignant (e.g. invasive melanoma or suspected melanoma) to benign (e.g. common acquired naevus, Spitz naevus, special type of naevus, dysplastic naevus or melanoma *in situ*). Under-diagnosis referred to changes from benign to malignant.
Scenario 2	-
Bruner 1997	Major discrepancies were defined as discrepancies that would have caused an immediate alteration in therapy, excessive increased cost in terms of patient quality of life or ineffective utilisation of resources, or potential for medical malpractice liability for the treating clinician.

B.5.3. Safety

In the majority of studies, there is an implicit assumption that the second, expert opinion is correct, without sufficient follow-up to confirm whether this is indeed the case. Therefore, very limited data are available from the included studies regarding the safety outcomes outlined in the PPICO criteria, which include incorrect diagnosis/interpretation, incorrect revisions of diagnosis/interpretation and incorrect treatment (see Table B.5-1 and Table B.5-2). As mentioned in Section B.3.3, only two of the included studies provided any patient follow-up information (Hutton Klein et al, 2010; Tavora et al, 2009); however, Hutton Klein et al (2010) only obtained follow-up in cases where the second, expert opinion was not confident (i.e. a probable or broad differential diagnosis was provided).

B.5.4. Effectiveness

None of the included studies reported relevant effectiveness outcomes such as mortality, morbidity or quality of life (see Table B.5-1 and Table B.5-2).

B.6. Systematic overview of the results

As discussed in Section A.2, an initial pathology opinion may include: (i) no diagnostic interpretation; (ii) a differential diagnosis; or (iii) a provisional diagnosis. While the nature of the initial pathology opinion is not an outcome explicitly evaluated in the Assessment Report, the interpretation of certain outcomes requires consideration of whether or not a provisional diagnosis was provided by the initial pathologist. In particular, in circumstances where the initial pathologist acknowledges their limitations and does not provide a diagnosis, the expert opinion would not usually be regarded as a true diagnostic discrepancy, as it would technically be the first diagnosis upon which patient management decisions could be based.

The nature of the initial pathology opinions provided in the *Scenario 1* and *Scenario 2* studies (including the number and proportion of cases referred for second, expert opinion without an initial diagnosis) are shown in Table B.6-1 and Table B.6-2, respectively. The proportion of studies referred for expert opinion with no initial diagnosis varies substantially between studies from 0.3% in Hsu et al (2010), which included pathology specimens from any anatomical site, to 46.8% in Arbiser et al (2001), which included soft tissue lesions only. The large variation is likely to result from differences in the complexity of the tissue being studied, but could also be an artefact of the availability of funding for second, expert opinions, which may alter referral patterns.

Importantly, there was also inconsistency between the studies regarding the way in which cases without an initial diagnosis were handled during the analysis of results. For example, some studies reported major discrepancies as a proportion of all cases, whereas other studies removed the number of cases with no initial diagnosis from the denominator. For consistency, the results shown throughout Section B.6 were recalculated, where necessary, to reflect the latter approach. For example, the concordance rates shown in Section B.6.1 reflect the proportion of concordant diagnoses out of those cases that had a provisional diagnosis.

The rationale behind omitting cases with no initial opinion from the results (particularly major discrepancy results, where major discrepancy is a surrogate for change in clinical management) is that it is not possible to determine what type of treatment (or other diagnostic techniques) would have been initiated in the absence of a second, expert opinion.

Tables B.6-1 and Tables B.6-2 also provide information about the characteristics of corresponding expert pathology opinions. For example, 13 cases in the study by Cook et al (2001) were referred without an initial pathology opinion. Of those 13 cases, the expert pathologist was able to provide a confident diagnosis in four cases, a probable diagnosis in five cases and was unable to provide a diagnosis in four cases (see Table B.6-1).

Table B.6-1 Summary of the nature of initial and expert pathology opinions – *Scenario 1 studies*

Study ID	Population (N)	Initial pathology opinion	Results n/N (%)	Expert pathology opinion	Results n/N (%)
ALL SURGICAL PATHOLOGY	-	-	-	-	-
Cook 2001	All histopathology; any organ system N=128 cases[a]	Cases with no initial diagnosis Cases with a differential diagnosis Cases with a provisional diagnosis: pathologist-initiated expert opinion Cases with a provisional diagnosis: clinician-initiated expert opinion Number of cases with a confident, final diagnosis prior to expert opinion[b]	13/116 (11.2%) 18/116 (15.5%) 55/116 (47.4%) 3/116 (2.6%) 27/116 (23.3%)	Confident diagnosis made in cases with no initial diagnosis Probable diagnosis made in cases with no initial diagnosis No diagnosis reached in cases with no initial diagnosis Confident diagnosis by expert pathologist after initial differential diagnosis Provisional diagnosis altered or a confident diagnosis made where there was previously no definite diagnosis	4/13 (30.8%) 5/13 (38.5%) 4/13 (30.8%) 15/18 (83.3%) 36/89[c] (40.4%)
Hsu 2010	Anatomic pathology; any organ system N=2686 cases	Cases with no initial diagnosis Cases with a differential diagnosis Cases with a provisional diagnosis Cases with a 'specific' provisional diagnosis	7/2686 (0.3%) 816/2686 (30.4%) 1863/2686 (69.4%) 1670/2686 (62.2%)	NR	NR
SOFT TISSUE/ SARCOMA	-	-	-	-	-
Arbiser 2001	Soft tissue lesions N=500 cases	Cases with no initial diagnosis Cases with a provisional diagnosis	234/500 (46.8%) 266/500 (53.2%)	NR	NR
Ray-Coquard 2012	Soft tissue or visceral sarcoma N=1463 cases[d]	Cases with a provisional diagnosis	564/564 (100%)	Expert pathologist provided a diagnosis	564/564 (100%)
DERMATOLOGY	-	-	-	-	-
Gaudi 2013	Dermatopathology N=405 cases[e]	Cases with no initial diagnosis Cases with a provisional diagnosis	51/405 (12.6%) 354/405 (87.4%)	NR	NR

Study ID	Population (N)	Initial pathology opinion	Results n/N (%)	Expert pathology opinion	Results n/N (%)
van Dijk 2008	Cutaneous melanocytic lesions N=1837	Cases with no initial diagnosis Cases with a differential diagnosis Cases with a provisional diagnosis	160/1837 (8.7%) 435/1837 (23.7%) 1217/1837 (66.2%)	Expert pathology panel unable to provide specific diagnosis Expert pathology panel unable to provide specific diagnosis but able to provide a presumed working diagnosis Expert pathology panel unable to provide specific diagnosis but able to provide a presumed working diagnosis + advice for further diagnostic and/or therapeutic procedures	67/1837 (3.6%) 42/1837 (2.3%) 25/1837 (1.4%)
Veenhuizen 1997	Skin lesions N=1069	Cases with no initial diagnosis Cases with a differential diagnosis Cases with a provisional diagnosis	90/1069 (8.4%) 131/1069 (12.3%) 798/1069 (74.6%)	Expert or expert pathology panel unable to provide a diagnosis Expert or expert pathology panel able to provide differential diagnosis Expert pathology panel provided unequivocal diagnosis in cases with no initial diagnosis Expert pathology panel provided unequivocal diagnosis in cases with initial differential diagnosis	7/1069 (0.7%) 23/1069 (2.2%) 81/90 (90.0%) 122/131 (93.1%)
ORAL AND MAXILLOFACIAL	-	-	-	-	-
Jones 2010	Oral and maxillofacial pathology N=142 cases	Cases with no initial diagnosis Cases with a provisional diagnosis	7/142 (4.9%) 135/142 (95.1%)	NR	NR
UROTHELIAL	-	-	-	-	-
Tavora 2009	Urothelial lesions of the renal pelvis and mid-upper ureter N=76	Cases with no initial diagnosis Cases with a provisional diagnosis	0/76 (0%) 76/76 (100%)	NR	NR
LUNG	-	-	-	-	-
Hutton Klein 2010	Granulomatous or giant cell reactions in the lung	Cases with no initial diagnosis Cases with a provisional diagnosis	25/80 (31.3%) 55/80 (68.8%)	Expert pathologist provided a confident diagnosis Expert pathologist provided a probable (strongly favoured) diagnosis	27/100 (27.0%)[g] 34/100 (34.0%)[g]

Study ID	Population (N)	Initial pathology opinion	Results n/N (%)	Expert pathology opinion	Results n/N (%)
	N=100 cases[f]			Expert pathologist provided a differential diagnosis	39/100 (39.0%)[g]

Abbreviations: NR, not reported.

[a] Details of the initial pathology opinion were available in 116 cases (i.e. cases for which the original referring Consultant's referral letter was found).

[b] A diagnosis of malignant lymphoma had been made prior to referral. The expert was asked to provide further lymphoma classification and grading.

[c] The study reports 36/116 (31.0%). The denominator has been altered to remove 27 cases in which a diagnosis of malignant lymphoma had already been made and the case was only referred for further lymphoma classification and grading.

[d] The study included a total of 1463 cases: 564 cases were initially examined by a 'non-expert' pathologist who requested a second opinion to confirm the diagnosis; 899 cases were initially examined by a 'non-expert' pathologist who did not request confirmation of the diagnosis. The study referred to the latter group as the 'systematic review' or 'control' group.

[e] 404 out of 405 cases were relevant expert opinion cases, in which an outside pathologist sought an expert opinion. One case was a mandatory second review case, in which an expert opinion was required prior to definitive medical or surgical treatment.

[f] The study included a total of 100 cases: 80 requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[g] The results were not provided separately according to pathologist/clinician-initiated referrals.

Table B.6-2 Summary of the nature of initial and expert pathology opinions – *Scenario 2 studies*

Study ID	Population (N)	Outcome	Results n/N (%)	Expert pathology opinion	Results n/N (%)
ALL SURGICAL PATHOLOGY	-	-	-	-	-
Ahmed 2004	Surgical pathology; any organ system N=381 cases	Cases with no initial diagnosis Cases with a provisional diagnosis	45/381 (11.8%) 336/381 (88.2%)	Expert pathologist unable to provide a diagnosis	12/336 (3.6%)
BRAIN AND SPINAL CORD	-	-	-	-	-
Bruner 1997	Brain and spinal cord biopsy for suspected neoplastic disease N=500 cases[a]	Cases with no initial diagnosis Cases with a provisional diagnosis	23/284 (8.1%) 261/284 (91.9%)	Expert pathologist provided a diagnosis	284/284 (100%)
LUNG	-	-	-	-	-
Hutton Klein 2010	Granulomatous or giant cell reactions in the lung N=100 cases[b]	Cases with no initial diagnosis Cases with a provisional diagnosis	0/20 (0%) 20/20 (100%)	Expert pathologist provided a confident diagnosis Expert pathologist provided a probable (strongly favoured) diagnosis Expert pathologist provided a differential diagnosis	27/100 (27.0%)[c] 34/100 (34.0%)[c] 39/100 (39.0%)[c]
LABIAL SALIVARY GLAND	-	-	-	-	-
Vivino 2002	LSG biopsy for possible Sjögren's syndrome N=60 cases	Cases with no initial diagnosis[d] Cases with a provisional diagnosis	1/60 (1.7%) 59/60 (98.3%)	Expert unable to provide diagnosis[d]	7/60 (11.7%)[d]

Abbreviation: LSG, labial salivary gland.

[a] The study included a total of 500 cases: 284 "consultation-only" cases were submitted because of some doubt about the original diagnosis on the part of pathologists or other attending physicians (e.g. surgeons, internists, or radiotherapists) at an outside institution; 216 cases were reviewed after the patient was referred to the Texas M. D. Anderson Cancer Center for management.

[b] The study included a total of 100 cases: 80 requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[c] The results were not provided separately according to pathologist/clinician-initiated referrals.

[d] The tissue biopsy was insufficient for diagnosis.

B.6.1. Diagnostic accuracy

As discussed in Section B.5.1, the 10 *Scenario 1* studies assessed diagnostic accuracy by comparing the initial pathology diagnosis (usually undertaken by a general, non-expert pathologist) with that of an expert pathologist. However, one study (Tavora et al, 2009) did not provide concordance or discordance rates. The primary focus of the study was the number of major discrepancies; however, broader diagnostic accuracy results were not reported. The evidence from that study will therefore be discussed in Section B.6.2.

Five of the *Scenario 1* studies reported both concordance and discordance (Cook et al, 2001; Gaudi et al, 2013; Hsu et al, 2010; Hutton Klein et al, 2010; Ray-Coquard et al, 2012), while others reported concordance data only (Arbiser et al, 2001; Jones and Jordan, 2010; van Dijk et al, 2008; Veenhuizen et al, 1997). In the latter four studies, it is not necessarily correct to assume that non-concordant cases were completely discordant. It is possible that cases excluded from concordance results were assigned the same broad diagnostic category by the initial and expert pathologists and that the diagnoses differed only on specific details such as grade or subtype (which may or may not have therapeutic significance). As a result, some studies categorise diagnostic accuracy results into several subgroups including total concordance, partial concordance and complete discordance (Ray-Coquard et al, 2012).

While misdiagnosis by the initial pathologist is often the cause of discordance, some studies also report a number of discordant cases where the source was different reporting styles or classification systems used by the initial and expert pathologists (Gaudi et al, 2013). Most studies did not specify whether diagnoses that used incomparable reporting styles were considered to be discordant or were simply excluded from the analysis.

As a result of different interpretations and definitions of concordance and discordance, it is difficult to compare the measures of diagnostic accuracy across multiple studies. For example, the two *Scenario 1* studies of all surgical pathology (Cook et al, 2001 and Hsu et al, 2010) reported concordance rates of 69.1% and 35.7%, respectively, which is likely to be due, in part, to different definitions of concordance (see Table B.6-3).

The broad nature of the conditions considered in the Assessment Report also adds to the variability of results between studies. For example, a concordance rate of 65.9% was reported in a study of oral and maxillofacial pathology (Jones and Jordan, 2010), whereas a study of granulomatous or giant cell reactions in the lung found that only 12.7% of initial pathologist and expert pathologist diagnoses were concordant (Hutton Klein et al, 2010), see Table B.6-3.

The five additional *Scenario 2* studies all provided some information about concordance and/or discordance rates between the initial and expert pathology opinions. Similarly, the definitions of concordance and discordance significantly differed between studies and it was not possible to pool the results. Table B.6-4 shows that the only study that reported diagnostic accuracy based on all surgical pathology types reported 60.7% concordance and 35.7% discordance (Ahmed et al, 2004). The other studies, which focussed on specific tissue types, had higher discordance rates: 41.1% for prostate needle biopsies (Chan and Epstein, 2005); 46.7% in brain and spinal cord biopsies (Bruner et al, 1997); 54.2% in labial salivary gland biopsies (Vivino et al, 2002); and 82.7% in granulomatous or giant cell reactions in the lung (Hutton Klein et al, 2010). Importantly, Table B.6-3 and Table B.6-4 show diagnostic accuracy results excluding cases without an initial (provisional) diagnosis.

Table B.6-3 Diagnostic accuracy: level of concordance and/or discordance between initial and expert pathology opinion – *Scenario 1 studies*

Study ID	Population (N)	Outcome	Results n/N (%)
ALL SURGICAL PATHOLOGY	-	-	-
Cook 2001	All histopathology; any organ system N=128 cases[a]	Concordant with provisional diagnosis (pathologist-initiated EEO) Discordant with provisional diagnosis (pathologist-initiated EEO) Concordant with differential diagnosis Concordant with provisional diagnosis (clinician-initiated EEO)	38/55 (69.1%) 17/55 (30.9%) 17/18 (94.4%) 3/3 (100%)
Hsu 2010	Anatomic pathology; any organ system N=2686 cases	Concordant with specific[b] provisional diagnosis Discordant with specific[b] provisional diagnosis	596/1670 (35.7%) 1074/1670 (64.3%)
SOFT TISSUE/SARCOMA	-	-	-
Arbiser 2001	Soft tissue lesions N=500 cases	Essential concordance with provisional diagnosis	181/266 (68.0%)
Ray-Coquard 2012	Soft tissue or visceral sarcoma N=1463 cases[c]	Full concordance with provisional diagnosis Partial concordance with provisional diagnosis[d] Complete discordance[e] *Type of discordance[f] (as a proportion of all cases with a provisional diagnosis):* • Subtype alone • Grade alone • Histological type alone • Grade and subtype • Grade and histological type	230/564 (40.8%) 263/564 (46.6%) 71/564 (12.6%) 11/564 (2.0%) 104/564 (18.4%) 89/564 (15.8%) 114/564 (20.2%) 16/564 (2.8%)
DERMATOLOGY	-	-	-
Gaudi 2013	Dermatopathology N=405 cases[g]	Concordant with provisional diagnosis Discordant with provisional diagnosis Different reporting styles	128/354 (36.2%) 212/354 (59.9%) 14/354 (4.0%)
van Dijk 2008	Cutaneous melanocytic lesions N=1837	Concordant with provisional diagnosis	545/1217 (44.8%)
Veenhuizen 1997	Skin lesions N=1069	Concordant with provisional diagnosis (based on diagnostic category)[h] Concordant with provisional/differential diagnosis (based on diagnostic category)[h]	554/848 (65.3%) 559/979 (57.1%)
ORAL AND MAXILLOFACIAL	-	-	-
Jones 2010	Oral and maxillofacial pathology N=142 cases	Concordant with provisional diagnosis	89/135 (65.9%)
LUNG	-	-	-

Study ID	Population (N)	Outcome	Results n/N (%)
Hutton Klein 2010	Granulomatous or giant cell reactions in the lung N=100 cases[i]	Concordant with provisional diagnosis – pathologist-initiated cases only Discordant[j] with provisional diagnosis – pathologist-initiated cases only	7/55 (12.7%) 48/55 (87.3%)

Abbreviations: SO, second opinion.

[a] Details of the initial pathology opinion were available in 116 cases (i.e. cases for which the original referring Consultant's referral letter was found).

[b] Of the total cases received for consultation, 1863 had a single tentative diagnosis (i.e. not a differential diagnosis or no initial diagnosis). Of those 1863 cases, 1670 had a 'specific' tentative diagnosis (i.e. precise terminology, including an indication of benignancy or malignancy).

[c] The study included a total of 1463 cases: 564 cases were initially examined by a 'non-expert' pathologist who requested a second opinion to confirm the diagnosis; 899 cases were initially examined by a 'non-expert' pathologist who did not request confirmation of the diagnosis. The study referred to the latter group as the 'systematic review' or 'control' group.

[d] Identical diagnosis of connective tumour but different grade or histological subtype.

[e] Change in benign versus malignant, different histological type or invalidation of the diagnosis of sarcoma.

[f] Breakdown includes all discordant cases, including 263 partially concordant cases and 71 completely discordant cases.

[g] 404 out of 405 cases were relevant expert opinion cases, in which an outside pathologist sought an expert opinion. One case was a mandatory second review case, in which an expert opinion was required prior to definitive medical or surgical treatment.

[h] The paper summarised concordance based on specific diagnosis and also broader diagnostic categories. Results presented above are based on concordance within the broader diagnostic categories which included: (i) invasive melanoma; (ii) suspected melanoma; (iii) differential diagnosis; (iv) benign (common acquired naevus, Spitz naevus, other special types of naevus), dysplastic naevus or melanoma *in situ*; and (v) Other. This outcome was not reported in the paper but was calculated using information in Tables III and IV, pg. 269-70.

[i] The study included a total of 100 cases: 80 requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[j] Refers to a disagreement between the expert and outside pathologists' diagnoses. Discordance refers to outright disagreement, a narrowing of the differential diagnosis to one being strongly favoured by the expert, or the differential diagnosis being expanded by the expert.

Table B.6-4 Diagnostic accuracy: level of concordance and/or discordance between initial and expert pathology opinion – *Scenario 2 studies*

Study ID	Population (N)	Outcome	Results n/N (%)
ALL SURGICAL PATHOLOGY	-	-	-
Ahmed 2004	Surgical pathology; any organ system N=381 cases	Concordant with provisional diagnosis Discordant with provisional diagnosis *Discordant cases by tissue origin[a]:* • Bone and joint • Female genital tract • Male genital tract • Lymph node • Skin • Head and neck • Gastrointestinal	204/336 (60.7%) 120/336 (35.7%) 11/30 (36.7%) 5/27 (18.5%) 5/13 (38.5%) 22/72 (30.6%) 35/65 (53.8%) 12/27 (44.4%) 17/52 (32.7%)
BRAIN AND SPINAL CORD	-	-	-
Bruner 1997	Brain and spinal cord biopsy for suspected neoplastic disease N=500 cases[b]	Concordant with provisional diagnosis Discordant with provisional diagnosis	139/261 (53.3%) 122/261 (46.7%)
PROSTATE	-	-	-
Chan 2005	Prostate needle biopsy N=684	Discordant with provisional diagnosis[c]	181/437 (41.4%)
LUNG	-	-	-
Hutton Klein 2010	Granulomatous or giant cell reactions in the lung N=100 cases[d]	Concordant with provisional diagnosis – clinician-initiated cases only Discordant[e] with provisional diagnosis – clinician-initiated cases only	6/20 (30.0%) 14/20 (70.0%)
LABIAL SALIVARY GLAND	-	-	-
Vivino 2002	LSG biopsy for possible Sjögren's syndrome N=60 cases	Discordant with provisional diagnosis ("diagnostic revision")	32/59[f] (54.2%)

[a] This information was not reported for all tissue types.

[b] The study included a total of 500 cases: 284 "consultation-only" cases were submitted because of some doubt about the original diagnosis on the part of pathologists or other attending physicians (e.g. surgeons, internists, or radiotherapists) at an outside institution; 216 cases were reviewed after the patient was referred to the Texas M. D. Anderson Cancer Center for management.

[c] The study included cases sent at the request of the patient or urologist. This outcome includes the subset of urologist-referred cases only.

[d] The study included a total of 100 cases: 80 requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

[e] Refers to a disagreement between the expert and outside pathologists' diagnoses. Discordance refers to outright disagreement, a narrowing of the differential diagnosis to one being strongly favoured by the expert, or the differential diagnosis being expanded by the expert.

[f] Paper reported 32/60. The denominator has been altered for consistency with other studies – the one case without a provisional diagnosis has been removed.

B.6.2. Clinically relevant change in diagnosis or interpretation

As discussed in Section B.5.1, discordant or discrepant cases can be categorised into major and minor discrepancies. While the rate of minor discrepancies is therefore an important measure of diagnostic accuracy, it has little value in terms of clinically relevant changes in diagnosis. As such, the minor discrepancy results from the included studies are presented in Appendix 4.

As discussed in Section B.5.2, the majority of the included studies used the terminology 'major discrepancy' to refer to clinically relevant changes in diagnosis that would result in a change in patient management. It could therefore be argued that the rate of major discrepancies represents the best available evidence from the current body of literature to determine the value of second, expert opinions.

Like overall discordance (or discrepancy) rates, there was substantial variation in the proportion of major discrepancies across the included studies, as shown in Table B.6-5 and Table B.6-6. Of the *Scenario 1* studies, the highest proportion of major discrepancies was 26.5% from a study of cutaneous melanocytic lesions (van Dijk et al, 2008). Similarly, 23.2% of skin lesions sent for expert review resulted in a change from malignant to benign or vice versa (Veenhuizen et al, 1997) and 24.4% of cases in a sarcoma study resulted in major discrepancies (Arbiser et al, 2001). In contrast, a study of urothelial lesions (Tavora et al, 2009) reported a major discrepancy rate of only 9.2% and one of the studies of all surgical pathology (Hsu et al, 2010) found major discrepancies in only 12.3% of cases, indicating that major discrepancies are uncommon in some tissue types. Hsu et al (2010) provided a breakdown of the number of major discrepancies according to the tissue of origin (see Table B.6-7).

Only one *Scenario 2* study reported the number of major discrepancies detected during expert review. Bruner et al (1997) reported a major discrepancy rate of 12.3% for brain and spinal cord biopsies. The study also assessed the number of patients who had initiated therapy (other than biopsy or surgery) before the second, expert opinion had been conducted. Of the 32 cases with major discrepancies, four (12.5%) had initiated therapy before the diagnosis was changed; 26 (81.3%) had not undergone therapy; and the status of two (6.3%) patients was unknown.

In most cases, the nature of the major discrepancy (e.g. a change from benign to malignant) was also provided. Those results are also shown in Table B.6-5 and Table B.6-6 as a proportion of cases with a provisional diagnosis.

Table B.6-5 Major discrepancies between initial and expert pathology opinions – *Scenario 1 studies*

Study ID	Population (N)	Outcome	Results n/N (%)
ALL SURGICAL PATHOLOGY	-	-	-
Cook 2001	All histopathology; any organ system N=128 cases[a]	Major discrepancy in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Change from benign to malignant • Change from malignant to benign	10/55 (18.2%) 5/55 (9.1%) 5/55 (9.1%)
Hsu 2010	Anatomic pathology; any organ system N=2686 cases[b]	Major discrepancy in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Change from benign to malignant • Change from malignant to benign • Change from one category of malignancy to another	205/1670 (12.3%) 43/1670 (2.6%) 137/1670 (8.2%) 25/1670 (1.5%)
SOFT TISSUE/SARCOMA	-	-	-
Arbiser 2001	Soft tissue lesions N=500 cases	Major discrepancy[c] in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Change from sarcoma to benign mesenchymal lesion • Change from benign mesenchymal lesion to sarcoma • Change from mesenchymal to nonmesenchymal tumour • Grading discrepancy	65/266 (24.4%) 29/266 (10.9%) 15/266 (5.6%) 13/266 (4.9%) 8/266 (3.0%)
Ray-Coquard 2012	Soft tissue or visceral sarcoma N=1463 cases[d]	Complete discordance[e] with initial diagnosis (i.e. major discrepancies) *Nature of major and minor discrepancies[i] (as a proportion of all cases with a provisional diagnosis):* • Subtype alone • Grade alone • Histological type alone • Grade and subtype • Grade and histological type	71/564 (12.6%) 11/564 (2.0%) 104/564 (18.4%) 89/564 (15.8%) 114/564 (20.2%) 16/564 (2.8%)

Study ID	Population (N)	Outcome	Results n/N (%)
DERMATOLOGY	-	-	-
Gaudi 2013	Dermatopathology N=405 cases[f]	Major discrepancy[g] in cases with a provisional diagnosis	24/354[h] (6.8%)
van Dijk 2008	Cutaneous melanocytic lesions N=1837	Major discrepancy[i] in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Over-diagnosis of naevi • Over-diagnosis of melanoma in situ • Under-diagnosis of melanoma • Under-diagnosis of melanoma in situ	322/1217 (26.5%) 170/1217 (14.0%) 8/1217 (0.7%) 132/1217 (10.8%) 12/1217 (1.0%)
Veenhuizen 1997	Skin lesions N=1069	Major discrepancy[j] in cases with a provisional diagnosis[k] *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Over-diagnosis of naevi or melanoma in situ • Under-diagnosis of suspected or invasive melanoma	185/798 (23.2%) 77/798 (9.6%) 108/798 (13.5%)
ORAL AND MAXILLOFACIAL	-	-	-
Jones 2010	Oral and maxillofacial pathology N=142 cases	Major discrepancy[l] in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of all cases with a provisional diagnosis):* • Change from malignant to benign • Change from benign to malignant • No change in diagnostic category (benign or malignant), but the second opinion diagnosis would significantly alter treatment plan	22/135 (16.3%) 9/135 (6.7%) 7/135 (5.2%) 6/135 (4.4%)
UROTHELIAL	-	-	-
Tavora 2009	Urothelial lesions of the renal pelvis and mid-upper ureter N=76 (39 biopsies from the ureter and 37 from the renal pelvis)	Major discrepancy in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Change from urothelial neoplasm to non-neoplastic	7/76 (9.2%) 7/76 (9.2%)[m]

[a] Details of the initial pathology opinion were available in 116 cases (i.e. cases for which the original referring Consultant's referral letter was found).

[b] Of the total cases received for consultation, 1863 had a single tentative diagnosis (i.e. not a differential diagnosis or no initial diagnosis). Of those 1863 cases, 1670 had a 'specific' tentative diagnosis (i.e. precise terminology, including an indication of benignancy or malignancy).

[c] Major discrepancies were defined as those that had a significant impact on therapy, such as distinguishing a reactive process from a sarcoma or significant mis-grading of a sarcoma (i.e. mis-grading by two grades in a three-tiered system).

[d] The study included a total of 1463 cases: 564 cases were initially examined by a 'non-expert' pathologist who requested a second opinion to confirm the diagnosis; 899 cases were initially examined by a 'non-expert' pathologist who did not request confirmation of the diagnosis. The study referred to the latter group as the 'systematic review' or 'control' group.

[e] Change in benign versus malignant, different histological type or invalidation of the diagnosis of sarcoma.

[f] 404 out of 405 cases were relevant expert opinion cases, in which an outside pathologist sought an expert opinion. One case was a mandatory second review case, in which an expert opinion was required prior to definitive medical or surgical treatment.

[g] Gaudi et al (2013) used a broader definition of major discrepancy than most of the other included studies. As such, the number of cases in Gaudi et al (2013) that underwent a benign-malignant or malignant-benign change has been calculated using information in Table I, pg. 122, rather than reporting major discrepancies as per study definition, in order to maximise consistency between studies.

[h] The paper reported this outcome using a denominator of 405. For consistency with other studies, the denominator has been altered to remove the cases in which no diagnosis was provided by the initial pathologist.

[i] Cases reported in the study as having been over- or under-diagnosed were those that underwent a shift from malignant to benign or benign to malignant, respectively, as a result of expert opinion. The authors stated that over- or under-diagnosis would have inevitable consequences for therapy, follow-up and prognosis. For the purposes of this table they are referred to collectively as 'Major discrepancies'.

[j] Includes cases categorised as having been over- or under-diagnosed. The study reported that over-diagnosis and under-diagnosis were defined and calculated from a perspective of clinical relevance, including therapeutic consequences. Over-diagnosis refers to situations where the expert diagnosis was 'common acquired naevus', 'Spitz naevus', 'special types of naevus', 'dysplastic naevus', or 'melanoma *in situ*', while the referring pathologist had diagnosed 'suspected melanoma' or 'invasive melanoma'. Under-diagnosis refers to situations where the expert diagnosis was 'suspected melanoma' or 'invasive melanoma', while the referring pathologist had diagnosed 'common acquired naevus', 'Spitz naevus', 'special types of naevus', 'dysplastic naevus', or 'melanoma *in situ*'. Lesions classified as 'other' were not considered in this outcome.

[k] Excluding cases with no initial diagnosis, a differential diagnosis or a diagnosis categorised as 'other', none of which had the potential to be a major discrepancy.

[l] Changes in diagnosis that would significantly alter the evaluation plan, treatment and/or prognosis of the patient.

[m] Five of the seven cases originated from the ureter; two cases originated from the pelvis.

Table B.6-6 Major discrepancies between initial and expert pathology opinions – *Scenario 2 studies*

Study ID	Population (N)	Outcome	Results n/N (%)
BRAIN AND SPINAL CORD	-	-	-
Bruner 1997	Brain and spinal cord biopsy for suspected neoplastic disease N=500 cases[a]	Major discrepancy[b] in cases with a provisional diagnosis *Nature of major discrepancy (as a proportion of cases with a provisional diagnosis):* • Tumour diagnosis changed to nontumour • Nontumour diagnosis changed to tumour • Malignant tumour changed to benign • Benign tumour changed to malignant • Diagnosis changed within benign or malignant	32/261 (12.3%) 7/261 (2.7%) 4/261 (1.5%) 4/261 (1.5%) 4/261 (1.5%) 13/261 (5.0%)

[a] The study included a total of 500 cases: 284 "consultation-only" cases were submitted because of some doubt about the original diagnosis on the part of pathologists or other attending physicians (e.g. surgeons, internists, or radiotherapists) at an outside institution; 216 cases were reviewed after the patient was referred to the Texas M. D. Anderson Cancer Center for management.

[b] Discrepancies that would have caused an immediate alteration in therapy, excessive increased cost in terms of patient quality of life or ineffective utilisation of resources, or potential for medical malpractice liability for the treating physician.

Interestingly, the *Scenario 1* study by Hsu et al (2010) also provided a breakdown of major discrepancies (as well as discordance and the use of additional special stains) according to tissue of origin (see Table B.6-7).

Relatively high major discrepancies rates were observed in specimens originating from endocrine glands (26.4%), lymph nodes, bone marrow and spleen (19.8%), nervous system (19.0%), and skin (15.4%). Conversely, major discrepancies rarely occurred between initial and expert pathologists' diagnoses in specimens from the female genital tract (3.2%) and breast tissue (3.6%), implying that those tissues may be less diagnostically challenging. It is difficult to comment on the relative diagnostic difficulty of nephrology and cardiovascular tissues due to the low number of cases included in the study (see Table B.6-7).

Table B.6-7 Summary of findings from the study by Hsu et al (2010)

Tissue origin	No.(%) of surgical pathology cases sent for expert consultation	No. (%) with specific tentative diagnosis[a]	No. (%) with discordance[b]	No. (%) with major discrepancy[c]	No. (%) with additional special stains performed
Skin	489 (18.2)	286 (58.5)	215 (75.2)	44 (15.4)	94 (19.2)
Lymph node, bone marrow, spleen	409 (15.2)	248 (60.6)	164 (66.1)	49 (19.8)	261 (63.8)
Bone and soft tissue	401 (14.9)	218 (54.4)	153 (70.2)	21 (9.6)	139 (34.7)
Female genital tract	259 (9.6)	188 (72.6)	120 (63.8)	6 (3.2)	61 (23.6)
Breast	242 (9.0)	165 (68.2)	81 (49.1)	6 (3.6)	83 (34.3)
Gastrointestinal tract and liver	212 (7.9)	139 (65.6)	83 (59.7)	11 (7.9)	127 (59.9)
Head and neck	189 (7.0)	106 (56.1)	56 (52.8)	16 (15.1)	87 (46.0)
Nervous system	155 (5.8)	100 (64.5)	65 (65.0)	19 (19.0)	69 (44.5)
Pulmonary system and mediastinum	107 (4.0)	62 (57.9)	41 (66.1)	7 (11.3)	51 (47.7)
Urinary tract and male genital tract	106 (3.9)	78 (73.6)	39 (50.0)	7 (9.0)	37 (34.9)
Endocrine glands	105 (3.9)	72 (68.6)	50 (69.4)	19 (26.4)	24 (22.9)
Nephropathology	7 (0.3)	5 (71.4)	5 (100.0)	0 (0)	4 (57.1)
Cardiovascular system	5 (0.2)	3 (60.0)	2 (66.7)	0 (0)	2 (40.0)
TOTAL	2686 (100)	1670 (69.7)	1074 (64.3)	205 (12.3)	1039 (38.7)

Source: Hsu et al (2010), Table II (p432), Table IV (p433), Table V (p433)

[a] Excludes cases from the referring (initial) pathologist with no diagnosis, a differential diagnosis, or a diagnosis using a general term (with or without indicating benignancy or malignancy).

[b] Discordance was defined as difference of specific tentative diagnosis and consultation (expert) diagnosis.

[c] Major discrepancy was defined as the diagnosis being changed from benign to malignant or vice versa, and from one category of malignancy to another (e.g. carcinoma to lymphoma).

B.6.3. Safety

According to the PPICO criteria (Section A.8) the main safety outcomes of interest in the Assessment Report are: (i) harms due to delay in diagnosis; (ii) incorrect diagnosis/interpretation; (iii) incorrect treatment; and (iv) incorrect revisions of diagnosis/interpretation. While several of the included studies provided information regarding turnaround time, none of the studies attempted to quantify harms due to a delay in diagnosis.

In order to assess the other safety outcomes, adequate patient follow-up (e.g. repeat biopsy) is required. As mentioned in Section B.3.3, only two of the included studies provided any patient follow-up information upon which an assessment of the safety (i.e. accuracy) of the expert pathologist's diagnosis could be made (Hutton Klein et al, 2010; Tavora et al, 2009). Hutton Klein et al (2010) only sought follow-up information in the 73 cases in which the second, expert opinion was not confident (i.e. a probable or broad differential diagnosis was provided). Table B.6-8 shows that follow-up information was only obtained in 36 of those cases and the results were difficult to interpret.

With the exception of the studies by Hutton Klein et al (2010) and Tavora et al (2009), there was an implicit assumption that the second, expert opinion was correct, without sufficient follow-up to confirm whether this was indeed the case. Due to the limitations in Hutton Klein et al (2010), the best available evidence regarding the incorrect diagnosis/interpretation or incorrect revisions of diagnosis/interpretation was provided in Tavora et al (2009). The study reported major discrepancies between the initial and expert diagnoses in seven of out 76 cases. In all seven cases, the diagnosis at follow-up supported the diagnosis of the expert pathologist. However the small number of cases for which follow-up was reported limits the value of the evidence.

Table B.6-8 Incorrect diagnosis or interpretation according to follow-up information

Study ID	Population (N)	Outcome	Results n/N (%)
LUNG	-	-	-
Hutton Klein 2010	Granulomatous or giant cell reactions in the lung N=100 cases[a]	Clinical follow-up confirmed or supported the probable specific diagnosis Clinical follow-up suggested that cultures were negative Further clinical information did not resolve the pathologic differential diagnosis	14/36 (38.9%) 15/36 (41.7%) 7/36 (19.4%)
UROTHELIAL LESIONS	-	-	-
Tavora 2009	Urothelial lesions of the renal pelvis and mid-upper ureter N=76	Proportion of cases in which clinical follow-up was concordant with initial pathologist's diagnosis Proportion of cases in which clinical follow-up was concordant with expert pathologist's diagnosis	0/7 (0%) 7/7 (100%)

[a] The study included a total of 100 cases: 80 requests for expert opinion were initiated by the pathologist; 20 expert opinion requests were initiated by the clinician.

B.7. Interpretation of the clinical evidence

A relatively small body of evidence exists that is precisely related to the type of second, expert opinion proposed for MBS funding in the Assessment Report. Many of the studies reported a single institution's experience of second, expert opinion, and as such, there is considerable variation across the studies, depending on the case mix of patients encountered by the initial pathologist, the complexity of the tissue being studied, the availability of intra-institutional consultation prior to referral, and the experience and qualifications of the expert pathologist who reviewed the case. The availability of funding for expert opinions may also alter referral patterns.

Furthermore, the precise nature of the second, expert opinions examined in the studies was not necessarily reflective of the conditions under which the service would be funded in Australia. For example, in some of the included studies, a third opinion (i.e. second expert opinion) was sought when the first and second diagnoses were discrepant. It is possible that this would occur in practice in Australia; however, it is also possible that the expert pathologist's diagnosis would be assumed to be correct and the patient would be managed accordingly. It is also not the intention of the proposed service to allow for multiple MBS-funded expert opinions on the same patient sample.

No studies were identified that examined the value of expert opinion using the evidentiary standard. Most of the included studies simply compared the diagnosis of the initial reporting pathologist with that of one expert pathologist. In several studies the expert pathologist could refer the case to a panel of experts for an expert consensus; however, none of these studies compared the initial opinion to a true consensus pathology opinion, as per the evidentiary standard.

Despite the shortcomings, the studies consistently demonstrated that there is value in seeking a second, expert opinion in cases where the pathologist is unable to confidently reach a diagnosis or where the clinician desires diagnostic input from an expert to verify a diagnosis or to provide further clinical information. The best available evidence is presented in Section B.6.2, which demonstrated that major discrepancies between an initial and expert pathologist are not uncommon and could lead to a change in patient management, with the expectation that this would positively impact on patient care.

However, it is important to acknowledge that there are major limitations associated with using major discrepancies as a surrogate for change in management. In most cases of diagnostic uncertainty, treatment is withheld until after an expert diagnosis is received. Thus, a major discrepancy between the initial and expert pathologist does not necessarily translate into a change in management, but rather the potential for more accurate classification of disease. This, in turn, could lead to more appropriate planning and selection of therapy, which should translate into better health outcomes and more effective utilisation of resources. However, due to lack of reliable follow-up data, this claim was not substantiated on the basis of the existing evidence. In the majority of studies, there was an implicit assumption that the expert opinion is correct; however, this may not always be the case. Furthermore, in some difficult cases the expert pathologist may not even be able to provide a definitive diagnosis.

Nonetheless, the high proportion of major discrepancies across some tissue types is an important outcome, as it provides a compelling clinical argument for second, expert opinions when there is diagnostic uncertainty or a rare or complex case that warrants verification.

Section C. Translating the clinical evaluation to the economic evaluation

C.1. Identification of issues to be addressed

Over the course of developing the economic evaluation, it became clear that the model required a number of transition probabilities to determine patients' transition from their initial pathology opinion to the definitive diagnosis.

For example, a proportion of patients would require a second, expert opinion, some of which would be 'complex' and others 'non-complex'. Similarly, a proportion of these patients would require additional (ancillary) testing on their pathology samples before a definitive diagnosis could be reached. Data were required to inform these proportions.

This section presents a summary of how these data were generated and applied to the economic evaluation.

C.2. Focussed analytical plan

An Expert Opinion Survey was developed with the aim of obtaining information from a number of large public and private pathology laboratories about the number and nature of pathology cases that are currently referred for second, expert opinion in Australia (presented in Appendix 5). The intention of the included questions was to obtain estimates regarding general referral patterns across Australia. Estimates were not sought about intra-institutional referrals, in which a pathologist seeks advice from a co-located colleague. The referrals of interest related to formal, written second opinions by an expert pathologist who is external to the initial pathologist, but may be co-located with a referring clinician (e.g. at a tertiary treatment centre).

Similarly, the survey sought to obtain estimates of the number and nature of pathology cases which would be referred for second, expert opinion if the proposed changes to MBS funding are implemented.

These data, applied to the economic evaluation presented in Section D, were calculated as means from the responses provided. Note that blank or empty responses were not included. Where respondents provided a range, the midpoint of the range was used in the calculation of the average. Similarly, where respondents provided an upper limit (e.g. "<5%"), this upper limit was applied as the point estimate used to calculate the mean. Such assumptions have a negligible impact on the results of the model. Finally note that, in order to correspond with the data required by the structure of the economic model, some responses were modified. For example, rather than follow the survey's lead of estimating the proportion of *Scenario 1* cases that were thought to fall within the confines of a 'complex' second, expert opinion, data were modified to find the proportion of cases that were both complex and under the definition of *Scenario 1* (i.e. the product of two raw results from the survey).

C.3. Population and circumstances of use reflected in the economic evaluation

The population considered in the economic evaluation comprises patients undergoing a morphology-based pathology test, as per the PPICO criteria outlined in Section A. The population in the model is representative of the population for whom MBS listing is sought. As discussed previously, where data are available, a number of subgroups are also considered in sensitivity analyses.

C.4. Results of the pre-modelling studies

The results of the pre-modelling study to inform these transition probabilities are presented in Table C.4-1.

Table C.4-1 Data from the Expert Opinion Survey used to inform the economic evaluation

Estimation of the percentage of cases	Average under the proposed funding arrangements	Average under the current funding arrangements
Tissue pathology	-	-
Proportion of cases referred for second, expert opinion	1.41%	0.570%
Proportion of cases initiated by Pathologist (*Scenario 1*)	74.38%	64.38%
Proportion of cases initiated by Clinician (*Scenario 2*)	25.63%	35.63%
Proportion of cases which are 'complex' and *Scenario 1*	39.98%	38.63%
Proportion of cases which are 'non-complex' and *Scenario 1*	34.40%	25.75%
Proportion of cases which are 'complex' and *Scenario 2*	7.69%	11.13%
Proportion of cases which are 'non-complex' and *Scenario 2*	17.94%	24.49%
Proportion of 'non-complex' cases requiring ancillary tests	23.75%	25.00%
Proportion of 'non-complex' cases not requiring ancillary tests	76.25%	75.00%
Proportion of 'complex' cases requiring ancillary tests	62.50%	62.63%
Proportion of 'complex' cases not requiring ancillary tests	37.50%	37.38%
Cytopathology	-	-
Proportion of cases referred for second, expert opinion	1.17%	0.33%
Proportion of cases initiated by Pathologist (*Scenario 1*)	59.50%	76.43%
Proportion of cases initiated by Clinician (*Scenario 2*)	40.50%	23.57%
Proportion of cases which are 'complex' and *Scenario 1*	11.05%	14.74%
Proportion of cases which are 'non-complex' and *Scenario 1*	48.45%	61.69%
Proportion of cases which are 'complex' and *Scenario 2*	7.43%	4.32%
Proportion of cases which are 'non-complex' and *Scenario 2*	33.08%	19.25%
Proportion of 'non-complex' cases requiring ancillary tests	11.57%	10.14%
Proportion of 'non-complex' cases not requiring ancillary tests	88.43%	89.86%
Proportion of 'complex' cases requiring ancillary tests	32.14%	30.43%
Proportion of 'complex' cases not requiring ancillary tests	67.86%	69.57%

Source: Expert Opinion Survey (Appendix 5)

C.5. Relationship of each pre-modelling study to the economic evaluation

The data presented in Table C.4-1 were applied to the economic evaluation, as described in Section D. The tissue pathology data were applied to the base case analysis, while the cytopathology data were used to generate a sensitivity analysis (see Section D.5). Additionally, a number of the tissue pathology data were modified in a series of sensitivity analyses to determine the impact they may have on the results generated.

Section D. Economic evaluation for the main indication

D.1. Overview of the economic evaluation

The Assessment Report presents an economic evaluation in the form of a Decision Analytic model. This model, discussed in greater detail below, is based upon the Decision Analytic structure presented in the revised Final Protocol. It enables the cost-effectiveness of MBS funding for a second, expert opinion on pathology items to be formally assessed.

On the health outcomes side, the economic evaluation is based on data sourced from the studies presented in Section B. Though the selected studies are mostly retrospective reviews, they nonetheless represent the best available data to capture the health outcome of interest.

There are a number of differences between the economic evaluation presented here and the Decision Analytic suggested in the revised Final Protocol. The general difference being that the structure presented in this Assessment Report is simplified due to limitations in the evidence base.

The most notable simplification of the structure is that there is no explicit consideration of either improved or inferior treatment outcomes. Instead, on the basis of available data, the economic evaluation estimates the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. As such, a distinction between improved and inferior outcomes is not required. The focus is, instead, on the attainment of a definitive diagnosis.

As a consequence of this, the economic evaluation does not extrapolate to final health outcomes, as was suggested by the revised Final Protocol. This is discussed in greater detail below.

Other notable differences between that the economic evaluation presented in this Assessment Report and that suggested by the revised Final Protocol include:

- *Explicit consideration of individual pathology types*. That is, the incremental cost-effectiveness of tissue pathology and cytopathology are considered independently, with tissue pathology forming the base case analysis.
- *Explicit consideration of the overall cost-effectiveness of the requested listings and that of subgroups for which data are available*. This is consistent with the recommendations of the revised Final Protocol.

The absence of any extrapolation to final health outcomes limits both the need and the value of a stepped economic evaluation. On this basis, a stepped evaluation was not undertaken.

D.2. Structure and rationale of the economic evaluation

The structure and rationale of the economic evaluation are presented in detail below. This includes discussion of the literature review used to inform the economic evaluation, as well as a comprehensive discussion of the differences between the present structure and that proposed by the revised Final Protocol.

D.2.1. Economic evaluation literature review

The literature search for clinical evidence (see Section B.1) was intentionally broad so that economic studies relating to second, expert opinion would also be captured within the citations identified. The search of EMBASE and Medline identified 4,181 citations in total and the search of the Cochrane Library identified 141 citations. A search was then conducted within the EndNote libraries into which the citations were downloaded, using the broad economic terms 'cost', 'price', 'economic', 'utility' and 'utilities' (within any field). The search identified 641 potentially relevant citations from EMBASE and Medline and 83 potentially relevant citations from the Cochrane Library. The 724 titles and abstracts were screened and 25 publications were obtained in full text.

Of the full text publications retrieved, there were seven studies that provided information relevant to Section D, and another two studies that were identified through the reference lists of included studies. However, all nine studies reported on 'routine' review of pathology cases, and thus are not directly relevant to the assessment. Furthermore, none of the studies were conducted in Australia – eight were from the United States and one was from Hong Kong. Appendix 6 presents a brief summary of the study characteristics and economic findings.

D.2.2. Structure of the economic evaluation

The economic evaluation is based on the structure proposed by the revised Final Protocol, although a number of important differences are present. Where these differences exist, they are described in detail below.

The model commences once a patient has an initial pathology opinion. Cases in which no diagnosis is offered by the initial pathologist are excluded from the model. As no data are available to inform how such patients may be managed, or how clinical management may change in the event of a second, expert opinion, their exclusion is reasonable. Further, as there is no reason to expect that the proportion of such cases would vary between the arms of the model, there is no reason to expect inclusion of such cases would impact on the cost-effectiveness results.

Following this, probabilities are applied to the model to reflect whether cases requiring a second, expert opinion are either at the behest of a recommendation from the initial pathologist (*Scenario 1*) or due to further need for clarification from the clinician managing the patient (*Scenario 2*). By applying probabilities (derived in Section C), the model considers *Scenario 1* and *Scenario 2* simultaneously. The model allows for different rates of second, expert opinion to be considered in the arm representing the current funding arrangements and in the arm representing the proposed funding arrangements. Since it is expected that the rate of second, expert opinion sought would increase with MBS funding (Expert Opinion Survey, Appendix 5), this distinction is crucial. The model does not consider the funding mechanism of second, expert opinions sought under the current arrangement. That is, the model does not consider whether second opinions are sought ex gratis or via alternative funding methods.

In cases in which second, expert opinion is sought, the evaluation distinguishes between 'complex' (>30 minutes) and 'non-complex' (≤30 minutes) expert opinion on a patient sample. This is consistent with the requested listing presented in Section A.3. The distinction is important in the arm representing the requested listing, as it enables costs to be correctly applied.

In the arm representing the current funding arrangement, the base case does not explicitly consider any costs associated with second, expert opinion.

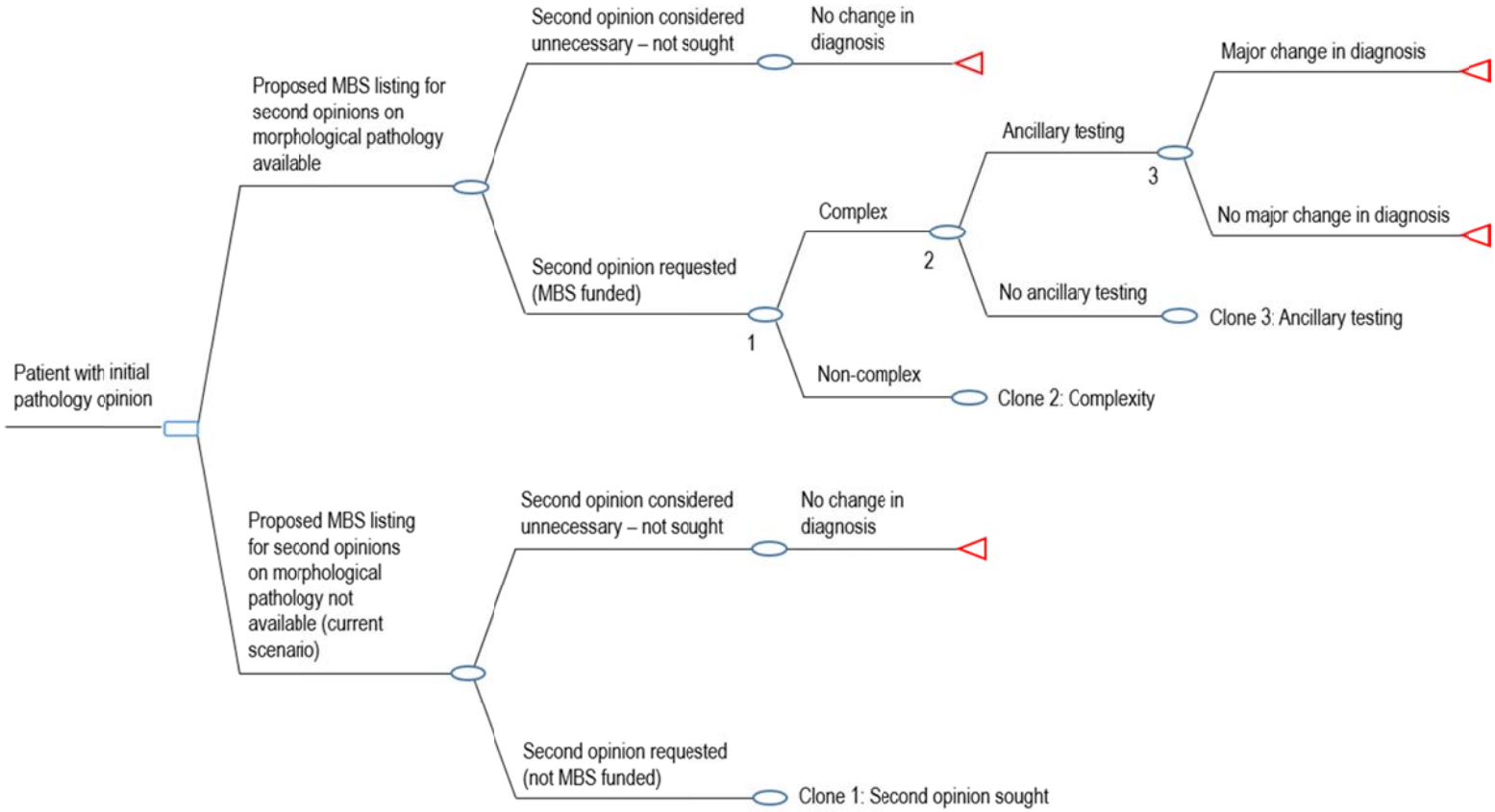
Subsequently, the evaluation considers whether healthcare resources will be required for ancillary testing to settle upon a diagnosis.

The evaluation is truncated at the point of diagnosis. This stopping point is sufficient for the incremental cost per significant (clinically relevant) change in diagnosis or interpretation to be assessed. While it may be argued that comprehensive modelling beyond this point would be warranted, there are several reasons why this is unlikely to be informative to decision-makers in the current case. The main reasons include:

- *The general nature of the requested listings render it very difficult to accurately assess the cost-effectiveness beyond the point of definitive diagnosis.* For example, it is not feasible to comprehensively consider the differential impacts of significant changes in diagnosis on all illnesses/conditions to which the listing would apply; the range of illnesses means that the range of different treatments, natural histories and subsequent mortality/morbidity implications is enormous. As such, a pragmatic approach was taken. To do otherwise would introduce unreasonable uncertainty to the model. This uncertainty would render the model misleading and/or impossible to interpret.
- *The paucity of data imposes very real limitations on the ability to extrapolate beyond diagnosis.* Long term data describing the transition from final diagnosis to mortality (and intermediate morbidity) do not exist for the research questions at hand. To illustrate one example, the absence of staging data at diagnosis means that it is not possible extrapolate/model to final outcomes without introducing unreasonable amounts of uncertainty to the analysis.

These, among other considerations, mean that the economic evaluation presented here is admittedly simple. Rather than attempting complex downstream modelling of a wide range of illnesses, the evaluation focusses on providing decision-makers with the most informative assessment of cost-effectiveness. Specifically, the evaluation provides an assessment of how much it will cost, on average, to provide information to trigger a change in diagnosis where required if second, expert opinions are funded by the MBS. Figure D-1 illustrates the structure of the economic evaluation.

Figure D-1 Decision tree summarising structure of the economic evaluation



Abbreviations: MBS, Medicare Benefits Schedule

The economic evaluation was conducted using Microsoft® Excel X for Mac®. An electronic workbook *<1332_Section D workbook.FINALxls>* accompanies this Assessment Report.

The time horizon is not explicitly considered in the economic evaluation. The application of a Decision Analytic model assumes an instant process by default. As the process of obtaining a second opinion is likely to unfold over a short time duration, the assumption is unlikely to pose any difficulties or render the analysis inappropriate. On this basis, discounting was not applied to the model.

Finally, the economic evaluation considers tissue pathology and cytopathology independently, appropriately applying data relevant to each analysis. As discussed below, cytopathology is considered in a sensitivity analysis while tissue pathology forms the base case analysis.

D.3. Variables in the economic evaluation

The variables applied to the economic evaluation comprise healthcare resource items, intermediate health outcomes and transition probabilities. Each of these are described in turn below.

D.3.1. Healthcare resource items

The short-term time horizon considered in the economic evaluation means that limited healthcare resource items were applied to the model. These comprise the requested MBS fee for second, expert opinion ('complex' defined as >30 minute; 'non-complex' defined as ≤30 minutes) and the ancillary tests required – in some circumstances – to enable a definitive diagnosis to be made. Downstream treatment costs (including those related to surgery, for example) are not considered, as these are unrelated to the total cost of attaining a definitive diagnosis.

The healthcare resource items applied to the model are presented in Table D.3-1 and described in turn below. For reasons detailed below, the base case applied the unit cost for tissue pathology ancillary tests, while the cytopathology unit cost was used in a sensitivity analysis.

Table D.3-1 Unit costs applied to the economic evaluation for healthcare resource items

Resource item	Unit cost applied to the model	Reference
Second, expert opinion under current funding arrangements	$0.00	Assumption
'Complex' expert opinion under proposed funding arrangements	$370.00	Requested fee (see Section A.3)
'Non-complex' expert opinion under proposed funding arrangements	$180.00	Requested fee (see Section A.3)
Ancillary tests, tissue pathology	$61.76	Calculated
Ancillary tests, cytopathology	$48.13	Calculated

As described previously in Section A, fees of $180 and $370 were proposed by the Applicant for non-complex (≤30 minutes) and complex (>30 minutes) second opinions, respectively. The proposed fees were based on the existing fees for initial pathology opinions. The 'non-complex' fee of $180 is approximately equal to the initial fee for

examination of a complexity level 4 biopsy with at least 12 separately identified specimens. The Applicant suggested that the lower fee should be used for any second opinion involving up to 30 minutes of work and also indicated that it would be appropriate to use the non-complex item number for second opinions on bone marrow specimens. The 'complex' fee of $370 is approximately equal to the average of the initial fees for examination of complexity level 5 and 7 biopsy materials and would be claimed when the expert review required more than 30 minutes of pathologists' time.

The provision of a second, expert opinion would include the examination of processed biopsy material and, if necessary, additional specimen dissection, processing of additional tissue, plus staining and light microscopy, and the production of a full, second written report. As discussed above, in addition to claiming reimbursement for the second opinion, expert pathologists would have the ability to recharge for ancillary items (such as IHC staining, molecular testing) in conjunction with one of the proposed new items. These may be required to provide a definitive diagnosis.

The 'non-core' items listed in Table D.3-2 include ancillary tests from Groups P5 and P6 that may be undertaken by a pathologist, such as IHC, electron microscopy, ICC and enzyme histochemistry. These data were then used, by calculating averages, to estimate the ancillary unit costs applied to the model (as per Table D.3-1). The applied costs were differentiated by tissue pathology and cytopathology.

Since Rule 13 of the Pathology Services Table maintains that only the most costly of these services can be charged in instances of multiple items being delivered, there is no risk that this simple averaging will underestimate the cost of ancillary services due to the existence of cases where multiple ancillary tests are required. Nonetheless, the sensitivity analyses in Section D.5 consider the impact of varying the estimated cost per patient of these services.

Table D.3-2 All 'non-core' ancillary MBS items in Groups P5 and P6 processed Jul 2012 to Jun 2013

Item Number	Service Fee	Number of Services	Total Value of Benefits
Group P5 – Tissue pathology	-	-	-
72844	$30.75	285	$7,134
72846	$59.60	86,378	$4,240,011
72847	$89.40	41,575	$3,034,995
72848	$74.50	6,465	$395,978
72849	$104.30	14,393	$1,202,532
72850	$119.20	6,961	$661,737
72851	$184.35	976	$146,160
72852	$245.80	78	$15,219
Total – All ancillary items	-	157,111	$9,703,766
Group P6 – Cytology	-	-	-
73059	$43.00	1,629	$59,021
73060	$57.35	2,006	$94,584
73061	$51.20	336	$14,396
73064	$71.70	1,092	$64,137
73065	$86.00	479	$34,570
Total – All ancillary items	-	5,542	$266,709

Abbreviations: MBS, Medicare Benefits Schedule
Data Source: Medicare Australia Statistics website.
Note: Group P5 ancillary items (e.g. item 72846 for immunohistochemical stains) are also regularly claimed in conjunction with the core bone marrow items (65084-65087) in Group P1.

D.3.2. Health outcomes

The economic evaluation, for reasons provided above, relies on intermediate, rather than final, health outcomes. Specifically, the model calculates the incremental cost per significant (clinically relevant) change in diagnosis or interpretation.

As is described in detail below, this was derived from the rate of major discrepancies from the original (provisional) diagnosis generated from the initial pathology sample. Such cases are representative of those which could potentially results in a change in clinical management from the initial pathology opinion. Moreover, these cases are often those in which diagnosis is modified from benign to malignant or vice versa and can, therefore, be thought of as 'significant'.

D.3.3. Transition probabilities

The transition probabilities applied to the economic evaluation comprise those governing the proportion of patients requiring expert opinion, the complexity level of expert opinions, the proportion of expert opinions with a need for ancillary tests, and the proportion of patients who have their diagnosis confirmed or changed. The latter are calculated from the major discrepancy rates presented in the included studies from Section B.6.2 (as described below), while the others are derived from the Expert Opinion Survey undertaken in preparation for this Assessment Report (see Section C and Appendix 5).

As described in Section D.3.2 above, the economic model calculates the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. To do this, data relating to major discrepancies in cases with a provisional diagnosis were applied to the economic model. Note, it is not clear that definitive diagnoses following second, expert opinion lead to treatment changes in cases of non-provisional diagnoses (e.g. no diagnosis). Moreover, there are no data available which could be used to shed light on this consideration. Consequently, the economic evaluation must give focus to major discrepancies in provisional cases alone if it is to be used to calculate the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. The impact of this is tested in the sensitivity analyses presented in Section D.5.

The health outcomes data used in the economic evaluation are based on data presented in Section B.6.2 of this Assessment Report. The data applied to the base case analysis are presented in Table D.3-3 for transparency.

Table D.3-3 Major discrepancies with provisional diagnosis applied to the base case economic evaluation

Study ID	Population (N)	Outcome	Results n/N (%)
Cook 2001	All histopathology; any organ system N=128 cases	Major discrepancy in cases with provisional diagnosis	10/55 (18.2%)
Hsu 2010	Anatomic pathology; any organ system N=2,686 cases	Major discrepancy in cases with a 'specific' provisional diagnosis	205/1670 (12.3%)
Average	-	-	215/1725 (12.5%)

Source: Table B.6-5 of the Assessment Report

The base case data relate to studies reporting major discrepancies in surgical pathology. Further, they relate to second, expert opinion sought by pathologists rather than

clinicians (i.e. *Scenario 1*). Nonetheless, due to the limited data available, it was assumed for the purposes of this evaluation that there is no difference in the major discrepancy rates between *Scenario 1* and *Scenario 2*. The impact of this assumption is tested in the sensitivity analyses presented in Section D.5.

As there are no analogous data relating to cytopathology, the incremental cost-effectiveness in cytopathology cases cannot be reliably estimated; the base case considers tissue pathology only. The uncertain cost-effectiveness estimate in cytopathology cases is investigated in the sensitivity analyses.

As described in Section C, the aim of the Expert Opinion Survey was to obtain information about the number and nature of pathology cases referred for second, expert opinion in Australia. Table D.3-4 repeats the data summarised in Section C for transparency, as applied to the base case analysis. These were derived from the tissue pathology responses of the survey.

Table D.3-4 Data from the Expert Opinion Survey used to inform the base case economic evaluation

Types of cases	Average under the proposed funding arrangements	Average under the current funding arrangements
Proportion of cases referred for second, expert opinion	0.0141	0.0057
Proportion of cases initiated by Pathologist (*Scenario 1*)	0.7438	0.6438
Proportion of cases initiated by Clinician (*Scenario 2*)	0.2563	0.3563
Proportion of cases which are *Scenario 1* and 'complex'	0.3998	0.3863
Proportion of cases which are *Scenario 1* and 'non-complex'	0.3440	0.2575
Proportion of cases which are *Scenario 2* and 'complex'	0.0769	0.1113
Proportion of cases which are *Scenario 2* and 'non-complex'	0.1794	0.2449
Proportion of 'non-complex' cases requiring ancillary tests	0.2375	0.2500
Proportion of 'non-complex' cases not requiring ancillary tests	0.7625	0.7500
Proportion of 'complex' cases requiring ancillary tests	0.6250	0.6263
Proportion of 'complex' cases not requiring ancillary tests	0.3750	0.3738

Source: Table C.4-1, Appendix 5 of the Assessment Report

By applying these data to the economic evaluation, the model allows for the estimation of the incremental cost-effectiveness of *Scenario 1* and *Scenario 2* simultaneously, accounting for the proportionate split between these (as per the survey responses).

D.4. Results of the economic evaluation

As described previously, the economic evaluation considers *Scenario 1* and *Scenario 2* simultaneously using the data obtained via the survey. Alternatively, the cost-effectiveness of tissue pathology and cytopathology are considered separately, with data limitations being such that the base case considers tissue pathology only. In doing so, the economic evaluation presents a single base case analysis, supplemented by a series of sensitivity analyses.

While a series of independent base case analyses of multiple populations (e.g. different pathology types) may be preferred *a priori*, uncertainty due to data limitations means that there would be very real risks of misrepresenting the cost-effectiveness of second, expert opinion. So, while it may be reasonable to assume discrepancy rates are similar in *Scenario 1* and *Scenario 2* (when considering supplementary sensitivity analyses), it is not

reasonable to assume the same of tissue pathology and cytopathology. As such, the latter is considered in Section D.5.

Similarly, while further differentiation of the base case could be informative on the basis of disease type, comprehensive data such as these were not available at the time of the analysis. Again, where possible, this is considered in sensitivity analyses.

The results of the base case economic evaluation are presented below. To ensure transparency, these are provided in a disaggregated manner presenting costs and outcomes in turn before presenting the incremental cost per significant (clinically relevant) change in diagnosis or interpretation.

D.4.1. Costs

Table D.4-1 presents the average cost per patient, disaggregated by healthcare resource item in each arm of the model. Table D.4-2 presents the average cost per patient, disaggregated by health state of the economic evaluation.

As can be seen from each of these tables, the cost of second, expert opinion is the largest cost driver. Ancillary costs, due to their relative use, comprise only a small portion of the total incremental cost. Further, with the low relative use of second, expert opinion – even with MBS funding – the average cost of second, expert opinion per patient is low compared with the unit cost.

Table D.4-1 Healthcare resource items and summary of incremental cost, average cost per patient

Type of resource item	Proposed funding arrangements	Current funding arrangements	Incremental cost
Intervention	-	-	-
Second, expert opinion (current funding arrangements)	$0.00	$0.00	$0.00
Second, expert opinion (proposed funding arrangements), 'complex' (>30 minutes)	$2.49	$0.00	$2.49
Second, expert opinion (proposed funding arrangements), 'non-complex' (≤30 minutes)	$1.33	$0.00	$1.33
Other relevant services	-	-	-
Ancillary testing	$0.37	$0.15	$0.21
Total	*$4.19*	*$0.15*	*$4.04*

Note: Figures may not sum due to rounding

Table D.4-2 Health states and summary of cost impacts

Health state in model	Proposed funding arrangements	Current funding arrangements	Incremental cost
No second, expert opinion sought	$0.00	$0.00	$0.00
Complex second, expert opinion sought and ancillary tests required, diagnosis confirmed	$1.59	$0.10	$1.49
Complex second, expert opinion sought and ancillary tests required, diagnosis changed	$0.23	$0.01	$0.21
Complex second, expert opinion sought and ancillary tests not required, diagnosis confirmed	$0.82	$0.00	$0.82
Complex second, expert opinion sought and ancillary tests not required, diagnosis changed	$0.12	$0.00	$0.12
Non-complex second, expert opinion sought and ancillary tests required, diagnosis confirmed	$0.37	$0.04	$0.33
Non-complex second, expert opinion sought and ancillary tests required, diagnosis changed	$0.05	$0.01	$0.05
Non-complex second, expert opinion sought and ancillary tests not required, diagnosis confirmed	$0.89	$0.00	$0.89
Non-complex second, expert opinion sought and ancillary tests not required, diagnosis changed	$0.13	$0.00	$0.13
Total	$4.19	$0.15	$4.04

Note: Figures may not sum due to rounding

D.4.2. Health outcomes

As described previously, the economic evaluation adopts the rate of significant change in diagnosis as the health outcome of interest. Table D.4-3 presents the number of significant changes in diagnosis per patient, disaggregated by health state of the economic evaluation.

Table D.4-3 Health states and significant changes in diagnosis, per patient

Health state in model	Proposed funding arrangements	Current funding arrangements	Incremental cost
No second, expert opinion sought	0.0000	0.0000	0.0000
Complex second, expert opinion sought and ancillary tests required, diagnosis confirmed	0.0000	0.0000	0.0000
Complex second, expert opinion sought and ancillary tests required, diagnosis changed	0.0005	0.0002	0.0003
Complex second, expert opinion sought and ancillary tests not required, diagnosis confirmed	0.0000	0.0000	0.0000
Complex second, expert opinion sought and ancillary tests not required, diagnosis changed	0.0003	0.0001	0.0002
Non-complex second, expert opinion sought and ancillary tests required, diagnosis confirmed	0.0000	0.0000	0.0000
Non-complex second, expert opinion sought and ancillary tests required, diagnosis changed	0.0002	0.0001	0.0001
Non-complex second, expert opinion sought and ancillary tests not required, diagnosis confirmed	0.0000	0.0000	0.0000
Non-complex second, expert opinion sought and ancillary tests not required, diagnosis changed	0.0007	0.0003	0.0004
Total	0.0018	0.0007	0.0011

Note: Figures may not sum due to rounding

On average, there are 0.0018 significant changes in diagnosis per patient if second, expert opinions are funded by the MBS. This compares with 0.0007 under the current funding

arrangements. In a population of 1,000 patients with a tissue pathology diagnosis, this translates to an additional 1.1 significant changes in diagnosis.

D.4.3. Incremental cost per significant (clinically relevant) change in diagnosis or interpretation

On the basis of the results above, the incremental cost-effectiveness shown in Table D.4-4 was calculated.

Table D.4-4 Incremental cost per significant (clinically relevant) change in diagnosis or interpretation

	Proposed funding arrangements	Current funding arrangements	Incremental
Average cost per patient	$4.19	$0.15	$4.04
Average rate of significant change in diagnosis per patient	0.0018	0.0007	0.0011
Incremental cost per significant (clinically relevant) change in diagnosis or interpretation	-	-	$3,838.26

Note: Figures may not sum due to rounding

The economic evaluation demonstrates that if second, expert opinions were to be funded by the MBS as per the requested listing, it would cost an additional $3,838 to generate one significant change in diagnosis in the case of tissue pathology.

Importantly, this analysis assumes that there is a zero cost associated with second, expert opinions under the current funding arrangements. As such, it represents a worst-case scenario in that sense. If the analysis were able to also include these costs, and the frequency with which they are incurred by respective parties, the incremental cost would be lower per patient, thereby improving the incremental cost per significant (clinically relevant) change in diagnosis or interpretation. This, and other sensitivity analyses, is investigated in Section D.5 below.

D.5. Sensitivity analyses

To better inform decision-makers on the incremental cost-effectiveness of MBS funding of second, expert opinions, a series of sensitivity analyses were conducted to highlight potential areas of uncertainty with regards to the base case presented in Section D.4.

The first of these analyses presents the potential cost-effectiveness of second, expert opinion in cytopathology. This was omitted from consideration in the base case, as described previously, due to a lack of reliable data upon which the analysis could be based. Specifically, there were no data relating to the rate of change in diagnosis (analogous to the major discrepancy rates for any organ system tissue pathology presented in Table D.3-3). The analysis presented in this Section, while unsuitable for a base case analysis, assumed that the rate of change in diagnosis for cytopathology is equal to that observed in surgical pathology (i.e. from Cook et al, 2001, and Hsu et al, 2010). While such an analysis is not without fault, it is presented here in the event that it could be informative to decision-makers since it demonstrates the sensitivity of the incremental cost-effectiveness to the cytopathology-specific responses generated by the Expert Opinion Survey discussed in Section C (and Appendix 5).

To undertake this analysis, the data from Table D.3-3 were used in conjunction with the appropriate Expert Opinion Survey data presented in Table C.4-1 and the appropriate

unit cost data for ancillary tests from Table D.3-1. The cytopathology data from the survey are presented again in Table D.5-1 for transparency.

Table D.5-1 Data from the Expert Opinion Survey used to inform the sensitivity analysis, cytopathology

Types of cases	Average under the proposed funding arrangements	Average under the current funding arrangements
Proportion of cases referred for second, expert opinion	0.0117	0.0033
Proportion of cases initiated by Pathologist (*Scenario 1*)	0.5886	0.7643
Proportion of cases initiated by Clinician (*Scenario 2*)	0.4114	0.2357
Proportion of *Scenario 1* cases which are 'complex'	0.1093	0.1474
Proportion of *Scenario 1* cases which are 'non-complex'	0.4793	0.6169
Proportion of *Scenario 2* cases which are 'complex'	0.0754	0.0432
Proportion of *Scenario 2* cases which are 'non-complex'	0.3360	0.1925
Proportion of 'non-complex' cases requiring ancillary tests	0.1157	0.1014
Proportion of 'non-complex' cases not requiring ancillary tests	0.8843	0.8986
Proportion of 'complex' cases requiring ancillary tests	0.3214	0.3043
Proportion of 'complex' cases not requiring ancillary tests	0.6786	0.6957

Additionally, sensitivity analyses were conducted to examine the uncertainty inherent in the base case regarding the merging of *Scenario 1* and *Scenario 2*. As described previously, major discrepancy data were available for *Scenario 1* only. Since no data specific to *Scenario 2* – any organ system – were available, it was assumed that the rates were representative of both. An unintended consequence of this approach is that the impact of other data relating to each of the scenarios is masked. That is, even in the absence of major discrepancy data for *Scenario 2*, it is possible that survey responses uniquely relating to *Scenario 1* and *Scenario 2* could have a marked impact on the estimated cost per additional significant (clinically relevant) change in diagnosis or interpretation. To explore this possibility, each is considered independently in a sensitivity analysis. Of course, the result for *Scenario 2* alone should be treated with caution as it does not include scenario-specific discrepancy data.

Similarly, sensitivity analyses relating to 'complex' (i.e. >30 minutes) second, expert opinions and 'non-complex' (i.e. ≤30 minutes) second, expert opinions are independently presented for transparency. Again, while it was not possible to apply differential discrepancy data to each of these categories, these sensitivity analyses were aimed at demonstrating the impact of other data generated from the Expert Opinion Survey as well as the impact of the requested list price on the cost-effectiveness of each of these complexity categories independently. The impact of this data limitation is potentially greater when *Scenario 2* is considered in isolation.

Following this, sensitivity analyses relating to specific diseases are presented. While it would be beneficial to generate incremental cost-effectiveness ratios (ICERs) for a wide range of diseases for which second, expert opinions will be used in clinical practice, the analyses are limited to those for which there are reasonable data available (soft tissue/ sarcoma and dermatology, both of which fall under the tissue pathology heading).

The major discrepancy data pertaining to specific diseases (analogous to Table D.3-3) are presented in Table D.5-2. Note that the Ray-Coquard et al (2012) data were based on those discrepancies with zero agreement with initial diagnosis, rather than those with

partial agreement; these data appear to better correspond with those from the other studies. Similarly, the Gaudi et al (2013) data relating to dermatology were based on the malignant to benign and benign to malignant data only, again because they appeared to better match data available from other studies. The sensitivity analyses for second, expert opinion on soft tissue/sarcoma and dermatology do not assume that the proportion of expert opinions considered to be 'complex' or 'non-complex' are any different to the base case analysis for any organ system.

Table D.5-2 Major discrepancies with provisional diagnosis applied to the sensitivity analysis

Study ID	Population (N)	Outcome	Results n/N (%)
Soft tissue/sarcoma	-	-	-
Hsu 2010	Anatomic pathology; any organ system N=2686 cases	Major discrepancy in bone and soft tissue cases with a specific provisional diagnosis	21/218 (9.6%)
Arbiser 2001	Soft tissue lesions N=500 cases	Major discrepancy in cases with a provisional diagnosis	65/266 (24.4%)
Ray-Coquard 2012	Soft tissue or visceral sarcoma N=1463 cases	Zero agreement with initial diagnosis	71/564 (12.6%)
Average	-	-	*157/1048 (15.0%)*
Dermatology	-	-	-
Hsu 2010	Anatomic pathology; any organ system N=2686 cases	Major discrepancy in skin (dermatology) cases with a specific provisional diagnosis	44/286 (15.4%)
Gaudi 2013	Dermatopathology N=405 cases	Major discrepancy (malignant-benign and benign-malignant only)	24/354 (6.8%)
van Dijk 2008	Cutaneous melanocytic lesions N=1837	Major discrepancy in cases with a provisional diagnosis	322/1217 (26.5%)
Veenhuizen 1997	Skin lesions N=1069	Major discrepancy in cases with a provisional diagnosis	185/798 (23.2%)
Average	-	-	*575/2655 (21.7%)*

Source: Table B.6-5 of the Assessment Report

Additionally, a sensitivity analysis of the base case was undertaken to examine the impact of the structural assumption of including major discrepancies with provisional diagnoses only. Both Cook et al (2001) and Hsu et al (2010) also report data relating to cases with no initial diagnosis. As it is not possible to determine what clinical management would have been initiated in the absence of second, expert opinion, these data were omitted from the base case. In a sensitivity analysis, however, the impact of their inclusion is assessed. In the case of Cook et al (2001), there were 13 cases with no initial diagnosis; in the case of Hsu et al (2010), there were seven cases. In both instances, these were added to the numerator and the denominator to recalculate the major discrepancy rates (see Table D.5-3). The underlying assumption, albeit unrealistic, is that a diagnosis can be rendered by second, expert opinion in all cases where there is no initial pathology opinion, and that this diagnosis is associated with a change in clinical management.

Table D.5-3 Major discrepancies with provisional diagnosis applied to sensitivity analysis, no initial diagnosis data included

Study ID	Population (N)	Outcome	Results n/N (%)[a]
Cook 2001	All histopathology; any organ system N=128 cases	Major discrepancy in cases with provisional diagnosis or no initial diagnosis	23/68 (33.8%)
Hsu 2010	Anatomic pathology; any organ system N=2686 cases	Major discrepancy in cases with a 'specific' provisional diagnosis or no initial diagnosis	212/1677 (12.6%)
Average	-	-	*235/1725 (13.6%)*

Source: Table B.6-1 of the Assessment Report

[a] All reported cases with no initial pathology opinion have been incorporated into the numerator and the denominator

Other sensitivity analyses were conducted around the requested price, the discrepancy rates, the cost of second, expert opinion in the comparator arm, the incidence of second, expert opinion in the arm representing the proposed changes to MBS funding and the frequency of ancillary testing in the investigative arm.

Table D.5-4 Sensitivity analyses conducted over the course of the economic evaluation

Description	Incremental cost	Incremental outcome	Incremental cost per significant change in diagnosis
Base case	*$4.04*	*0.0011*	*$3,838.26*
Cytopathology	$2.58	0.0011	$2,460.01
Scenario 1 alone	$4.21	0.0011	$4,000.26
Scenario 2 alone	$3.53	0.0011	$3,353.95
'Complex' second, expert opinions alone	$5.55	0.0011	$5,278.96
'Non-complex' second, expert opinions alone	$2.66	0.0011	$2,531.19
Soft tissue/sarcoma	$4.04	0.0013	$3,193.34
Dermatology	$4.04	0.0018	$2,208.92
Including cases with no initial diagnosis	$4.04	0.0011	$3,552.31
List price increased 10%	$4.42	0.0011	$4,201.67
List price decreased 10%	$3.65	0.0011	$3,474.85
Major discrepancy rate increased by 10%	$4.04	0.0012	$3,489.33
Major discrepancy rate decreased by 10%	$4.04	0.0009	$4,264.73
Average cost of second, expert opinion in the comparator arm set to unit cost of 'non-complex' second, expert opinion	$1.49	0.0011	$1,420.59
Rate of second, expert opinions set to upper limit from survey results (1% in current arm, 2% in proposed arm)	$5.66	0.0012	$4,543.35
Rate of second, expert opinions set to lower limit from survey results (0.1% in current arm, 0.3% in proposed arm)	$0.86	0.0002	$3,461.68
Cost of ancillary tests increased by 10%	$4.06	0.0011	$3,858.68
Cost of ancillary tests decreased by 10%	$4.01	0.0011	$3,817.84

Among the analyses conducted, the greatest downside sensitivity risk relates to consideration of 'complex' second, expert opinions alone. Given that these would attract twice the price under the proposed listing, this result is intuitive. While this result should be noted in itself, it must also be noted that it is a partial analysis. Specifically, it is reasonable to assume that the rate of major discrepancies among 'complex' cases may be

different to the average case. There are, however, no data upon which a modification of the base case can be estimated to tailor an analysis relevant 'complex' cases alone. As such, we cannot be certain of the true impact of considering 'complex' cases in isolation and the partial analysis presented above must be viewed in light of its limitations.

The greatest upside risk stems from the inclusion of a unit cost associated with second, expert opinion in the arm representing current funding arrangements. While the MBS does not currently fund any second opinions, payment may be appropriate in some cases. The revised Final Protocol, for example, maintains that a proportion of second, expert opinions are conducted ex gratis, while the funding of others is met either by the patient or by other funding mechanisms. While both the distribution of these possibilities, and the applicable unit costs, are unknown, it can be seen that a simplistic approach of using the requested fee for 'non-complex' second, expert opinions has a marked effect. This reduces the ICER to $1,421 per significant change in diagnosis. This demonstrates that inclusion of a figure representing the true cost of the current arrangements would improve the cost-effectiveness of the requested listing by reducing the incremental cost.

Another particularly sensitive analysis can be seen in the increase in the rate of second, expert opinions to the upper limit of the survey results. This was a two-way sensitivity analysis, incorporating the upper limit into both arms of the model (1% in the arm representing current practice and 2% in the arm representing the proposed listing). With such low rates of second, expert opinions in the base case, it is unsurprising that this would have a notable effect on the results. In fact, it could be that the sensitivity to this parameter is more than simply academic, as it may be difficult to predict how the rate of second, expert opinions may increase in true clinical practice in the event of a change to the funding mechanism. If the rate increases more than is expected, this will increase the ICER, reducing the cost-effectiveness offered. Moreover, it is worth considering the possibility that an increase in the rate of second, expert opinions may be due to expert opinions being requested for cases which are unlikely to benefit from the second opinion (i.e. cases which are currently omitted from requests for second, expert opinion due to their relative, but limited, certainty). If this were the case, this could have a more pronounced impact by lowering the rate of major discrepancies, which would increase the ICER further. Of course, there are currently no data to indicate this outcome would eventuate, but it may warrant consideration nonetheless.

Another notable result is that the inclusion of cases with no initial diagnosis has been shown to have negligible effect on the result. While the ICER itself does change when these data are applied, the impact on the incremental outcome is not observable at the level of four decimal places. When considering the low number of cases without an initial diagnosis, this result is intuitive.

The results are not particularly sensitive to the unit costs used. Neither the list price nor the cost of ancillary tests appear to have a marked impact on the results when varied to reasonable limits. Similarly, the ICER does not exhibit pronounced sensitivity to reasonable variation in the major discrepancy rates.

The incremental cost-effectiveness appears to improve when diseases are considered in isolation, or at least in the case of soft tissue/sarcoma and dermatology. Each of the ICERs for these is lower than in the base case. Of course, the results should be interpreted with caution since, in both cases, they include additional studies not included in the base case. They, therefore, lack internal consistency with the base case.

Nonetheless, at the very least, these serve to highlight how the cost-effectiveness may change between subgroups.

Finally, the analysis focussing on cytopathology is worth highlighting. Data limitations weigh heavily on this analysis, with it relying on tissue pathology data rather than data applicable to cytopathology. This markedly hinders the ability to draw conclusions from the analysis. Nonetheless, the analysis does reveal that, other things being equal, resource use estimates from the survey indicate that cytopathology may be more cost-effective than tissue pathology. Of course, variations to the major discrepancy rate could reverse this finding, but it remains an interesting result nonetheless. Further research into the likely rates of major discrepancies among cytopathology second, expert opinions could be of great value.

Section E. Estimated utilisation and financial implications

E.1. Justification of the selection of sources of data

As discussed in Section A.2.4, second, expert opinions on tissue pathology and cytology specimens are not funded on the MBS. Hence there is no MBS data available to show the number of second opinions that are currently performed by expert pathologists in Australia.

Furthermore, there is limited data available in the published literature regarding the number of second, expert pathology opinions undertaken in Australia or internationally, nor the proportion of initial tissue pathology or cytology cases that are usually referred for expert opinion. Of the included studies in Section B, two reported second, expert opinion rates (see Table E.1-1). The Cook et al (2001) study from the United Kingdom showed that second, expert opinion rates increased over time from 0.35% in 1990 to 0.56% in 1998. The Hsu et al (2010) study from Taiwan reported a second, expert opinion rate of 0.7%. In addition, a study from the College of American Pathologists (Azam and Nakhleh, 2002), excluded in Section B.2, suggested that approximately 0.5% of initial tissue pathology cases are referred to an expert pathologist to resolve diagnostic uncertainty. However the study included some patient-requested referrals and had a very low proportion of Australian sites (<4%), which limits the applicability of the results.

Table E.1-1 Rates of second, expert opinion – as reported in the included studies

Study ID	Source of estimate	Outcome	Second opinion rate
ALL SURGICAL PATHOLOGY	-	-	-
Cook 2001	(1) Consultants' correspondence files (2) Centralised laboratory records from Portsmouth Hospitals' NHS Trust (Queen Alexandra and St Mary's Hospitals)	Referrals for expert opinion in 1990 (as a proportion of total histopathology accessions): n/N (%) Referrals for expert opinion in 1998 (as a proportion of total histopathology accessions): n/N (%)	60/16953 (0.35%) 128/22990 (0.56%)
Hsu 2010	A survey of 87 Taiwan Society of Pathology members regarding extra-departmental pathology referrals	Estimated percentage of cases referred for expert opinion per year: mean (median, range) Estimated rate of referral in institutes having five or less pathologists: mean (median, range) Estimated rate of referral in institutes having six or more pathologists: mean (median, range)	0.7% (0.5%; 0.01-5%) 0.8% (0.5%; 0.01-5%) 0.7% (0.5%; 0.2-1%)

Abbreviations: NHS, National Health Service.

In their pre-assessment documentation, the Applicant estimated that approximately 1-2% of specimens would require a second, expert opinion in Australia. In their feedback to the Consultation Protocol, the Applicant revised that estimate to "substantially less than 1%", acknowledging that the figure came from a major metropolitan referral centre with

specific expertise and was not representative of the vast majority of community laboratory practices. Other submissions received during public consultation suggested that the proportion of cases referred for second, expert opinion may vary by an order of magnitude from less than 0.1% in large metropolitan laboratories to around 1% in remote, single-pathologist laboratories. The huge variation in referral patterns across different institutions and regions throughout Australia demonstrates the difficulty of providing an accurate estimate of the proportion of all tissue pathology and cytology cases that are referred for expert opinion in Australia. As such, the overall utilisation of second, expert opinion in Australia is highly uncertain.

E.1.1. Estimated utilisation of the proposed medical service

An electronic workbook *<1332_Section E workbook.FINAL.xls>* accompanies this Assessment Report.

The approach used to estimate the utilisation of the proposed medical service in the financial analysis is largely reliant on MBS data that shows the number of initial pathology opinions (also referred to in the Assessment Report as 'core' tissue pathology and cytology items) that have been provided through the MBS in recent years. Historical MBS data showing 'core' item utilisation are used to forecast future utilisation of those MBS items. Estimates of the proportion of those cases likely to be referred for second, expert opinion under both current and proposed funding arrangements can then be applied to the projected figures.

Historical MBS data from July 2008 to June 2013 for the 'core' bone marrow, tissue pathology and cytology items were used to project estimated utilisation of those 'core' MBS items for 2013-14[10] through to 2019-20 (the fifth year of listing on the MBS). The historical MBS data and utilisation projections, estimated using simple linear regression, are shown in Table E.1-2.

Importantly, the historical MBS data and estimated utilisation for 'core' cytopathology items is shown both with and without MBS items 73053, 73055 and 73057, which relate to gynaecological cytology. As discussed in Section A.2.5, MSAC should consider whether the inclusion of gynaecological cytology cases in the proposed second, expert opinion MBS items is appropriate. As such, both possible funding circumstances (with and without the three gynaecological cytology items) are explored in the financial estimates throughout Section E.

[10] Actual MBS data for the financial year 2013-2014 were not available as at 22 July, 2014.

Table E.1-2 Estimated number of services for 'core' MBS items for initial pathology opinions, over the first five years of the proposed MBS listing

MBS item	June 2011	June 2012	June 2013	June 2014	Current (2014-15)	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Tissue pathology[a]	-	-	-	-	-	-	-	-	-	-
MBS item 65084	14,062	14,166	15,382	16,029	16,809	17,590	18,371	19,151	19,932	20,713
MBS item 65087	2,547	2,714	2,643	2,662	2,663	2,664	2,664	2,665	2,666	2,667
MBS item 72813	13,477	12,527	10,983	12,141	12,224	12,306	12,389	12,472	12,554	12,637
MBS item 72816	1,163,546	1,220,087	1,266,752	1,284,319	1,315,560	1,346,802	1,378,043	1,409,284	1,440,526	1,471,767
MBS item 72817	278,907	297,290	313,420	321,131	332,762	344,393	356,024	367,655	379,286	390,917
MBS item 72818	13,376	15,206	17,076	17,252	18,218	19,185	20,151	21,118	22,084	23,051
MBS item 72823	579,280	599,118	633,867	669,302	703,132	736,962	770,792	804,623	838,453	872,283
MBS item 72824	315,683	330,324	356,323	382,450	407,461	432,471	457,482	482,492	507,502	532,513
MBS item 72825	46,208	51,495	56,333	60,163	64,498	68,833	73,168	77,503	81,838	86,173
MBS item 72826	16,966	18,251	18,392	17,733	17,629	17,525	17,420	17,316	17,212	17,108
MBS item 72827	6,153	6,085	5,618	7,143	7,779	8,415	9,051	9,687	10,324	10,960
MBS item 72828	958	1,290	2,018	2,168	2,517	2,865	3,214	3,562	3,911	4,259
MBS item 72830	73,275	75,372	80,498	84,328	88,399	92,469	96,539	100,610	104,680	108,751
MBS item 72836	21,679	21,070	22,469	21,980	22,128	22,277	22,425	22,574	22,723	22,871
MBS item 72838	12,570	12,658	12,872	14,268	15,084	15,901	16,718	17,535	18,352	19,168
Total	2,558,687	2,677,653	2,814,646	2,913,069	3,026,863	3,140,658	3,254,451	3,368,247	3,482,043	3,595,838
Cytology	-	-	-	-	-	-	-	-	-	-
MBS item 73043	2,534	2,326	2,370	2,211	2,110	2,008	1,907	1,805	1,704	1,602
MBS item 73045	90,638	93,632	99,501	101,331	104,692	108,054	111,415	114,777	118,138	121,500
MBS item 73047	37,875	39,889	44,010	45,566	48,027	50,488	52,949	55,410	57,870	60,331
MBS item 73049	46,165	54,030	58,404	51,444	50,448	49,452	48,456	47,460	46,465	45,469
MBS item 73051	12,952	9,867	10,063	7,147	5,181	3,215	1,249	-717	-2,683	-4,649
MBS item 73053	1,423,872	1,535,752	1,548,645	1,581,686	1,618,954	1,656,221	1,693,489	1,730,756	1,768,023	1,805,291
MBS item 73055	225,815	203,470	213,220	173,855	152,878	131,901	110,924	89,947	68,969	47,992
MBS item 73057	33,288	32,483	30,916	29,876	28,706	27,536	26,366	25,196	24,026	22,856
MBS item 73062	14,818	6,368	7,524	10,260	10,728	11,196	11,664	12,132	12,600	13,068
MBS item 73063	15,070	15,511	16,189	22,061	25,376	28,690	32,005	35,319	38,634	41,949
MBS item 73066	0	2,023	2,380	2,737	3,094	3,451	3,808	4,165	4,522	4,879
MBS item 73067	0	1,813	2,488	3,163	3,838	4,513	5,188	5,863	6,538	7,213
Total (Non-gynaecological only)	220,052	225,459	242,929	245,920	253,494	261,067	268,641	276,214	283,788	291,362
Total (All cytology)	1,903,027	1,997,164	2,035,710	2,031,337	2,054,032	2,076,725	2,099,420	2,122,113	2,144,806	2,167,501

Source: Excel Section E workbook <Service utilisation assumptions>

Note: Projections were calculated based on Medicare Australia data from 2008-09 to 2012-13; however, not all historical data used in projections are presented in Table E.1-2.

[a] Includes bone marrow items (MBS items 65084 and 65087).

As discussed above, Australian estimates of the proportion of initial pathology specimens that are referred for second, expert opinion are not available from the literature. To address the data gap, a targeted Expert Opinion Survey[11] was sent to eight Chief Executive Officers or Heads of Pathology Departments in Australia (see Appendix 1). In order to determine the utilisation of the proposed second, expert opinion items, the respondents were asked to estimate the proportion of initial cases that would be referred to an external expert pathologist. Separate estimates were obtained according to current and proposed funding arrangements as well as tissue pathology (including bone marrow) and non-gynaecological cytology. For the purpose of the financial estimates, and in lieu of other data, it was assumed that the proportion of gynaecological cytology cases that would require a second, expert opinion would not differ from non-gynaecological cytology.

The estimated proportion of tissue pathology and cytology cases referred for second, expert opinion under the current and proposed funding arrangements are shown in Table E.1-3. The estimates represent the average (mean) of the responses obtained through the Expert Opinion Survey (eight responses for tissue pathology and seven for non-gynaecological cytology). The expected increase in the proportion of cases referred for second, expert opinion supports the clinical claim that second, expert opinions are not sought as frequently as they should be (particularly from isolated regional or remote pathologists) due to the cost, lack of funding, and perceived impost on colleagues (see Section A.7). The estimates from Table E.1-3 were applied in the base case financial analysis, with alternative values tested in sensitivity analyses in Section E.6.

Table E.1-3 Base case estimates of proportion of cases referred for second, expert opinion

	Average estimate (%) - Proposed funding arrangements	Average estimate (%) - Current funding arrangements
Tissue pathology	-	-
Proportion of cases referred for second, expert opinion	1.41%	0.57%
Cytology[a]	-	-
Proportion of cases referred for second, expert opinion	1.17%	0.33%

Source: Expert Opinion Survey (Appendix 5)

[a] The estimate refers to the proportion of non-gynaecological cytology cases referred for second, expert opinion. The base case financial analysis assumes that a similar rate would apply to gynaecological cytology cases.

The second, expert opinion rates from the Expert Opinion Survey (Table E.1-3) are applied to the estimated number of 'core' services in Table E.1-2 to estimate the number of second, expert opinion services that would be expected to occur under the current and proposed funding arrangements (see Section E.2).

As discussed in Section A.3 it is possible, though highly unlikely, that in some cases a third opinion would be required in order to obtain a definitive diagnosis. The financial analysis assumes that MBS funding would only be available for one expert opinion per patient episode.

As discussed in Section A.3, the Applicant suggested a two-tiered fee structure with different rebates reflecting the time and work involved in second, expert opinions. It would be up to the expert pathologist to determine the workload involved in providing

[11] The Expert Opinion Survey was developed by HealthConsult Pty Ltd to inform the financial estimates in the Assessment Report. The survey was distributed to experts in the field who were selected by the Applicant.

the second opinion and bill the item accordingly as 'complex' or 'non-complex'. The proposed fee structure therefore necessitated the attainment of estimates relating to the proportion of cases that would be 'complex' and 'non-complex', also taking into consideration whether the initial pathologist or clinician initiated the referral (i.e. *Scenario 1* and *Scenario 2* described in Section A.2). Those estimates, which are applied in the base case, were obtained from the Expert Opinion Survey and are presented in Table E.1-4.

Table E.1-4 Base case estimates of proportion of second, expert opinions which are 'complex' and 'non-complex'

	Average estimate (%) - Proposed funding arrangements	Average estimate (%) - Current funding arrangements
Tissue pathology	-	-
Proportion of *Scenario 1* cases which are 'complex'	53.75%	60.00%
Proportion of *Scenario 1* cases which are 'non-complex'	46.25%	40.00%
Proportion of *Scenario 2* cases which are 'complex'	30.00%	31.25%
Proportion of *Scenario 2* cases which are 'non-complex'	70.00%	68.75%
Cytology[a]	-	-
Proportion of *Scenario 1* cases which are 'complex'	18.57%	19.29%
Proportion of *Scenario 1* cases which are 'non-complex'	81.43%	80.71%
Proportion of *Scenario 2* cases which are 'complex'	18.33%	18.33%
Proportion of *Scenario 2* cases which are 'non-complex'	81.67%	81.67%

Source: Excel Section E workbook <Service utilisation assumptions>

Note: For the purposes of the financial estimates, *Scenario 1* refers to requests for a second, expert opinion initiated by the pathologist. *Scenario 2* refers to requests for a second, expert opinion initiated by the clinician.

[a] The estimate refers to the proportion of non-gynaecological cytology cases. The base case financial analysis assumes that the estimated proportion of 'complex' and 'non-complex' cases are the same for gynaecological cytology.

E.1.2. Estimated utilisation of the associated services

The financial analysis also takes into consideration additional MBS items that may be used in conjunction with the proposed MBS items for second, expert opinion. In particular, it is anticipated that ancillary tests (e.g. IHC, molecular testing) undertaken as part of the second, expert opinion would be charged to the MBS in the usual way. The Expert Opinion Survey (Appendix 1) asked respondents to estimate the proportion of 'complex' and 'non-complex' second, expert opinions that would require ancillary tests in both the proposed and current funding arrangements. Separate estimates were also provided for tissue pathology and cytology, as shown in Table E.1-5. In general, the average estimates were similar under the proposed and current funding arrangements.

Table E.1-5 Base case estimates of changes in use of ancillary tests according to availability of MBS funding for second, expert opinions

	Average estimate (%) - Proposed funding arrangements	Average estimate (%) - Current funding arrangements
Tissue pathology	-	-
Proportion of 'complex' cases requiring ancillary tests	62.50%	62.63%
Proportion of 'non-complex' cases requiring ancillary tests	23.75%	25.00%
Cytology[a]	-	-
Proportion of 'complex' cases requiring ancillary tests	32.14%	30.43%
Proportion of 'non-complex' cases requiring ancillary tests	11.57%	10.14%

Source: Excel Section E workbook <Service utilisation assumptions>

[a] The estimate refers to the proportion of non-gynaecological cytology cases. The base case financial analysis assumes that use of ancillary tests is the same for gynaecological cytology.

Several other existing MBS items may be affected by an MBS listing for second, expert pathology opinions. As discussed in Section A.2.3, the provision of the proposed service may be associated with administrative and handling costs in order to transfer the original specimens/slides to and from an expert pathologist. As such, the utilisation of the 'specimen referred fee' (MBS Group 11, item 73940) may be affected by the proposed listing. Despite the fact that the first (referring) laboratory would incur costs associated with the second, expert opinion (e.g. retrieving slides from the archives, collating the case, sending the slides, refining the original diagnosis and re-filing the case material), the specimen referred fee is currently restricted to being claimed by the second (receiving) laboratory. Therefore, the base case assumption is that each case referred for second, expert opinion would result in one additional claim for MBS item 73940 (i.e. the number of services for MBS item 73940 would be equal to 100% of the estimate for second, expert opinion utilisation), see Table E.1-6. The current Schedule fee for the bulk billing incentive is $10.25.

In the Final Protocol (p14), PASC suggested that the costs incurred by the first laboratory may require separate consideration (similar to MSAC Application 1331 – Retrieval of tissue for further diagnostic testing specifically genetic testing for diagnostic/prognostic purposes); however such potential costs have not been included in the current financial analysis.

In addition to increased usage of the specimen referred fee, an MBS listing for second, expert opinions would be likely to result in additional utilisation of the 'bulk billing incentive' (MBS item 74996). As stated in the Final Protocol (p23), pathology items have a greater than 90% bulk billing rate. For simplicity, the base case assumes that 100% of cases referred for second, expert opinion would result in one additional claim for MBS item 74996 (Table E.1-6). The current Schedule fee for the bulk billing incentive is $3.70.

Finally, while the Final Protocol (p23) suggested a possible increase in utilisation of clinician consultation items (MBS items 23 and 105), it is considered to be highly unlikely that the referral of case material to an expert pathologist would require an additional consultation between the treating clinician and the patient. Under the proposed funding arrangements, a second, expert opinion could not be conducted at the behest of the patient. Furthermore, any additional consultations between the treating clinician and patient may unnecessarily increase the time taken to obtain a definitive diagnosis. Therefore it is assumed that no additional use of MBS items 23 and 105 would result from the proposed listing, regardless of whether the pathologist or treating clinician initiated the referral.

Table E.1-6 Base case estimates of changes in use of other associated MBS items

	Proportion applied in financial analysis (%) - Proposed funding arrangements	Proportion applied in financial analysis (%) - Current funding arrangements
Proportion of second, expert opinions incurring specimen referred fee (MBS item 73940)	100%	0%
Proportion of second, expert opinions incurring bulk billing incentive (MBS item 74996)	100%	0%

Note: Assumes no difference in use of MBS items 73940 and 74996 between tissue pathology and cytology cases.

E.1.3. Summary of the sources of data and assumptions underpinning the financial analysis

Table E.1-7 provides a summary of the assumptions and sources of data that contribute to the estimate of financial impact provided in the Assessment Report.

Table E.1-7 Key assumptions and data sources used for the financial analysis

Input	Assumption(s) and source of data
Future utilisation of 'core' MBS items for initial pathology opinions	Assume that future utilisation follows recent trends. Projections are calculated using simple linear regression of historical MBS data from 2008-09 to 2012-13. The relevant MBS items are: MBS items 65084-87; 72813-38; 73043-57; 73062-63; and 73066-67.
Proportion of initial pathology opinions referred for second, expert opinion	Mean estimates sourced from Expert Opinion Survey (see Appendix 1). Survey respondents were asked to base their estimate on the proposed conditions for MBS-funded second, expert opinions, as specified in Section A.2.
Proportion of second, expert opinions that would be 'complex' and 'non-complex'	Mean estimates sourced from Expert Opinion Survey (see Appendix 1).
Change in utilisation of ancillary tests associated with second, expert opinions	Assume that the use of ancillary tests may vary between 'complex' and 'non-complex' expert opinions. Mean estimates for both 'complex' and 'non-complex' second, expert opinions were obtained from the Expert Opinion Survey (see Appendix 1).
Change in utilisation of specimen referred fee (MBS item 73940)	Financial analysis assumes that (i) under current funding arrangements no specimen referred fees would be charged to the MBS because second, expert opinions are not currently funded on the MBS; and (ii) under proposed funding arrangements all cases (100%) referred for second, expert opinion would result in one additional use of MBS item 73940.
Change in utilisation of bulk billing incentive (MBS item 74996)	Financial analysis assumes that (i) under current funding arrangements no bulk billing incentives would be charged to the MBS because second, expert opinions are not currently funded on the MBS; and (ii) under proposed funding arrangements all cases (100%) referred for second, expert opinion would result in one additional use of MBS item 74996.
Change in utilisation of clinician consultation items (MBS item 23 or 105)	In lieu of data, assume that 0% of referrals for second, expert opinion require additional consultation between the referring clinician and patient.
Estimates for gynaecological cytology cases (initial MBS items 73053, 73055 and 73057)	In lieu of data, assume that the estimates obtained in the Expert Opinion Survey for non-gynaecological cytology also apply to gynaecological cytology. This assumption applies to all estimates (e.g. referral rate, complexity, use of ancillary tests).

E.1.4. Costing assumptions

Table E.1-8 summarises the proposed second, expert opinion items and fees that contribute to the estimate of financial impact provided in the Assessment Report. As discussed in Section A.3, the proposed Schedule fees were suggested by the Applicant and were set at a level that is commensurate with the existing fees for initial pathology items on the MBS.

The financial analysis assumes that all MBS services undertaken by expert pathologists are bulk-billed using the 85% benefit (as shown in Table E.1-6). Importantly, it is possible that some patients may receive a second, expert opinion as an inpatient (i.e. patients who have been transferred from regional or rural areas for definitive treatment). Expert opinion services undertaken on public inpatients would be non-reimbursable under Medicare. Private inpatients are not expected to represent a large proportion of

expert opinion services as patients would not often be admitted for treatment before a definitive diagnosis has been obtained. As such, and for simplicity, the financial estimates assume that 100% of cases are outpatients, bulk-billed using the 85% benefit. Any use of the proposed service for private inpatients would reduce the financial impact to the MBS.

Finally, for simplicity, the financial analysis assumes that the MBS fees, for both proposed and associated items, do not change over the five-year projection period. The Medicare Safety Net, Extended Medicare Safety Net (EMSN) and EMSN capping are not taken into consideration.

Table E.1-8 Second, expert opinion items and fees used in the base case financial analysis

	Proposed Schedule fee	Proposed 85% benefit
Proposed funding arrangements	-	-
'Non-complex' second, expert opinion	$180.00	$153.00
'Complex' second, expert opinion	$370.00	$314.50
Current funding arrangements	-	-
'Non-complex' second, expert opinion	$0.00	$0.00
'Complex' second, expert opinion	$0.00	$0.00

Source: Schedule fees proposed by the Applicant (see Section A.2), currently unfunded. Excel Section E workbook <Costing inputs>

For the purpose of the financial estimates, an average cost of ancillary tests for tissue pathology was calculated by dividing the total value of benefits of ancillary tests (i.e. Group P5, MBS items 72844-72852) in 2012-13 by the total number of services of those items in the same year (Table E.1-9). This method of calculation, as opposed to simply averaging the Schedule fees of the eight 'non-core' items, was chosen to account for higher use of some 'non-core' (ancillary) items over others and also the impact of 'coning' on the total cost to the MBS, given that multiple different tests can be conducted on the same patient sample. The same approach was used to calculate the average cost of ancillary tests used on cytological samples, see Table E.1-9.

Despite the absence of MBS funding for second, expert opinions, expert pathologists may still conduct ancillary tests as part of the service, either without payment, at the expense of the referring institution, or at the expense of the patient. Under current funding arrangements, new ancillary tests undertaken in conjunction with a second, expert opinion may be charged by the expert pathologist through the existing MBS items. However, under current arrangements, if an expert pathologist providing second opinion repeats an ancillary test that has already been undertaken as part of the initial pathology opinion, an MBS item cannot be charged by the expert pathologist (unless it is conducted as part of a new patient episode). As such, there may well be a cost associated with ancillary tests conducted for the purposes of second, expert opinion under the current funding arrangements.

The Expert Opinion Survey did not provide an estimate of the proportion of current MBS claims for ancillary test items which are likely to be associated with a second, expert opinion. Furthermore, MBS data that could provide insight into the current utilisation of those items for the purpose of second, expert opinions (e.g. an analysis of whether claims for 'non-core' items are regularly made at a later date to that of the initial pathology opinion) are not readily available. As such, it is difficult to quantify the current cost to the MBS of ancillary items associated with second, expert opinions. The financial analysis therefore assumes that ancillary tests undertaken as part of second, expert opinion bear

no cost to the MBS under current funding arrangements. As such, the incremental cost of ancillary tests under the proposed listing may be overestimated (see Section E.3).

Table E.1-9 Ancillary items and fees used in the financial analysis

	Total number of services in 2012-13	Total value of benefits ($) in 2012-13	Average cost of ancillary items under proposed funding arrangements	Average cost of ancillary items under current funding arrangements
Tissue pathology[a]	157,111	$9,703,766	$61.76	$0.00
Cytology[b]	5,542	$266,709	$48.13	$0.00

Source: Excel Section E workbook <Costing inputs> and <MBS Data>
Note: Items and fees sourced from Medicare Australia, accessed 10 June 2014
[a] Ancillary tests include MBS items 72844-72852.
[b] Ancillary tests include MBS items 73059-73061 and 73064-73065.

The cost assumptions for other associated MBS items included in the financial analysis are presented in Table E.1-10. For simplicity, the financial analysis assumes that the cost of the associated MBS items do not change over the five-year projection period.

Table E.1-10 Other associated MBS items and fees used in the financial analysis

	MBS item	Schedule fee – Proposed funding arrangements	85% benefit – Proposed funding arrangements	Cost assumption – Current funding arrangements
Specimen referred fee	MBS item 73940	$10.25	$8.75	$0.00
Bulk billing incentive	MBS item 74996	$3.70	$3.15	$0.00

Source: Excel Section E workbook <Costing inputs>
Note: Items and fees sourced from MBS Online, accessed 24 July 2014

E.2. Estimation of use and costs of the proposed medical service

Table E.2-1 shows the number of second, expert opinion services that would be expected over the first five years of the proposed MBS listing. The estimates were obtained by multiplying the projected number of initial pathology opinions through to the fifth year of listing (Table E.1-2) by the proportion of initial cases that would be referred for second, expert opinion (Table E.1-3). The table also shows the number of second, expert opinions that would be expected to occur over the next five years if current funding arrangements continue, using the relevant estimates from Table E.1-2.

Table E.2-1 Estimated number of MBS services for second, expert opinions, over the first five years of the proposed MBS listing

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Proposed funding arrangements	-	-	-	-	-
Tissue pathology[a]	44,362	45,969	47,576	49,184	50,791
Non-gynaecological cytology	3,058	3,147	3,236	3,324	3,413
All cytology	24,327	24,593	24,859	25,125	25,391
Current funding arrangements	-	-	-	-	-
Tissue pathology[a]	17,862	18,510	19,157	19,804	20,451
Non-gynaecological cytology	858	883	908	932	957
All cytology	6,824	6,898	6,973	7,047	7,122

Source: Excel Section E workbook <MBS services (SO items)>

[a] Includes bone marrow items

The estimated utilisation shown in Table E.2-1 is broken down further in Table E.2-2 to indicate the proportion of cases that would be likely to be pathologist-initiated (*Scenario 1*) and clinician-initiated (*Scenario 2*), as well as those that would be 'complex' and 'non-complex' under the proposed funding arrangements. Table E.2-3 presents the equivalent breakdown using the survey estimates for the current funding arrangements and Table E.2-4 provides the incremental difference in service utilisation – showing the expected increase in utilisation under the proposed MBS listing.

Table E.2-2 Estimated number of MBS services for second, expert opinions, over the first five years of the proposed MBS listing – Proposed funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	32,994	34,190	35,385	36,580	37,776
Complex	17,734	18,377	19,019	19,662	20,305
Non-complex	15,260	15,813	16,366	16,918	17,471
Non-gynaecological cytology	1820	1872	1925	1978	2031
Complex	338	348	358	367	377
Non-complex	1482	1525	1568	1611	1654
All cytology	14,475	14,633	14,791	14,949	15,107
Complex	2,688	2,718	2,747	2,776	2,806
Non-complex	11,787	11,915	12,044	12,173	12,302
Sub-total (excluding gynaecological cytology)	*34,814*	*36,062*	*37,310*	*38,558*	*39,807*
Sub-total (including all cytology)	*47,469*	*48,822*	*50,176*	*51,530*	*52,883*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	11,368	11,780	12,191	12,603	13,015
Complex	3,410	3,534	3,657	3,781	3,905
Non-complex	7,957	8,246	8,534	8,822	9,111
Non-gynaecological cytology	1,239	1,275	1,310	1,346	1,382
Complex	227	234	240	247	253
Non-complex	1,012	1,041	1,070	1,100	1,129
All cytology	9,853	9,960	10,068	10,176	10,283
Complex	1,806	1,826	1,846	1,866	1,885
Non-complex	8,046	8,134	8,222	8,310	8,398
Sub-total (excluding gynaecological cytology)	*12,606*	*13,054*	*13,502*	*13,950*	*14,398*
Sub-total (including all cytology)	*21,220*	*21,740*	*22,259*	*22,779*	*23,298*
TOTAL (*S1* and S*2* – excluding gynaecological cytology)	47,420	49,116	50,812	52,508	54,204
TOTAL (*S1* and *S2* – all cytology)	68,689	70,562	72,436	74,309	76,182

Source: Excel Section E workbook <MBS services (SO items)>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.2-3 Estimated number of MBS services for second, expert opinions, over the first five years of the proposed MBS listing – Current funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	11,499	11,916	12,332	12,749	13,166
Complex	6,899	7,149	7,399	7,649	7,899
Non-complex	4,600	4,766	4,933	5,100	5,266
Non-gynaecological cytology	656	675	694	713	732
Complex	126	130	134	137	141
Non-complex	529	545	560	575	591
All cytology	5,215	5,272	5,329	5,386	5,443
Complex	1,006	1,017	1,028	1,039	1,050
Non-complex	4,209	4,255	4,301	4,347	4,393
Sub-total (excluding gynaecological cytology)	*12,155*	*12,590*	*13,026*	*13,462*	*13,897*
Sub-total (including all cytology)	*16,714*	*17,188*	*17,661*	*18,135*	*18,609*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	6,364	6,594	6,825	7,055	7,286
Complex	1,989	2,061	2,133	2,205	2,277
Non-complex	4,375	4,533	4,692	4,850	5,009
Non-gynaecological cytology	202	208	214	220	226
Complex	37	38	39	40	41
Non-complex	165	170	175	179	184
All cytology	1,608	1,626	1,644	1,661	1,679
Complex	295	298	301	305	308
Non-complex	1,314	1,328	1,342	1,357	1,371
Sub-total (excluding gynaecological cytology)	*6,566*	*6,802*	*7,039*	*7,275*	*7,511*
Sub-total (including all cytology)	*7,972*	*8,220*	*8,468*	*8,716*	*8,964*
TOTAL (*S1* and *S2* – excluding gynaecological cytology)	18,720	19,392	20,064	20,737	21,409
TOTAL (*S1* and *S2* – all cytology)	24,686	25,408	26,130	26,851	27,573

Source: Excel Section E workbook <MBS services (SO items)>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.2-4 Incremental number of MBS services for second, expert opinions, over the first five years of the proposed MBS listing

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	21,495	22,274	23,053	23,832	24,610
Complex	10,835	11,228	11,620	12,013	12,405
Non-complex	10,660	11,046	11,433	11,819	12,205
Non-gynaecological cytology	1164	1198	1232	1265	1299
Complex	211	218	224	230	236
Non-complex	953	980	1008	1035	1063
All cytology	9,260	9,361	9,462	9,563	9,664
Complex	1,682	1,701	1,719	1,738	1,756
Non-complex	7,577	7,660	7,743	7,826	7,908
Sub-total (excluding gynaecological cytology)	*22,659*	*23,472*	*24,284*	*25,097*	*25,910*
Sub-total (including all cytology)	*30,755*	*31,635*	*32,515*	*33,395*	*34,275*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	5,004	5,186	5,367	5,548	5,729
Complex	1,422	1,473	1,525	1,576	1,628
Non-complex	3,582	3,712	3,842	3,972	4,102
Non-gynaecological cytology	1,036	1,066	1,097	1,127	1,157
Complex	190	196	201	207	212
Non-complex	846	871	895	920	945
All cytology	8,244	8,334	8,424	8,514	8,605
Complex	1,511	1,528	1,544	1,561	1,577
Non-complex	6,733	6,806	6,880	6,953	7,027
Sub-total (excluding gynaecological cytology)	*6,041*	*6,252*	*6,463*	*6,675*	*6,886*
Sub-total (including all cytology)	*13,248*	*13,520*	*13,791*	*14,063*	*14,334*
TOTAL (*S1* and *S2* – excluding gynaecological cytology)	28,700	29,724	30,748	31,772	32,796
TOTAL (*S1* and *S2* – all cytology)	44,003	45,155	46,306	47,457	48,609

Source: Excel Section E workbook <Incremental services (SO items)>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.2-5 presents the estimated cost of the two second, expert opinion items over the first five years of the proposed listing. As discussed in Section E.1.4 the costs have been calculated using the 85% benefit for all cases – $153.00 and $314.50 for 'non-complex' and 'complex' second, expert opinions, respectively. The estimated total cost of the items also represents the incremental cost to the MBS, given that under current funding arrangements second, expert opinions are provided without MBS reimbursement; hence the current cost to the MBS is $0.

Table E.2-5 Estimated cost to the MBS of the proposed items for second, expert opinions, over the first five years of listing – Proposed funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	$7,912,188	$8,198,864	$8,485,547	$8,772,231	$9,058,912
Complex	$5,577,444	$5,779,527	$5,981,615	$6,183,704	$6,385,791
Non-complex	$2,334,744	$2,419,337	$2,503,932	$2,588,527	$2,673,122
Non-gynaecological cytology	$332,981	$342,641	$352,300	$361,960	$371,621
Complex	$106,280	$109,363	$112,446	$115,529	$118,613
Non-complex	$226,701	$233,278	$239,854	$246,431	$253,008
All cytology	$2,648,780	$2,677,727	$2,706,671	$2,735,615	$2,764,561
Complex	$845,430	$854,669	$863,908	$873,146	$882,385
Non-complex	$1,803,350	$1,823,057	$1,842,763	$1,862,469	$1,882,176
Sub-total (excluding gynaecological cytology)	*$8,245,168*	*$8,541,505*	*$8,837,847*	*$9,134,191*	*$9,430,533*
Sub-total (including all cytology)	*$10,560,968*	*$10,876,590*	*$11,192,218*	*$11,507,846*	*$11,823,473*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	$2,290,025	$2,372,998	$2,455,973	$2,538,948	$2,621,922
Complex	$1,072,543	$1,111,404	$1,150,266	$1,189,127	$1,227,989
Non-complex	$1,217,482	$1,261,594	$1,305,707	$1,349,820	$1,393,933
Non-gynaecological cytology	$226,174	$232,736	$239,297	$245,859	$252,420
Complex	$71,414	$73,486	$75,558	$77,630	$79,701
Non-complex	$154,760	$159,250	$163,739	$168,229	$172,719
All cytology	$1,799,163	$1,818,824	$1,838,484	$1,858,144	$1,877,806
Complex	$568,083	$574,291	$580,499	$586,707	$592,915
Non-complex	$1,231,079	$1,244,533	$1,257,985	$1,271,438	$1,284,891
Sub-total (excluding gynaecological cytology)	*$2,516,200*	*$2,605,734*	*$2,695,270*	*$2,784,806*	*$2,874,342*
Sub-total (including all cytology)	*$4,089,188*	*$4,191,822*	*$4,294,457*	*$4,397,092*	*$4,499,728*
TOTAL (*S1* and S*2* – excluding gynaecological cytology)	$10,761,368	$11,147,239	$11,533,117	$11,918,998	$12,304,875
TOTAL (*S1* and *S2* – all cytology)	$14,650,156	$15,068,413	$15,486,675	$15,904,938	$16,323,201

Source: Excel Section E workbook <MBS costs (SO items)>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

E.3. Estimation of changes in use and cost of other services

E.3.1. MBS items associated with the proposed service

As discussed in Section E.1.2, the financial analysis considers changes in use of ancillary tests (MBS items 72844-72852; 73059-73061; and 73064-73065), the specimen referred fee (MBS item 73940) and the bulk billing incentive (MBS item 74996) that are anticipated if second, expert opinions are funded through the MBS. Table E.3-1 shows the estimated number of services under the proposed funding arrangements and Table E.3-2 shows the corresponding information under the current funding arrangements.

Table E.3-1 Estimated number of services for other associated MBS items, over the first five years of the proposed MBS listing – Proposed funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	80,696	83,620	86,544	89,468	92,392
Ancillary tests	14,708	15,241	15,774	16,307	16,840
Specimen referred fee (MBS 73940)	32,994	34,190	35,385	36,580	37,776
Bulk billing incentive (MBS 74996)	32,994	34,190	35,385	36,580	37,776
Non-gynaecological cytology	3,919	4,033	4,147	4,260	4,374
Ancillary tests	280	288	296	304	313
Specimen referred fee (MBS 73940)	1,820	1,872	1,925	1,978	2,031
Bulk billing incentive (MBS 74996)	1,820	1,872	1,925	1,978	2,031
All cytology	31,177	31,518	31,859	32,200	32,540
Ancillary tests	2,228	2,252	2,277	2,301	2,325
Specimen referred fee (MBS 73940)	14,475	14,633	14,791	14,949	15,107
Bulk billing incentive (MBS 74996)	14,475	14,633	14,791	14,949	15,107
Sub-total (excluding gynaecological cytology)	*84,616*	*87,653*	*90,691*	*93,728*	*96,766*
Sub-total (including all cytology)	*111,874*	*115,138*	*118,403*	*121,667*	*124,932*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	26,757	27,726	28,696	29,665	30,635
Ancillary tests	4,021	4,167	4,313	4,458	4,604
Specimen referred fee (MBS 73940)	11,368	11,780	12,191	12,603	13,015
Bulk billing incentive (MBS 74996)	11,368	11,780	12,191	12,603	13,015
Non-gynaecological cytology	2,667	2,745	2,822	2,899	2,977
Ancillary tests	190	196	201	207	212
Specimen referred fee (MBS 73940)	1,239	1,275	1,310	1,346	1,382
Bulk billing incentive (MBS 74996)	1,239	1,275	1,310	1,346	1,382
All cytology	21,217	21,449	21,681	21,912	22,144
Ancillary tests	1,512	1,528	1,545	1,561	1,578
Specimen referred fee (MBS 73940)	9,853	9,960	10,068	10,176	10,283
Bulk billing incentive (MBS 74996)	9,853	9,960	10,068	10,176	10,283
Sub-total (excluding gynaecological cytology)	*29,424*	*30,471*	*31,518*	*32,564*	*33,611*
Sub-total (including all cytology)	*47,974*	*49,175*	*50,376*	*51,578*	*52,779*
TOTAL (*S1* and *S2* – excl. gynaecological cytology)	114,040	118,124	122,208	126,293	130,377
TOTAL (*S1* and *S2* – all cytology)	159,847	164,313	168,779	173,245	177,711

Source: Excel Section E workbook <MBS services (associated items)>, <Total MBS services>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.3-2 Estimated number of services for other associated MBS items, over the first five years of the proposed MBS listing – Current funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	5,471	5,669	5,867	6,065	6,264
Ancillary tests	5,471	5,669	5,867	6,065	6,264
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
Non-gynaecological cytology	92	95	97	100	103
Ancillary tests	92	95	97	100	103
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
All cytology	733	741	749	757	765
Ancillary tests	733	741	749	757	765
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
Sub-total (excluding gynaecological cytology)	*5,563*	*5,764*	*5,965*	*6,165*	*6,366*
Sub-total (including all cytology)	*6,204*	*6,410*	*6,616*	*6,822*	*7,029*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	2,339	2,424	2,509	2,593	2,678
Ancillary tests	2,339	2,424	2,509	2,593	2,678
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
Non-gynaecological cytology	28	29	30	30	31
Ancillary tests	28	29	30	30	31
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
All cytology	223	225	228	230	233
Ancillary tests	223	225	228	230	233
Specimen referred fee (MBS 73940)	0	0	0	0	0
Bulk billing incentive (MBS 74996)	0	0	0	0	0
Sub-total (excluding gynaecological cytology)	*2,367*	*2,453*	*2,538*	*2,624*	*2,709*
Sub-total (including all cytology)	*2,562*	*2,649*	*2,736*	*2,824*	*2,911*
TOTAL (*S1* and S*2* – excluding gynaecological cytology)	7,930	8,216	8,503	8,789	9,076
TOTAL (*S1* and *S2* – all cytology)	8,766	9,059	9,353	9,646	9,939

Source: Excel Section E workbook <MBS services (associated items)> , <Total MBS services>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.3-3 shows the incremental difference in service utilisation of ancillary items and other MBS items associated with second, expert opinion.

Table E.3-3 Incremental number of services for other associated MBS items, over the first five years of the proposed MBS listing

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	75,226	77,951	80,677	83,403	86,128
Ancillary tests	9,238	9,572	9,907	10,242	10,576
Specimen referred fee (MBS 73940)	32,994	34,190	35,385	36,580	37,776
Bulk billing incentive (MBS 74996)	32,994	34,190	35,385	36,580	37,776
Non-gynaecological cytology	3,827	3,938	4,049	4,160	4,271
Ancillary tests	188	193	199	204	210
Specimen referred fee (MBS 73940)	1,820	1,872	1,925	1,978	2,031
Bulk billing incentive (MBS 74996)	1,820	1,872	1,925	1,978	2,031
All cytology	30,444	30,777	31,110	31,443	31,775
Ancillary tests	1,495	1,511	1,528	1,544	1,560
Specimen referred fee (MBS 73940)	14,475	14,633	14,791	14,949	15,107
Bulk billing incentive (MBS 74996)	14,475	14,633	14,791	14,949	15,107
Sub-total (excluding gynaecological cytology)	*79,053*	*81,890*	*84,726*	*87,563*	*90,400*
Sub-total (including all cytology)	*105,670*	*108,728*	*111,787*	*114,845*	*117,903*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	24,418	25,302	26,187	27,072	27,957
Ancillary tests	1,682	1,743	1,804	1,865	1,926
Specimen referred fee (MBS 73940)	11,368	11,780	12,191	12,603	13,015
Bulk billing incentive (MBS 74996)	11,368	11,780	12,191	12,603	13,015
Non-gynaecological cytology	2,639	2,716	2,792	2,869	2,945
Ancillary tests	162	167	171	176	181
Specimen referred fee (MBS 73940)	1,239	1,275	1,310	1,346	1,382
Bulk billing incentive (MBS 74996)	1,239	1,275	1,310	1,346	1,382
All cytology	20,994	21,223	21,453	21,682	21,912
Ancillary tests	1,289	1,303	1,317	1,331	1,345
Specimen referred fee (MBS 73940)	9,853	9,960	10,068	10,176	10,283
Bulk billing incentive (MBS 74996)	9,853	9,960	10,068	10,176	10,283
Sub-total (excluding gynaecological cytology)	*27,057*	*28,018*	*28,979*	*29,941*	*30,902*
Sub-total (including all cytology)	*45,412*	*46,526*	*47,640*	*48,754*	*49,868*
TOTAL (*S1* and *S2* – excluding gynaecological cytology)	106,110	109,908	113,706	117,504	121,302
TOTAL (*S1* and *S2* – all cytology)	151,082	155,254	159,427	163,599	167,772

Source: Excel Section E workbook <Incremental services (assoc.)> & <Incremental services (all items)

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

Table E.3-4 presents the approximate cost to the MBS of the associated services shown in Table E.3-3. As discussed in Section E.1.4, the financial analysis adopted two different fees for ancillary tests under the proposed funding arrangements, which represent the current average cost of ancillary tests within Group P5 (tissue pathology) and Group P6 (cytology) of the MBS. The costs to the MBS of ancillary tests, the specimen referred fee and bulk billing incentive were all assumed to be $0 under current funding arrangements.

Table E.3-4 Estimated cost of other associated MBS items, over the first five years of the proposed MBS listing – Proposed funding arrangements

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	$1,301,060	$1,348,200	$1,395,342	$1,442,483	$1,489,624
Ancillary tests	$908,430	$941,345	$974,260	$1,007,175	$1,040,090
Specimen referred fee[b]	$288,698	$299,158	$309,619	$320,079	$330,540
Bulk billing incentive[c]	$103,931	$107,697	$111,463	$115,229	$118,994
Non-gynaecological cytology	$35,132	$36,152	$37,171	$38,190	$39,209
Ancillary tests	$13,479	$13,870	$14,261	$14,652	$15,043
Specimen referred fee[b]	$15,922	$16,384	$16,846	$17,308	$17,769
Bulk billing incentive[c]	$5,732	$5,898	$6,064	$6,231	$6,397
All cytology	$279,469	$282,523	$285,577	$288,631	$291,685
Ancillary tests	$107,219	$108,391	$109,563	$110,734	$111,906
Specimen referred fee[b]	$126,654	$128,038	$129,422	$130,806	$132,190
Bulk billing incentive[c]	$45,596	$46,094	$46,592	$47,090	$47,589
Sub-total (excluding gynaecological cytology)	*$1,336,192*	*$1,384,352*	*$1,432,512*	*$1,480,673*	*$1,528,834*
Sub-total (including all cytology)	*$1,580,529*	*$1,630,723*	*$1,680,919*	*$1,731,114*	*$1,781,309*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	$383,648	$397,548	$411,449	$425,350	$439,251
Ancillary tests	$248,372	$257,371	$266,371	$275,370	$284,369
Specimen referred fee[b]	$99,467	$103,071	$106,675	$110,279	$113,883
Bulk billing incentive[c]	$35,808	$37,106	$38,403	$39,701	$40,998
Non-gynaecological cytology	$23,884	$24,577	$25,270	$25,963	$26,656
Ancillary tests	$9,145	$9,411	$9,676	$9,941	$10,207
Specimen referred fee[b]	$10,838	$11,152	$11,466	$11,781	$12,095
Bulk billing incentive[c]	$3,902	$4,015	$4,128	$4,241	$4,354
All cytology	$189,995	$192,071	$194,147	$196,223	$198,300
Ancillary tests	$72,749	$73,544	$74,339	$75,134	$75,929
Specimen referred fee[b]	$86,210	$87,152	$88,094	$89,036	$89,978
Bulk billing incentive[c]	$31,036	$31,375	$31,714	$32,053	$32,392
Sub-total (excluding gynaecological cytology)	*$407,532*	*$422,126*	*$436,719*	*$451,313*	*$465,907*
Sub-total (including all cytology)	*$573,643*	*$589,619*	*$605,596*	*$621,573*	*$637,550*
TOTAL (*S1* and S*2* – excluding gynaecological cytology)	$1,743,725	$1,806,478	$1,869,232	$1,931,986	$1,994,740
TOTAL (*S1* and *S2* – all cytology)	$2,154,172	$2,220,343	$2,286,515	$2,352,688	$2,418,860

Source: Excel Section E workbook <MBS costs (associated items)> , <Total MBS costs>
Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*
[a] Includes bone marrow items
[b] MBS item 73940
[c] MBS item 74996

E.3.2. Change in use and cost of other services on the MBS

The financial analysis does not attempt to capture the use and cost of MBS services that are downstream of the provision of second, expert opinion. As was the case in the economic evaluation (see Section D.3.1), the financial analysis only captures costs related to attaining a second, expert opinion. The general nature of the requested listing and the paucity of data imposes limitations on the ability to consider both the cost-effectiveness and overall financial impact of the proposed listing beyond the point of a definitive diagnosis.

In terms of downstream resource use, second, expert opinions may result in a subsequent increase or decrease in the use of other services, such as those associated with biopsy, imaging, treatment and/or monitoring. As discussed in Section A.2, where second, expert opinions are requested due to pathologist or clinician uncertainty or a clinical need for diagnostic refinement, input is actively sought to arrive at a definitive diagnosis. In such cases, treatment will often be postponed until the expert opinion is received. Where the expert pathologist is able to confirm a diagnosis that was in doubt by the initial pathologist or clinician, the expert may also add significant information that could support either the initiation or withholding of specific therapy. In cases where the expert pathologist makes a major change to the submitted diagnosis, there may be an immediate alteration in the choice and timing of therapy, leading to reduced costs in terms of quality of life and effective utilisation of resources.

Under the current funding scenario, where second, expert opinions are sometimes not sought due to the cost, lack of funding, and perceived impost on colleagues, this can lead to a sub-optimal diagnosis. Thus, the proposed MBS service has the potential to positively impact on patient care via the more accurate classification of disease and thus more accurate planning and selection of therapy, and more rapid diagnosis of rare and diagnostically challenging cases.

E.4. Estimated financial implications on the MBS

Table E.4-1 presents a summary of the total aggregated cost to the MBS of the proposed listing for second, expert opinion including associated costs related to ancillary tests, specimen referral and bulk billing.

Table E.4-1 Estimated total cost to the MBS of second, expert opinion and associated services, over the first five years of the proposed MBS listing

	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Scenario 1	-	-	-	-	-
Tissue pathology[a]	$9,213,248	$9,547,064	$9,880,889	$10,214,714	$10,548,537
Second, expert opinion	$7,912,188	$8,198,864	$8,485,547	$8,772,231	$9,058,912
Ancillary tests	$908,430	$941,345	$974,260	$1,007,175	$1,040,090
Specimen referred fee[b]	$288,698	$299,158	$309,619	$320,079	$330,540
Bulk billing incentive[c]	$103,931	$107,697	$111,463	$115,229	$118,994
Non-gynaecological cytology	$368,113	$378,792	$389,471	$400,150	$410,830
Second, expert opinion	$332,981	$342,641	$352,300	$361,960	$371,621
Ancillary tests	$13,479	$13,870	$14,261	$14,652	$15,043
Specimen referred fee[b]	$15,922	$16,384	$16,846	$17,308	$17,769
Bulk billing incentive[c]	$5,732	$5,898	$6,064	$6,231	$6,397
All cytology	$2,928,249	$2,960,250	$2,992,248	$3,024,246	$3,056,246
Second, expert opinion	$2,648,780	$2,677,727	$2,706,671	$2,735,615	$2,764,561
Ancillary tests	$107,219	$108,391	$109,563	$110,734	$111,906
Specimen referred fee[b]	$126,654	$128,038	$129,422	$130,806	$132,190
Bulk billing incentive[c]	$45,596	$46,094	$46,592	$47,090	$47,589
Sub-total (excluding gynaecological cytology)	*$9,581,360*	*$9,925,856*	*$10,270,360*	*$10,614,865*	*$10,959,366*
Sub-total (including all cytology)	*$12,141,497*	*$12,507,314*	*$12,873,137*	*$13,238,960*	*$13,604,783*
Scenario 2	-	-	-	-	-
Tissue pathology[a]	$2,673,673	$2,770,546	$2,867,422	$2,964,298	$3,061,172
Second, expert opinion	$2,290,025	$2,372,998	$2,455,973	$2,538,948	$2,621,922
Ancillary tests	$248,372	$257,371	$266,371	$275,370	$284,369
Specimen referred fee[b]	$99,467	$103,071	$106,675	$110,279	$113,883
Bulk billing incentive[c]	$35,808	$37,106	$38,403	$39,701	$40,998
Non-gynaecological cytology	$250,059	$257,313	$264,567	$271,822	$279,076
Second, expert opinion	$226,174	$232,736	$239,297	$245,859	$252,420
Ancillary tests	$9,145	$9,411	$9,676	$9,941	$10,207
Specimen referred fee[b]	$10,838	$11,152	$11,466	$11,781	$12,095
Bulk billing incentive[c]	$3,902	$4,015	$4,128	$4,241	$4,354
All cytology	$1,989,157	$2,010,895	$2,032,631	$2,054,368	$2,076,106
Second, expert opinion	$1,799,163	$1,818,824	$1,838,484	$1,858,144	$1,877,806
Ancillary tests	$72,749	$73,544	$74,339	$75,134	$75,929
Specimen referred fee[b]	$86,210	$87,152	$88,094	$89,036	$89,978
Bulk billing incentive[c]	$31,036	$31,375	$31,714	$32,053	$32,392
Sub-total (excluding gynaecological cytology)	*$2,923,732*	*$3,027,860*	*$3,131,989*	*$3,236,119*	*$3,340,249*
Sub-total (including all cytology)	*$4,662,830*	*$4,781,442*	*$4,900,053*	*$5,018,665*	*$5,137,278*
TOTAL (*S1* and S*2* – excluding gynaecological cytology)	$12,505,092	$12,953,716	$13,402,349	$13,850,984	$14,299,615
TOTAL (*S1* and *S2* – all cytology)	$16,804,327	$17,288,756	$17,773,190	$18,257,625	$18,742,061

Source: Excel Section E workbook <Total MBS costs>

Abbreviations: S1, *Scenario 1*; S2, *Scenario 2.*

[a] Includes bone marrow items

[b] MBS item 73940

[c] MBS item 74996

The estimated costs presented in Table E.4-1 also represent the total incremental cost of the proposed and associated services to the MBS, given that under current funding arrangements the relevant services are provided either without MBS reimbursement or not at all (i.e. specimen referred fee and bulk billing incentive). A simplified version is presented in Table E.4-2, which shows the total incremental costs including both *Scenario 1* and *Scenario 2* (pathologist- and clinician-initiated referrals), excluding and including gynaecological cytology.

Table E.4-2 Summary of total incremental cost of second, expert opinion and associated services, over the first five years of the proposed MBS listing

Total incremental cost	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Excluding gynaecological cytology	$12,505,092	$12,953,716	$13,402,349	$13,850,984	$14,299,615
Including gynaecological cytology	$16,804,327	$17,288,756	$17,773,190	$18,257,625	$18,742,061

Source: Excel Section E workbook <Incremental costs (all items)>

E.5. Estimated financial implications for Government health budgets

As discussed in Section E.3, the financial analysis does not attempt to capture the potential downstream costs or cost-savings that could be attributed to the proposed listing. For example, the revision of a diagnosis from malignant to benign could result in savings to other Government health budgets through the avoidance of unnecessary treatment (e.g. chemotherapy). Conversely, Government health budgets may face increased costs in some cases where a previously benign provisional diagnosis is changed to malignant. In such cases, increased downstream treatment costs would result from a need for therapy (chemotherapy, for example) that would otherwise have been withheld. On the other hand, where a previously benign provisional diagnosis is changed to malignant, there may be reduced costs to the MBS and other Government health budgets from treating early-stage cancer rather than advanced cancer.

E.6. Identification, estimation and reduction of uncertainty

Sensitivity analyses were performed to examine how robust the main findings of the financial analysis are to possible variations in key assumptions. Section E.6 presents a number of sensitivity analyses using a base case in which gynaecological cytology cases ('core' MBS items 73053, 73055 and 73057) are excluded from the proposed listing.

In contrast, the base case adopted in Section E.6.2 assumes that all cytology cases (along with all bone marrow and tissue pathology cases) are eligible for MBS reimbursement of second, expert opinions. The main reason for the separate analysis in Section E.6.2 is to show the financial impact of proposed changes to the NCSP.

E.6.1. Sensitivity analyses – base case excludes gynaecological cytology

It was anticipated that the financial estimates would be most sensitive to variations in the proportion of cases referred for second, expert opinion. In particular, the proportion of cases referred for second, expert opinion under the proposed funding arrangements are highly uncertain, given that the best available estimates rely on an Expert Opinion Survey

with a very small number of respondents (although representing large pathology practices; see Appendix 1). As such, four different sensitivity analyses were conducted using higher and lower estimates (see Table E.6-1).

In *Sensitivity analysis 1* the median was used to summarise the results of the Expert Opinion Survey rather than the mean. The rationale for *Sensitivity analysis 1* was that the results of the Expert Opinion Survey did not appear to be normally distributed and could arguably be better summarised using the median.

Furthermore, one set of expert responses contained several outliers and a sensitivity analysis (*Sensitivity analysis 2*) was therefore conducted using calculated averages which excluded their estimates. In order to maintain internal consistency, all of the responses from the respondent in question (not only the estimate of proportion of cases referred for second, expert opinion) were excluded from the averages. The same approach was adopted in *Sensitivity analyses 1* and *3*.

Sensitivity analysis 3 used the estimates from one of the HESP members assigned to MSAC Application 1332. These estimates were generally towards the lower end of the range of responses.

Finally, a sensitivity analysis was conducted using estimates for the proportion of cases referred that were higher than the mean. *Sensitivity analysis 4* used an estimated referral rate of 2% under proposed funding arrangements – equal to the higher end of the range provided by the Applicant in their pre-assessment documentation and also equal to the highest estimate for tissue pathology under the proposed funding arrangements (aside from the aforementioned outlier of who estimated "<5%"). In *Sensitivity analysis 4*, only the estimate for the proportion of cases referred for second, expert opinion under the proposed funding arrangements was altered. Changes to the proportion referred under current funding arrangements would have no impact on the total or incremental cost of the listing, as the service bears no cost to the MBS under current funding arrangements.

The results of the sensitivity analyses are presented in Table E.6-2.

Table E.6-1 Proportion of cases referred for second, expert opinion under the proposed funding arrangements – estimates used in sensitivity analyses

Analysis	Assumption	Proportion referred (%) – Tissue pathology	Proportion referred (%) – Cytology
Base case	Table E.1-3	1.41%	1.17%
Sensitivity analysis 1	Expert opinion survey results summarised using the median response (the mean was used in the base case).	1.00%	0.50%
Sensitivity analysis 2	Calculated averages excluded one respondent's estimates which contained several outliers.	0.90%	0.53%
Sensitivity analysis 3	Assume that calculated averages in the base case were generally overestimates. The sensitivity analysis uses lower estimates (provided by one of the HESP members who completed the survey).	0.30%	0.10%
Sensitivity analysis 4	Assume that the base case proportion of cases that would be referred to an expert under proposed funding arrangements was an underestimate. The sensitivity analysis tests a higher referral rate than the base case.	2.00%	2.00%

In addition, several other sensitivity analyses were conducted in which other key assumptions were altered:

- Assume no distinction between 'complex' and 'non-complex' second, expert opinions; thus only one MBS Schedule fee would be used. The sensitivity analysis assumes a Schedule fee of $200 and 85% benefit of $170 (*Sensitivity analysis 5*).
- Assume that 100% of pathologist-initiated second, expert opinions on tissue pathology samples require more than 30 minutes of the expert pathologist's time to review and produce a written report – i.e. 100% of *Scenario 1* tissue pathology cases would be charged according to the proposed 'complex' MBS item fee (*Sensitivity analysis 6*).
- Assume that second, expert opinions would not be requested for complexity 2 or 3 items – MBS items 72813-72818 (*Sensitivity analysis 7*).

The rationale for *Sensitivity analysis 7* is based on the possibility that the Expert Opinion Survey overestimated the proportion of all initial pathology cases that would be referred for second, expert opinion. It is reasonable to assume that expert pathologists (who often work in large hospital laboratories) may have overlooked the large number of initial opinions for relatively straightforward skin and gastrointestinal tract (GIT) biopsies that are conducted in private laboratories around Australia. Therefore, *Sensitivity analysis 7* was conducted by removing the number of initial pathology opinions that are charged to the lower complexity items (i.e. MBS items 72813-72818) and applying the base case estimates for the proportion of cases referred to a smaller overall number of services.

Table E.6-2 presents the results for the seven sensitivity analyses.

Table E.6-2 Estimated total incremental costs of the proposed and associated services over the first five years of the proposed MBS listing: Results of sensitivity analyses

Analysis	Assumption	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Base case	Table E.4-2	$12,505,092	$12,953,716	$13,402,349	$13,850,984	$14,299,615
Sensitivity analysis 1	Expert opinion survey results summarised using the median.	$8,976,757	$9,300,238	$9,623,726	$9,947,215	$10,270,701
Sensitivity analysis 2	Calculated averages excluded one respondent's set of estimates, which contained several outliers.	$8,234,843	$8,531,116	$8,827,395	$9,123,675	$9,419,953
Sensitivity analysis 3	The sensitivity analysis uses responses from one of a HESP member who completed the survey.	$2,545,984	$2,637,846	$2,729,710	$2,821,575	$2,913,439
Sensitivity analysis 4	The sensitivity analysis tests a higher second, expert opinion rate (under proposed funding arrangements) than the base case.	$17,886,453	$18,526,898	$19,167,356	$19,807,817	$20,448,273
Sensitivity analysis 5	Assume a one-tier fee structure – Schedule fee $200; 85% benefit $170.	$9,805,126	$10,156,207	$10,507,295	$10,858,386	$11,209,473
Sensitivity analysis 6	Assume that all Scenario 1 tissue pathology cases are 'complex' – involving more than 30 minutes of expert pathologist's time.	$15,334,763	$15,885,912	$16,437,073	$16,988,236	$17,539,394
Sensitivity analysis 7	Assume that second, expert opinion is not requested for complexity 2 or 3 items (MBS items 72813-72818).	$5,984,984	$6,267,373	$6,549,767	$6,832,168	$7,114,561

Source: Excel Section E workbook <Incremental costs (all items)>

E.6.2. Sensitivity analyses – base case includes gynaecological cytology

Table E.6-3 shows a base case in which all bone marrow, tissue pathology and cytology cases (including gynaecological cytology) are eligible for MBS reimbursement for second, expert opinions. As outlined in Section A.2.5, it is anticipated that a substantial decrease in overall cytology utilisation could occur in 2016, when proposed changes to the NCSP (recommended by MSAC in April 2014) could come into effect.

The renewed screening pathway involves five-yearly screening with HPV testing as the primary screening test. According to the Public Summary Document from the April 2014 MSAC meeting[12], the estimated use of cytology for cervical screening is expected to decrease from 2.4 million per year in 2016 to 0.34 million per year. The estimated reduction equates to an 86% decrease.

A sensitivity analysis (*Sensitivity analysis 8*) was conducted to show the impact that the proposed changes to the screening pathway may have on the cost to the MBS of second, expert opinions. The projected number of initial cytology services to Year 5 were recalculated based on the projected utilisation estimates for all 'core' cytology items (Table E.1-2), with an 86% decrease applied to MBS items 73053 and 73055 from 2016 (i.e. halfway through Year 1). The total incremental cost under the proposed changes is therefore lower, as the costs are applied to a smaller number of services (*Sensitivity analysis 8*, Table E.6-3).

Table E.6-3 Estimated total incremental costs of the proposed and associated services over the first five years of the proposed MBS listing: Results of sensitivity analysis

Analysis	Assumption	Year 1 (2015-16)	Year 2 (2016-17)	Year 3 (2017-18)	Year 4 (2018-19)	Year 5 (2019-20)
Base case	Table E.4-2	$16,804,327	$17,288,756	$17,773,190	$18,257,625	$18,742,061
Sensitivity analysis 8	Assume that proposed changes to the NCSP come into effect at the beginning of 2016. Assume an immediate 86% decrease in use of MBS items 73053 and 73055.	$14,983,693	$13,614,312	$14,065,575	$14,516,839	$14,968,101

Source: Excel Section E workbook <Incremental costs (all items)>
Abbreviations: NCSP, National Cervical Screening Program

[12] MSAC 61st Meeting (3-4 April 2014) Outcomes for Application No. 1276 – Renewal of the National Cervical Screening Program [available at http://www.msac.gov.au/]

Section F. Options to present additional relevant information

F.1. Issues relating to equity principles

The introduction of the proposed service for second, expert opinions is likely to be of particular value in regional and remote areas of Australia. Under current funding arrangements, pathologists working in small or single-pathologist laboratories in remote areas have little or no access to expert pathologists and may be less able to provide a primary or definitive diagnosis than pathologists in metropolitan areas who have a greater opportunity to approach colleagues for intra-institutional second and/or expert opinion. In addition, there may be a financial disincentive to seek a second, expert opinion because the patient or their laboratory/hospital are likely to be charged for the service, plus any associated transportation costs. As such, there is a justifiable argument for the funding of second, expert opinions for morphological pathology to address issues of inequity.

Appendix 1. Health Expert Standing Panel and Assessment Group

Health Expert Standing Panel

Member	Expertise or Affiliation
Professor Adrienne Morey	Expert on HER2 in breast cancer, Gastric anatomical pathology, Chair of the RCPA Anatomical Pathology Advisory Committee
Professor Jane Dahlstrom	Anatomical Pathology and Autopsy Pathology

Assessment Group

Name	Organisation
Ms Kate Applegarth	HealthConsult Pty Ltd
Dr Suzanne Campbell	HealthConsult Pty Ltd
Dr Lisa Fodero	HealthConsult Pty Ltd
Mr Joe Scuteri	HealthConsult Pty Ltd
Mr Paul Mernagh	Subcontractor for HealthConsult Pty Ltd

Appendix 2. Item numbers and descriptors

MBS item descriptors and fees are reproduced below for Group P1 (Haematology), Group P5 (Tissue pathology) and Group P6 (Cytology). The related Explanatory Notes are provided thereafter.

	GROUP P1 - HAEMATOLOGY
65084	Bone marrow trephine biopsy - histopathological examination of sections of bone marrow and examination of aspirated material (including clot sections where necessary), including (if performed): any test described in item 65060, 65066 or 65070 Fee: $165.85 Benefit: 75% = $124.40 85% = $141.00
65087	Bone marrow - examination of aspirated material (including clot sections where necessary), including (if performed): any test described in item 65060, 65066 or 65070 Fee: $83.10 Benefit: 75% = $62.35 85% = $70.65

Source: MBS Online, accessed 10 June 2014

	GROUP P5 – TISSUE PATHOLOGY
72813	Examination of complexity level 2 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 or more separately identified specimens (Item is subject to rule 13) Fee: $71.50 Benefit: 75% = $53.65 85% = $60.80
72816	Examination of complexity level 3 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 separately identified specimen (Item is subject to rule 13) Fee: $86.35 Benefit: 75% = $64.80 85% = $73.40
72817	Examination of complexity level 3 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 2 to 4 separately identified specimens (Item is subject to rule 13) Fee: $96.80 Benefit: 75% = $72.60 85% = $82.30
72818	Examination of complexity level 3 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 5 or more separately identified specimens (Item is subject to rule 13) Fee: $107.05 Benefit: 75% = $80.30 85% = $91.00
72823	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 separately identified specimen

	GROUP P5 – TISSUE PATHOLOGY
	(Item is subject to rule 13) Fee: $97.15 Benefit: 75% = $72.90 85% = $82.60
72824	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 2 to 4 separately identified specimens (Item is subject to rule 13) Fee: $141.35 Benefit: 75% = $106.05 85% = $120.15
72825	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 5 to 7 separately identified specimens (Item is subject to rule 13) Fee: $180.25 Benefit: 75% = $135.20 85% = $153.25
72826	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 8 to 11 separately identified specimens (Item is subject to rule 13) Fee: $194.60 Benefit: 75% = $145.95 85% = $165.45
72827	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions – 12 to 17 separately identified specimens (Item is subject to Rule 13) Fee: $208.95 Benefit: 75% = $156.75 85% = $177.65
72828	Examination of complexity level 4 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions – 18 or more separately identified specimens (Item is subject to Rule 13) Fee: $223.30 Benefit: 75% = $167.50 85% = $189.85
72830	Examination of complexity level 5 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 or more separately identified specimens (Item is subject to rule 13) Fee: $274.15 Benefit: 75% = $205.65 85% = $233.05
72836	Examination of complexity level 6 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 or more separately identified specimens (Item is subject to rule 13) Fee: $417.20 Benefit: 75% = $312.90 85% = $354.65
72838	Examination of complexity level 7 biopsy material with multiple tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 or more separately identified specimens. (Item is subject to rule 13) Fee: $466.85 Benefit: 75% = $350.15 85% = $396.85

	GROUP P5 – TISSUE PATHOLOGY
72844	Enzyme histochemistry of skeletal muscle for investigation of primary degenerative or metabolic muscle diseases or of muscle abnormalities secondary to disease of the central or peripheral nervous system - 1 or more tests Fee: $30.75 Benefit: 75% = $23.10 85% = $26.15
72846	Immunohistochemical examination of biopsy material by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 1 to 3 antibodies except those listed in 72848 (Item is subject to rule 13) Fee: $59.60 Benefit: 75% = $44.70 85% = $50.70
72847	Immunohistochemical examination of biopsy material by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 4-6 antibodies (Item is subject to rule 13) Fee: $89.40 Benefit: 75% = $67.05 85% = $76.00
72848	Immunohistochemical examination of biopsy material by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 1 to 3 of the following antibodies - oestrogen, progesterone and c-erb-B2 (HER2) (Item is subject to rule 13) Fee: $74.50 Benefit: 75% = $55.90 85% = $63.35
72849	Immunohistochemical examination of biopsy material by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen – 7-10 antibodies (Item is subject to rule 13) Fee: $104.30 Benefit: 75% = $78.25 85% = $88.70
72850	Immunohistochemical examination of biopsy material by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen – 11 or more antibodies (Item is subject to rule 13) Fee: $119.20 Benefit: 75% = $89.40 85% = $101.35
72851	Electron microscopic examination of biopsy material - 1 separately identified specimen (Item is subject to rule 13) Fee: $184.35 Benefit: 75% = $138.30 85% = $156.70
72852	Electron microscopic examination of biopsy material - 2 or more separately identified specimens (Item is subject to rule 13) Fee: $245.80 Benefit: 75% = $184.35 85% = $208.95
72855	Intraoperative consultation and examination of biopsy material by frozen section or tissue imprint or smear - 1 separately identified specimen (Item is subject to rule 13) Fee: $184.35 Benefit: 75% = $138.30 85% = $156.70
72856	Intraoperative consultation and examination of biopsy material by frozen section or tissue imprint or smear - 2 to 4 separately identified specimens (Item is subject to rule 13) Fee: $245.80 Benefit: 75% = $184.35 85% = $208.95

	GROUP P5 – TISSUE PATHOLOGY
72857	Intraoperative consultation and examination of biopsy material by frozen section or tissue imprint or smear - 5 or more separately identified specimens (Item is subject to rule 13) Fee: $286.75 Benefit: 75% = $215.10 85% = $243.75

Source: MBS Online, accessed 10 June 2014

	GROUP P6 - CYTOLOGY
73043	Cytology (including serial examinations) of nipple discharge or smears from skin, lip, mouth, nose or anus for detection of precancerous or cancerous changes 1 or more tests Fee: $22.85 Benefit: 75% = $17.15 85% = $19.45
73045	Cytology (including serial examinations) for malignancy (other than an examination mentioned in item 73053); and including any Group P5 service, if performed on: (a) specimens resulting from washings or brushings from sites not specified in item 73043; or (b) a single specimen of sputum or urine; or (c) 1 or more specimens of other body fluids; 1 or more tests Fee: $48.60 Benefit: 75% = $36.45 85% = $41.35
73047	Cytology of a series of 3 sputum or urine specimens for malignant cells Fee: $94.70 Benefit: 75% = $71.05 85% = $80.50
73049	Cytology of material obtained directly from a patient by fine needle aspiration of solid tissue or tissues - 1 identified site Fee: $68.15 Benefit: 75% = $51.15 85% = $57.95
73051	Cytology of material obtained directly from a patient at one identified site by fine needle aspiration of solid tissue or tissues if a recognized pathologist: (a) performs the aspiration; or (b) attends the aspiration and performs cytological examination during the attendance Fee: $170.35 Benefit: 75% = $127.80 85% = $144.80
73053	Cytology of a smear from cervix where the smear is prepared by direct application of the specimen to a slide, excluding the use of liquid based slide preparation techniques, and the stained smear is microscopically examined by or on behalf of a pathologist - each examination (a) for the detection of precancerous or cancerous changes in women with no symptoms, signs or recent history suggestive of cervical neoplasia, or (b) if a further specimen is taken due to an unsatisfactory smear taken for the purposes of paragraph (a); or (c) if there is inadequate information provided to use item 73055; (See para P16.11 of explanatory notes to this Category) Fee: $19.45 Benefit: 75% = $14.60 85% = $16.55
73055	Cytology of a smear from cervix, not associated with item 73053, where the smear is prepared by direct application of the specimen to a slide, excluding the use of liquid based slide preparation techniques, and the stained smear is microscopically examined by or on behalf of a pathologist - each test (a) for the management of previously detected abnormalities including precancerous or cancerous conditions; or (b) for the investigation of women with symptoms, signs or recent history suggestive of cervical neoplasia; (See para P16.11 of explanatory notes to this Category)

	GROUP P6 - CYTOLOGY
	Fee: $19.45 Benefit: 75% = $14.60 85% = $16.55
73057	Cytology of smears from vagina, not associated with item 73053 or 73055 and not to monitor hormone replacement therapy, where the smear is prepared by direct application of the specimen to a slide, excluding the use of liquid based slide preparation techniques, and the stained smear is microscopically examined by or on behalf of a pathologist - each test (See para P16.11 of explanatory notes to this Category) Fee: $19.45 Benefit: 75% = $14.60 85% = $16.55
73059	Immunocytochemical examination of material obtained by procedures described in items 73045, 73047, 73049, 73051, 73062, 73063, 73066 and 73067 for the characterisation of a malignancy by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 1 to 3 antibodies except those listed in 73061 (Item is subject to rule 13) Fee: $43.00 Benefit: 75% = $32.25 85% = $36.55
73060	Immunocytochemical examination of material obtained by procedures described in items 73045, 73047, 73049, 73051, 73062, 73063, 73066 and 73067 for the characterisation of a malignancy by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 4 to 6 antibodies (Item is subject to rule 13) Fee: $57.35 Benefit: 75% = $43.05 85% = $48.75
73061	Immunocytochemical examination of material obtained by procedures described in items 73045, 73047, 73049, 73051, 73062, 73063, 73066 and 73067 for the characterisation of a malignancy by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 1 to 3 of the following antibodies - oestrogen, progesterone and c-erb-B2 (HER2) (Item is subject to rule 13) Fee: $51.20 Benefit: 75% = $38.40 85% = $43.55
73062	Cytology of material obtained directly from a patient by fine needle aspiration of solid tissue or tissues – 2 or more separately identified sites. Fee: $89.00 Benefit: 75% = $66.75 85% = $75.65
73063	Cytology of material obtained directly from a patient at one identified site by fine needle aspiration of solid tissue or tissues if an employee of an approved pathology authority attends the aspiration for confirmation of sample adequacy Fee: $99.35 Benefit: 75% = $74.55 85% = $84.45
73064	Immunocytochemical examination of material obtained by procedures described in items 73045, 73047, 73049, 73051, 73062, 73063, 73066 and 73067 for the characterisation of a malignancy by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen – 7 to 10 antibodies (Item is subject to rule 13) Fee: $71.70 Benefit: 75% = $53.80 85% = $60.95
73065	Immunocytochemical examination of material obtained by procedures described in items 73045, 73047, 73049, 73051, 73062, 73063, 73066 and 73067 for the characterisation of a malignancy by immunofluorescence, immunoperoxidase or other labelled antibody techniques with multiple antigenic specificities per specimen - 11 or more antibodies

	GROUP P6 - CYTOLOGY
	(Item is subject to rule 13) Fee: $86.00 Benefit: 75% = $66.75 85% = $75.65
73066	Cytology of material obtained directly from a patient at 2 or more separately identified sites by fine needle aspiration of solid tissue or tissues if a recognized pathologist: (a) performs the aspiration; or (b) attends the aspiration and performs cytological examination during the attendance Fee: $221.45 Benefit: 75% = $166.10 85% = $188.25
73067	Cytology of material obtained directly from a patient at 2 or more separately identified sites by fine needle aspiration of solid tissue or tissues if an employee of an approved pathology authority attends the aspiration for confirmation of sample adequacy Fee: $129.15 Benefit: 75% = $96.90 85% = $109.80

Source: MBS Online, accessed 10 June 2014

P19.1 Rules for the Interpretation of the Pathology Services Table *(excerpts – relevant to this Assessment Report only)*

Please note that in the Health Insurance (Pathology Services Table) Regulations 2010 (effective 1 November 2010) rules and sub-rules are referred to as clauses and sub-clauses. In addition in the Regulations a rule that refers to specific items within a pathology group, for example Group P1 Haematology, is listed directly above the Schedule of Services for that group.

1. (1) In this table

patient episode means:

(a) a pathology service or pathology services (other than a pathology service to which paragraph 1 (1) (b) refers) provided for a single patient whose need for the service or services was determined under section 16A of the Act:

(i) on the same day; or

(ii) if more than 1 test is performed on the 1 specimen within 14 days - on the same or different days;

whether the services:

(iii) are requested by 1 or more practitioners; or

(iv) are described in a single item or in more than 1 item; or

(v) are rendered by 1 approved pathology practitioner or more than 1 approved pathology practitioner; or

(vi) are rendered on the same or different days; or

(b) a pathology service to which rule 4 refers that is provided in the circumstances set out in that rule that relates to the service.

receiving APP means an approved pathology practitioner in an approved pathology authority who performs one or more pathology services in respect of a single patient episode following receipt of a request for those services from a referring APP.

recognised pathologist means a medical practitioner recognised as a specialist in pathology by a

determination under section 3D, 3DB or 3E of the Act.

referring APP means an approved pathology practitioner in an approved pathology authority who:

(i) has been requested to render 1 or more pathology services, all of which are requested in a single patient episode; and

(ii) is unable, because of the lack of facilities in, or expertise or experience of the staff of, the laboratory of the authority, to render 1 or more of the pathology services; and

(iii) requests an approved pathology practitioner (the *receiving APP*) in another approved pathology authority to render the pathology service or services that the referring APP is unable to render; and

(iv) renders each pathology service (if any) included in that patient episode, other than the pathology service or services in respect of which the request mentioned in subparagraph (iii) is made.

serial examinations means a series of examinations requested on 1 occasion whether or not:

(a) the materials are received on different days by the approved pathology practitioner; or

(b) the examinations or cultures were requested on 1 or more request forms by the treating practitioner.

the Act means the *Health Insurance Act 1973.*

1. (2) In these rules, a reference to a request to an approved pathology practitioner includes a reference to a request for a pathologist-determinable service to which subsection 16A (6) of the Act applies.

1. (3) A reference in this table by number to an item that is not included in this table is a reference to the item that has that number in the general medical services table or the diagnostic imaging services table, as the case requires.

1. (4) A reference to a Group in the table includes every item in the Group and a reference to a Subgroup in the table includes every item in the Subgroup.

Precedence of items

2. (1) If a service is described:

(a) in an item in general terms; and

(b) in another item in specific terms;

only the item that describes the service in specific terms applies to the service.

2. (2) Subject to subrule (3), if:

(a) subrule (1) does not apply; and

(b) a service is described in 2 or more items;

only the item that provides the lower or lowest fee for the service applies to the service.

2. (3) If an item is expressed to include a pathology service that is described in another item, the other item does not apply to the service in addition to the first-mentioned item, whether or not the services described in the 2 items are

requested separately.

Circumstances in which services rendered following 2 requests to be taken to have been rendered following 1 request

3. (1) In subrule 3(2), *service* includes assay, estimation and test.

3. (2) Two or more pathology services (other than services to which, under rule 4, this rule does not apply) rendered for a patient following 2 or more requests are taken to have been rendered following a single request if:

(a) the services are listed in the same item; and

(ab) that item is not item 74990 or 74991; and

(b) the patient's need for the services was determined under subsection 16A (1) of the Act on the same day even if the services are rendered by an approved pathology practitioner on more than one day.

Services to which rule 3 does not apply

4. (1) Rule 3 does not apply to a pathology service described in item 65060, 65070, 65120, 65123, 65126, 65129, 65150, 65153, 65156, 66500, 66503, 66506, 66509, 66512, 66584 or 66800, if:

(a) the service is rendered in relation to one or more specimens taken on each of not more than 6 separate occasions in a period of 24 hours; and

(b) the service is rendered to an inpatient in a hospital; and

(c) each service must be rendered as soon as possible after collection and after authorization of the result of the previous specimen; and

(d) the account for the service is endorsed 'Rule 3 Exemption'.

4. (2) Rule 3 does not apply to any of the following pathology services:

(a) estimation of prothrombin time (INR) in respect of a patient undergoing anticoagulant therapy;

(b) quantitative estimation of lithium in respect of a patient undergoing lithium therapy;

(c) a service described in item 65070 in relation to a patient undergoing chemotherapy for neoplastic disease or immunosuppressant therapy;

(d) a service described in item 65070 in relation to clozaril, ticlopidine hydrochloride, methotrexate, gold, sulphasalazine or penicillamine therapy of a patient;

(e) a service described in item 66500 - 66512 in relation to methotrexate or leflunomide therapy of a patient;

(f) quantitative estimation of urea, creatinine and electrolytes in relation to:

(i) cis-platinum or cyclosporin therapy of a patient; or

(ii) chronic renal failure of a patient being treated in a dialysis program conducted by a recognised hospital;

(g) quantitative estimation of albumin and calcium in relation to therapy of a patient with vitamin D, its metabolites or analogues;

(h) quantitative estimation of calcium, phosphate, magnesium, urea, creatinine and electrolytes in cancer patients receiving bisphosphonate infusions.

if:

(i) under a request for a service, other than a request for a service described in paragraph (a), no more than 6 tests are requested; and

(ii) the tests are performed within 6 months of the request; and

(iii) the account for the service is endorsed "Rule 3 Exemption".

4. (3) Rule 3 does not apply to a pathology service described in items 65109 or 65110 if:

(a) The service is rendered on not more than 5 separate occasions in the case of item 65109 and 2 separate occasions in the case of item 65110 in a period of 24 hours; and

(b) The service is rendered in response to a written request separated in time from the previous request; and

(c) The account for the service is endorsed "Rule 3 Exemption".

Certain items not to apply to a service referred by one pathology practitioner to another

6. (1) In this rule:

designated pathology service means a pathology service in respect of tests relating to a single patient episode that are tests of the kind described in item 65150, 65175, 66650, 66695, 66711, 66722, 66785, 66800, 66812, 66819, 66825, 69384, 69494, 71089, 71153 or 71165.

6. (2) This rule applies in respect of a designated pathology service where:

(a) an approved pathology practitioner *(practitioner A)* in an approved pathology authority:

(i) has been requested to render the designated pathology service; and

(ii) is unable, because of the lack of facilities in, or expertise or experience of the staff of, the laboratory of the authority, to render 1 or more of the tests included in the service; and

(iii) requests an approved pathology practitioner *(practitioner B)* in another approved pathology authority to render the test or tests that practitioner A is unable to render; and

(iv) renders each test (if any) included in the service, other than the test or tests in respect of which the request mentioned in subparagraph (iii) is made; and

(b) the tests mentioned in subparagraph (a) (iv) that practitioner A renders are not tests constituting a service described in item 65156, 65179, 66653, 66712, 66734, 66788, 66806, 66815, 66822, 66828, 69496, 71093, 71159 or 71168.

6. (3) If this rule applies in respect of a designated pathology service:

(a) item 65150, 65153, 65175, 65176, 65177, 65178, 66650, 66695, 66698, 66701, 66704, 66707, 66711, 66722, 66725, 66728, 66731, 66785, 66800, 66803, 66812, 66819, 66825, 69384, 69387, 69390, 69393, 69396,

69494, 69495, 71089, 71091, 71153, 71155, 71157, 71165, 71166 or 71167 (as the case requires) applies in respect of the test or tests rendered by practitioner A; and

(b) where practitioner B renders a service under a request referred to in subparagraph (2) (a) (iii) and:

(i) practitioner A has rendered one or more of the tests that the service comprises - subject to subrule (4), the amount specified in item 65158, 65181, 66652, 66697, 66715, 66724, 66790, 66805, 66817, 66821, 66827, 69401, 69498, 71092, 71156 or 71170 (as the case requires) shall be taken to be the fee for each test that the service comprises; or

(ii) practitioner A has not rendered any of the tests that the service comprises -

(A) the amount specified in item 65157, 65180, 66651, 66696, 66714, 66723, 66789, 66804, 66816, 66820, 66826, 69400, 69497, 71090, 71154 or 71169 (as the case requires) shall be taken to be the fee for the first test that the service comprises; and

(B) subject to subrule (4), the amount specified in item 65158, 65181, 66652, 66697, 66715, 66724, 66790, 66805, 66817, 66821, 66827, 69401, 69498, 71092, 71156 or 71170 (as the case requires) shall be taken to be the fee for each subsequent test that the service comprises.

6. (4) For paragraph (3) (b), the maximum number of tests to which item 65158, 65181, 66652, 66697, 66715, 66724, 66790, 66805, 66817, 66821, 66827, 69401, 69498, 71092, 71156 or 71170 applies is:

(a) for item 66652, 66715, 66790, 66817, 66821 or 66827:

2 - X; and

(b) for item 66805, 69498 or 71092:

3 - X; and

(c) for item 71156 or 71170:

4 - X; and

(d) for item 66724:

5 - X; and

where X is the number of tests rendered by practitioner A in relation to the designated pathology service in respect of which the request mentioned in that paragraph is made.

6. (5) Items in Group P10 (Patient episode initiation) do not apply to the second mentioned approved pathology practitioner in subrule (2).

Items not to be split

7. Except as stated in rule 6, the amount specified in an item is payable only to one approved pathology practitioner in respect of a single patient episode.

Tests on biopsy material - Group P5 (Tissue pathology) and Group P6 (Cytology)

13. (1) For items in Group P5 (Tissue pathology):

(a) *biopsy material* means all tissue received by the Approved Pathology Practitioner:

(i) from a medical procedure or group of medical procedures performed on a patient at the same time; or

(ii) after being expelled spontaneously from a patient.

(b) *cytology* means microscopic examination of 1 or more stained preparations of cells separated naturally or artificially from their normal environment by methods recognised as adequate to demonstrate their structure to a degree sufficient to enable an opinion to be formed about whether they are likely to be normal, abnormal but benign, or abnormal and malignant but, in accordance with customary laboratory practice, does not include examination of a blood film and a bone marrow aspirate; and

(c) *separately identified specimen* means an individual specimen collected, identified so that it is clearly distinguished from any other specimen, and sent for testing by or on behalf of the treating practitioner responsible for the procedure in which the specimen was taken.

13. (2) For Groups P5 and P6 of the pathology services table, services in Group P6 include any services described in Group P5 on the material submitted for a test in Group P6.

13. (3) For subrule (2), any sample submitted for cytology from which a cell block is prepared does not qualify for a Group P5 item.

13.(4) If more than 1 of the services mentioned in items 72813, 72816, 72817, 72818, 72823, 72824, 72825, 72826, 72827, 72828, 72830, 72836 and 72838 are performed in a single patient episode, only the fee for the item performed having the highest specified fee is applicable to the services.

13.(5) If more than 1 histopathological examinations are performed on separate specimens, of different complexity levels, from a single patient episode, a medicare benefit is payable only for the examination that has the highest schedule fee.

13.(6) In items 72813, 72816, 72817, 72818, 72823, 72824, 72825, 72826, 72827, 72828, 72830, 72836 and 72838 a reference to a *complexity level* is a reference to the level given to a specimen type mentioned in Part 4 of this Table.

13.(7) If more than 1 of the services mentioned in items 72846, 72847, 72848; 72849 and 72850 or 73059, 73060, 73061, 73064 and 73065 are performed in a single patient episode, a medicare benefit is payable only for the item performed that has the highest scheduled fee.

13.(8) If more than 1 of the services mentioned in items 73049, 73051, 73062, 73063, 73066 and 73067 are performed in a single patient episode, only the fee for the item performed having the higher or highest specified fee applies to the services.

Items in Groups P10 (Patient episode initiation) and P11 (Specimen referred) not to apply in certain circumstances

14. (1) For this rule and items in Groups P10 (Patient episode initiation) and P11 (Specimen referred):

approved collection centre has the same meaning as in Part IIA of the Act.

institution means a place at which residential accommodation or day care is, or both residential accommodation and day care are, made available to:

(a) disadvantaged children; or

(b) juvenile offenders; or

(c) aged persons; or

(d) chronically ill psychiatric patients; or

(e) homeless persons; or

(f) unemployed persons; or

(g) persons suffering from alcoholism; or

(h) persons addicted to drugs; or

(i) physically or mentally handicapped persons;

but does not include:

(j) a hospital; or

(k) a residential aged care home; or

(l) accommodation for aged persons that is attached to a residential aged care home or situated within a residential aged care home.

prescribed laboratory means a laboratory operated by:

(a) the Australian Government; or

(b) an authority of the Commonwealth; or

(c) a State or internal Territory; or

(d) an authority of a State or internal Territory; or

(e) an Australian tertiary education institution.

s*pecimen collection centre* has the same meaning as in Part IIA of the Act.

treating practitioner has the same meaning as in paragraph 16A(1)(a) of the Act.

14. (2) If a service described in an item in Group P10 is rendered by, or on behalf of, an approved pathology practitioner who is a recognised pathologist, the relevant one of those items does not apply to the service if:

(a) the service is rendered upon a request made in the course of a service provided to a public patient in a recognised hospital or when attending an outpatient service of a recognised hospital.

14. (3) An item in Group P10 or P11 does not apply to a pathology service to which subsection 16A (7) of the Act applies.

14. (4) An item in Group P10 or P11 does not apply to a pathology service unless at least 1 item in Groups P1 to P8 also applies to the service.

14. (5) Subject to subrule (7), if one item in Group P10 applies to a patient episode, no other item in the Group applies to the patient episode.

14. (6) An item in Group P11 applies only to the approved pathology practitioner or approved pathology authority to whom the specimen mentioned in the item was referred.

14. (7) If, in respect of the same patient episode:

(a) services referred to in 1 or more items in Group P5 and 1 or more of Groups P1, P2, P3, P4, P6, P7 and P8 are rendered by an approved pathology practitioner in the laboratory of another approved pathology authority; or

(b) services referred to in 1 or more items in Group P6 and 1 or more of Groups P1, P2, P3, P4, P5, P7 and P8 are rendered by another approved pathology practitioner in the laboratory of another approved pathology

authority;

the fee specified in the applicable item in Group P10 is payable to both approved pathology practitioners.

14. (8) If more than one specimen is collected from a person on the same day for the provision of pathology services:

(a) in accordance with more than 1 request; and

(b) in or by a single approved pathology authority;

the fee specified in the applicable item in Group P10 applies once only to the services unless an exemption listed in Rule 4 applies or an exemption has been granted under Rule 3 "S4B(3)".

14. (9) The amount specified in item 73940 is payable only once in respect of a single patient episode.

Application of an item in Group P11 (Specimen referred) to a service excludes certain other items

15. If item 73940 applies to a patient episode, none of the items in Group P10 applies to any pathology service rendered by the approved pathology authority or approved pathology practitioner who claimed item 73940 in respect of the patient episode.

Circumstances in which an item in Group P11 (Specimen referred) does not apply

16. (1) An item in Group P11 does not apply to a referral if:

(a) a service in respect of the same patient episode has been carried out by the referring approved pathology authority; and

(b) the approved pathology authority to which the referral is made is related to the referring approved pathology authority.

16. (2) An approved pathology authority is *related to* another approved pathology authority for subrule (1) if:

(a) both approved pathology authorities are employed (including employed under contract) by the same person, whether or not the person is also an approved pathology authority; or

(b) either of the approved pathology authorities is employed (including employed under contract) by the other; or

(c) both approved pathology authorities are corporations and are related corporations within the meaning of the Corporations Act; or

(d) the approved pathology authorities are partners (whether or not either or both of the approved pathology authorities are individuals and whether or not other persons are in partnership with either or both of the approved pathology authorities; or

(e) both approved pathology authorities are operated by the Commonwealth or an authority of the Commonwealth; or

(f) both approved pathology authorities are operated by the same State or internal Territory or an authority of the same State or internal Territory.

16. (3) An item in Group P11 does not apply to a referral if the following common tests are referred either singly or in combination (except if the following items are referred in combination with other items not similarly specified): 65060, 65070, 65120, 66500, 66503, 66506, 66509, 66512, 66536, 66596, 69300, 69303, 69333 or 73527.

Abbreviations

17. (1) The abbreviations in Part 4 of this table may be used to identify particular pathology services or groups of pathology services.

17. (2) The names of services or drugs not listed in Part 4 of this table must be written in full.

Certain pathology services to be treated as 1 service

18. (1) In this rule:

general practitioner means a medical practitioner who:

(a) is not a consultant physician in any specialty; and

(b) is not a specialist in any specialty.

set of pathology services means a group of pathology services:

(a) that consists of services that are described in at least 4 different items; and

(b) all of which are requested in a single patient episode; and

(c) each of which relates to a patient who is not an admitted patient of a hospital; and

(d) excludes services referred to in an item in Group P10, Group P11, Group P12 or Group P13, items 66900, 69484, 73053 and 73055; and

(e) excludes services described in the following items:

65079, 65082, 65157, 65158, 65166, 65180, 65181, 66606, 66609, 66610, 66639, 66642, 66651, 66652, 66663, 66666, 66696, 66697, 66714, 66715, 66723, 66724, 66780, 66783, 66789, 66790, 66792, 66804, 66805, 66816, 66817, 66820, 66821, 66826, 66827, 66832, 69325, 69328, 69331, 69379, 69383, 69400, 69401, 69419, 69451, 69500, 69484, 69489, 69492, 69497, 69498, 71076, 71090, 71092, 71096, 71148, 71154, 71156, 71169, 71170, 73309, 73312, 73315, 73318, 73321 and 73324;

where those services are performed by an approved pathology practitioner in an accredited pathology laboratory of an approved pathology authority following referral by another approved pathology practitioner in an accredited pathology laboratory of an approved pathology authority which is not related to the first mentioned approved pathology authority.

(1A) An approved pathology authority is related to another approved pathology authority for the purposes of paragraph 18(1)(e) if that approved pathology authority would be related to the other approved pathology authority for the purposes of rule 16(2).

18. (2) If a general practitioner requests a set of pathology services, the pathology services in the set are to be treated as individual pathology services in accordance with this rule.

18. (3) If the fee specified in 1 item that describes any of the services in the set of pathology services is higher than the fees specified in the other items that describe the services in the set:

(a) the pathology service described in the first-mentioned item is to be treated as 1 pathology service; and

(b) either:

(i) the pathology service in the set that is described in the item that specifies the second-highest fee is to be treated as 1 pathology service; or

(ii) if 2 or more items that describe any of those services specify the second-highest fee ¿ the pathology

service described in the item that specifies the second-highest fee, and has the lowest item number, is to be treated as 1 pathology service; and

(c) the pathology services in the set, other than the services that are to be treated as 1 pathology service under paragraphs (a) and (b), are to be treated as 1 pathology service.

18. (4) If the fees specified in 2 or more items that describe any of the services in the set of pathology services are the same, and higher than the fees specified in the other items that describe the services in the set:

(a) the pathology service in the set that is described in the item that specifies the highest fee, and has the lowest item number, is to be treated as 1 pathology service; and

(b) the pathology service in the set that is described in the item that specifies the highest fee, and has the second-lowest item number, is to be treated as 1 pathology service; and

(c) the pathology services in the set, other than the services that are to be treated as 1 pathology service under paragraphs (a) and (b), are to be treated as 1 pathology service.

18. (5) If pathology services are to be treated as 1 pathology service under paragraph (3) (c) or (4) (c), the fee for the 1 pathology service is the highest fee specified in any of the items that describe the pathology services that are to be treated as the 1 pathology service.

Limitation on certain items

25. (a) For any particular patient, items 66539, 66605, 66606, 66607, 66610, 69380, 69488, 69489, 71075, 71127, 71135 or 71137 is applicable not more than twice in a 12 month period.

25. (b) For any particular patient, item 66626 is applicable not more than 36 times in a 12 month period.

25. (c) For any particular patient, items 66655, 66659, 69482, 69491, 69499 or 69500 are applicable not more than once in a 12 month period.

25. (d) For any particular patient, item 66750 or 66751 is applicable not more than once in a pregnancy.

25. (e) For any particular patient, item 69336 is applicable not more than once in each period of 7 days.

25. (f) For any particular patient, items 66551, 66660, 69445, 69451, 69483, 71079 or 73523 are applicable not more than 4 times in a 12 month period.

25.(g) For any particular patient, items 66554, 66830 and 71077 are applicable not more than 6 times in a 12 month period.

25. (h) For any particular patient, item 66819, 66820, 66821, 66822, 66825, 66826, 66827 or 66828 is applicable not more than 3 times in a 6 month period.

25. (i) For any particular patient, items 69418 and 69419 are applicable not more than twice in a 24 month period.

Appendix 3. Search strategies

Table A3.1 and Table A3.2 provide the broad search strings used that were used to identify relevant literature in Embase.com (which concurrently searches EMBASE and Medline) and the Cochrane Library, respectively.

Table A3.1 Embase.com search terms and results (search conducted on 20 March 2014)

#	Query	No. of citations
#1	(morpholog* NEAR/3 referral OR (interinstitutional AND 'consultation'/exp) OR interinstitutional NEAR/3 consultation OR ('inter institutional' AND 'consultation'/exp) OR 'inter institutional' NEAR/3 consultation OR 'interinstitutional pathology consultation' OR 'inter-institutional pathology consultation' OR 'inter-institutional pathology consultations' OR ('second opinion' OR 'second opinions') OR ('expert opinion' OR 'expert opinions') OR morpholog* NEAR/3 referral* OR patholog* NEAR/3 referral* OR second NEAR/2 opinion* OR expert NEAR/2 opinion* OR voluntary NEAR/3 opinion* OR 'extra-departmental pathology consultation' OR 'extradepartmental pathology consultation' OR extradepartmental NEAR/3 consultation* OR 'extra departmental' NEAR/3 consultation* OR ('personal consultation' OR 'personal consultations') OR (extradepartmental AND 'consultation'/exp) OR ('extra departmental' AND 'consultation'/exp) OR ('second opinion diagnosis') OR (opinion NEAR/4 pathology) OR ('second opinion' NEAR/4 pathology) OR ('morphology referrals') OR ('expert pathologist' OR 'expert pathologists'))	27,969
#2	('pathology'/exp OR 'anatomical pathology' OR 'histology'/exp OR histologic* OR 'histopathology'/exp OR histopathologic* OR 'cytology'/exp OR cytologic* OR 'pathological anatomy'/exp OR 'cytopathology'/exp OR cytopathologic* OR 'tissue pathology' OR morpholog* OR morpholog* NEAR/2 pathology OR morpholog* NEAR/2 diagnos* OR 'biopsy'/exp OR 'smear'/exp OR 'pathologist'/exp OR pathologists OR ('pathology'/de OR pathology) OR ('pathologist'/de OR pathologist)	3,367,571
#3	#1 AND #2 NOT ((forensic OR forensics) OR ('case report'/exp OR 'case report'))	4,181

Table A3.2 Cochrane Library search terms and results (search conducted on 15 April 2014)

#	Query	No. of citations
#1	"second opinion" OR "second-opinion" OR "expert opinion" OR "voluntary opinion" OR "personal consultation" OR "extradepartmental consultation" OR "extra-departmental consultation" OR "extradepartmental pathology consultation" OR "extra-departmental pathology consultation" OR "interinstitutional consultation" OR "Inter-institutional consultation" OR "interinstitutional pathology consultation" OR "inter-institutional pathology consultation"	1,444
#2	"pathology":ti,ab,kw OR histology OR histologic OR histopathology OR histopathologic OR "anatomical pathology" OR cytology OR cytologic OR cytopathology OR cytopathologic OR "tissue pathology" OR pathologist OR biopsy OR smear OR morphology OR morphological OR "morphological pathology"	32,260
#3	#1 AND #2	141

Appendix 4. Minor discrepancy rates

As mentioned in Section B.5, in general, minor discrepancies were those that indicated a difference of opinion between the initial and expert pathologist that would have no significant (clinically relevant) effect on treatment or prognosis. For example, van Dijk et al (2008) reported the number of marginal modifications, not resulting in clinically relevant changes in patient management. Similarly, Jones and Jordan (2010) defined minor discrepancies as differences in diagnostic opinion that would not significantly alter the treatment and/or prognosis of the patient. Van Dijk et al (2008) reported that 350 (28.8%) out of 1217 dermatology cases with a provisional diagnosis were minor discrepancies. Jones and Jordan (2010) found 24 (17.8%) minor discrepancies out of 135 oral and maxillofacial pathology cases with a provisional diagnosis.

Minor discrepancies in soft tissue or sarcoma cases were reported in two studies (Arbiser et al 2001 and Ray-Coquard et al 2012). There was a substantial difference in the proportion of cases with a provisional diagnosis in which there were minor discrepancies between the initial and expert diagnoses. Arbiser et al (2001) reported 20 (7.5%) out of 266 cases, while Ray-Coquard et al 2012 reported 'partial concordance' in 263 (46.6%) out of 564 cases with a provisional diagnosis. Partial concordance was defined as identical diagnosis of connective tumour with differences of grade or histological subtype.

Gaudi et al (2013) reported minor discrepancies in dermatology cases in three separate categories: minimal disagreements; minor disagreements; and defects in diagnosis with minimal effect on patient care. In total, minor discrepancies occurred in 121/354 (34.2%) cases with a provisional diagnosis. Minimal disagreements, including spelling errors, accounted for only 10 (8.3%) of those cases; whereas, minor disagreements (the use of alternate nomenclature, a lack of clarity in diagnosis, or unfamiliarity with the most up-to-date terminology and reporting requirements) and defects in diagnosis (histopathologic differences that did not influence prognosis, or failures to review relevant prior pathologic diagnosis and/or margin status) made up 56 (46.3%) and 55 (45.5%) of the 121 discrepant cases, respectively.

Table A4.1 Minor discrepancy rates – as reported in *Scenario 1* studies

Study ID	Population (N)	Outcome	Results n/N (%)
SOFT TISSUE/ SARCOMA	-	-	-
Arbiser 2001	Cases of soft tissue lesions N=500 cases	Number of cases with a provisional diagnosis Minor discrepancy	266/500 (53.2%) 20/266 (7.5%)
Ray-Coquard 2012	Soft tissue or visceral sarcoma N=1463 cases[a]	Number of cases with a provisional diagnosis Partial concordance with initial diagnosis[b] (i.e. minor discrepancies) *Nature of major and minor discrepancies[c]:* • Subtype alone • Grade alone • Histological type alone • Grade and subtype • Grade and histological type	564/564 (100%) 263/564 (46.6%) 11/334 (3.3%) 104/334 (31.1%) 89/334 (26.6%) 114/334 (34.1%) 16/334 (4.8%)
DERMATOLOGY	-	-	-
Gaudi 2013	Dermatopathology N=405 cases[d]	Number of cases with a provisional diagnosis Minor discrepancy *Nature of minor discrepancies (as a proportion of cases with a provisional diagnosis):* • Minimal disagreements (e.g. errors in spelling) • Minor disagreements[e] • Defects in diagnosis with minimal effect on patient care[f] *Nature of minor discrepancies (as a proportion of total minor discrepancies):* • Minimal disagreements (e.g. errors in spelling) • Minor disagreements[e] • Defects in diagnosis with minimal effect on patient care[f]	354/405 (87.4%) 121/354 (34.2%) 10/354 (2.8%) 56/354 (15.8%) 55/354 (15.5%) 10/121 (8.3%) 56/121 (46.3%) 55/121 (45.5%)
van Dijk 2008	Cutaneous melanocytic lesions N=1837	Number of cases with a provisional diagnosis Minor discrepancy[g]	1217/1837 (66.2%) 350/1217 (28.8%)

Study ID	Population (N)	Outcome	Results n/N (%)
ORAL AND MAXILLOFACIAL	-	-	
Jones 2010	Oral and maxillofacial pathology N=142 cases	Number of cases with a provisional diagnosis Minor discrepancy[h]	135/142 (95.1%) 24/135 (17.8%)

[a] The study included a total of 1463 cases: 564 cases were initially examined by a 'non-expert' pathologist who requested a second opinion to confirm the diagnosis; 899 cases were initially examined by a 'non-expert' pathologist who did not request confirmation of the diagnosis. The study referred to the latter group as the 'systematic review' or 'control' group.
[b] Identical diagnosis of connective tumour but different grade or histological subtype.
[c] Includes all discordant cases, including 263 partially concordant cases (minor discrepancies) and 71 completely discordant cases (major discrepancies). The results were not presented separately.
[d] 404 out of 405 cases were relevant expert opinion cases, in which an outside pathologist sought an expert opinion. One case was a mandatory second review case, in which an expert opinion was required prior to definitive medical or surgical treatment.
[e] Differences in the rendered report that were attributed to the use of alternate nomenclature, the lack of clarity in diagnosis, or the unfamiliarity with the most up-to-date terminology and reporting requirements.
[f] Defects in diagnosis that caused minimal effect on patient care – histopathologic differences that did not influence prognosis and failures to review relevant prior pathologic diagnosis and/or margin status.
[g] Refers to marginal modifications, not resulting in clinically relevant changes in patient management.
[h] Differences in diagnostic opinion that would not significantly alter the treatment and/or prognosis of the patient.

Table A4.2 Minor discrepancy rates reported in Scenario 2 studies

Study ID	Population (N)	Outcome	Results n/N (%)
BRAIN AND SPINAL CORD	-	-	-
Bruner 1997	Brain and spinal cord biopsy for suspected neoplastic disease N=500 cases[a]	Number of cases with a provisional diagnosis Minor discrepancy in cases with a provisional diagnosis *Nature of minor discrepancy (as a proportion of cases with a provisional diagnosis):* • Tentative or doubtful diagnosis confirmed • Information added or deleted *Nature of minor discrepancy (as a proportion of cases with a minor discrepancy):* • Tentative or doubtful diagnosis confirmed • Information added or deleted	261/284 (91.9%) 39/261 (14.9%) 21/261 (8.0%) 18/261 (6.9%) 21/39 (53.8%) 18/39 (46.2%)

[a] The study included a total of 500 cases: 284 "consultation-only" cases were submitted because of some doubt about the original diagnosis on the part of pathologists or other attending physicians (e.g. surgeons, internists, or radiotherapists) at an outside institution; 216 cases were reviewed after the patient was referred to the Texas M. D. Anderson Cancer Center for management.

Appendix 5. Expert opinion survey

An Expert Opinion Survey was developed by the Assessment Group in order to obtain data to inform the economic and financial estimates used in the Assessment Report. The survey was initially pilot-tested with the two HESP members allocated to MSAC Application 1332 (see Appendix 1). Upon their advice, the order of the questions were altered – primarily to improve the flow of the survey and to reduce repetition.

The final survey was distributed to eight experts (Chief Executive Officers or Heads of Departments) who were selected and contacted by the Applicant. Due to time constraints, it was not feasible for the Applicant to approach a large/random group of experts or to collate a large number of responses. The eight selected experts came from both public and private laboratories in New South Wales, Queensland, South Australia, Western Australia and the Australian Capital Territory. Survey recipients were offered phone support from the Applicant to assist them in completing the survey if required.

The survey itself contained 16 questions, some of which had multiple parts. All of the questions required the respondents to provide answers using percentages. No restrictions were placed on their answers (e.g. there were no multiple choice questions) and where the respondents felt it necessary they were able to respond using a range of percentages (e.g. 1-2% or <0.1%). Respondents were also able to add comments after their estimates if they felt that clarification of their estimate was required or if they had made assumptions that warranted further explanation.

The survey contained two main parts: Part 1 – Tissue pathology; and Part 2 – Non-gynaecological cytology.

The following background information was provided at the start of the survey:

> The aim of this survey is to obtain information about the number and nature of pathology cases that are referred for second, expert opinion (also known as personal or expert consultations) in Australia. The intention of the following questions is to obtain estimates about general referral patterns across Australia, rather than your individual experience or that of your pathology department. Estimates should not include intra-institutional referrals, in which a pathologist seeks advice from a co-located colleague. The referrals of interest relate to formal, written second opinions by an expert pathologist that is external to the initial pathologist, but may be co-located with a referring clinician (e.g. at a tertiary treatment centre).
>
> The survey relates to the fields of tissue pathology and cytopathology (Groups P5 and P6 on the Medicare Benefits Schedule, MBS). Bone marrow cases (included in Group P1 on the MBS) are also of interest and should be considered in responses relating to tissue pathology.
>
> Each question includes two parts: (a) Current funding conditions, in which no MBS funding is available for pathology second, expert opinions; and (b) Proposed funding conditions, in which MBS funding is available for pathology second, expert opinions and any ancillary tests that are undertaken by the expert pathologist. The purpose of part (b) is to determine whether MBS funding of second, expert opinions is likely to impact on the number and nature of pathology cases that are referred.

A relevant publication has been identified that forms the basis for some of the following questions. A brief summary of that publication (Azam et al, 2002) is provided below:

As part of their Q-Probes program, the College of American Pathologists conducted a study of expert opinion referrals from 180 institutions in the United States, Canada and Australia. Over a period of 4 months, participating institutions were asked to document up to 20 cases sent for second, expert opinion to resolve diagnostic uncertainty or to obtain input on a case from an expert. Referrals were initiated by the initial pathologist, a treating clinician or the patient. The study established an expert opinion referral rate of 0.5% for tissue pathology cases.

The results of the survey are summarised below. All eight respondents provided answers to Part 1; while Part 2 contained answers from seven respondents. The estimates represent the average (mean) of the responses (eight for tissue pathology and seven for non-gynaecological cytology)

Question	Mean (SD)	Median [Range]
Part 1 – Tissue pathology	N=8	-
1. Is 0.5% a reasonable estimate of the proportion of initial tissue pathology cases, including bone marrow cases, that are currently referred for second, expert opinion in Australia across all types of pathology institutions (e.g. remote single-pathologist laboratories, large pathology departments at metropolitan hospitals, tertiary treatment centres)? If no, specify a figure.	0.57% (0.31%)	0.5% [0.10% to 1%]
2. What is a reasonable estimate of the proportion of initial tissue pathology cases that would be referred for second, expert opinion in Australia if an MBS rebate was available? Note that the two Schedule fees that have been proposed by the RCPA are $180 and $370 for second, expert opinions requiring ≤ or >30 minutes of expert pathologist's time, respectively.	1.41% (1.54%)	1.0% [0.3% to <5%]
3. The study by Azam et al (2002) also found that approximately 85% of requests for a second, expert opinion were initiated by the pathologist. Does this reflect current referral patterns in Australia, assuming that all referrals are from the initial pathologist, the clinician who requested the initial pathology, or the clinician in charge of treatment? If no, specify a figure.	64.38% (32.23%)	85% [5% to 90%]
4. If an MBS rebate was available for pathology second, expert opinions, what proportion of requests for a second, expert opinion are likely to be initiated by the pathologist (see Question 2 for the proposed MBS fee)?	74.38% (29.69%)	85% [10% to >95%]
5. It is expected that difficult cases would be referred to a pathologist with particular expertise in the condition or type of disease (e.g. breast pathologist, dermatopathologist, urogenital pathologist). Due to their expertise, some cases considered difficult by the initial pathologist may be relatively straightforward or 'non-complex' for the expert pathologist. Non-complex cases may be defined as those that take up to 30 minutes for an expert pathologist to review, while 'complex' cases may be defined as cases which involve over 30 minutes of the expert pathologist's time (excluding administrative tasks such as unpacking, accessioning, data entry etc.).	-	-
a) In your opinion, what proportion of tissue pathology cases that are referred by a pathologist for expert opinion are 'complex', involving over 30 minutes of the expert pathologist's time?	60.00% (33.49%)	67.5% [<5% to 100%]
b) In your opinion, what proportion of tissue pathology cases that are referred by a clinician for expert opinion are 'complex', involving over 30 minutes of the expert pathologist's time?	31.25% (21.67%)	40.0% [0% to 50%]
6. If an MBS rebate was available for pathology second, expert opinions:	-	-
(a) What proportion of tissue pathology cases that are referred by a pathologist for expert opinion would be 'complex', involving over 30 minutes of the expert pathologist's time?	53.75% (31.71%)	55% [<5% to 100%]

Question	Mean (SD)	Median [Range]
(b) What proportion of tissue pathology cases that are referred by a clinician for expert opinion would be 'complex', involving over 30 minutes of the expert pathologist's time?	30.00% (20.70%)	35.0% [0% to 50%]
7. In some cases, the second, expert opinion may only involve the examination of slides that were previously prepared (with or without staining) by the initial pathologist, while in other cases additional sectioning may be required. Furthermore, the expert pathologist may conduct ancillary tests (such as immunohistochemical staining) to aid diagnosis. The proportion of cases in which ancillary tests are used may vary between 'non-complex' and 'complex' expert opinions, outlined in Question 5.	-	-
(a) Please estimate the proportion of 'non-complex' second, expert opinions in which ancillary tests (e.g. immunohistochemistry) are currently used.	25.00% (12.82%)	22.5% [5% to 50%]
(b) Please estimate the proportion of 'complex' second, expert opinions in which ancillary tests (e.g. immunohistochemistry) are currently used.	62.63% (27.71%)	72.5% [1% to 90%]
8. If an MBS rebate was available for pathology second, expert opinions and expert pathologists were able to bill the MBS for any ancillary tests conducted (regardless of whether or not the initial pathologist had already billed the MBS for the test(s)), please estimate:	-	-
(a) The proportion of 'non-complex' second, expert opinions in which ancillary tests (e.g. immunohistochemistry) would be used.	23.75% (10.26%)	22.5% [5% to 40%]
(b) The proportion of 'complex' second, expert opinions in which ancillary tests (e.g. immunohistochemistry) would be used.	62.50% (24.78%)	70.0% [10% to 90%]
Part 2 – Non-gynaecological cytology	N=7	-
Approximately 75% of all cytopathology claims received by the MBS relate to item 73053 (i.e. cytology of a smear from the cervix in women with no symptoms, signs or recent history suggestive of cervical neoplasia). Expert pathologists have suggested that a second, expert opinion for this and other gynaecological cytology items are rarely required. As such, the following section relates to non-gynaecological cytology cases only.	-	-
9. An expert opinion referral rate of 0.5% (Azam et al, 2002) was used as a starting point for estimating second, expert opinion referral rates for tissue pathology cases in Australia. Is it reasonable to assume that the proportion of initial non-gynaecological cytopathology cases that are referred for second, expert opinion in Australia across all types of pathology institutions (e.g. remote single-pathologist laboratories, pathology departments at large, metropolitan hospitals, tertiary treatment centres) is approximately 0.5%? If no, specify a figure.	0.33% (0.21%)	0.5% [<0.1% to 0.5%]
10. What is a reasonable estimate of the proportion of initial non-gynaecological cytopathology cases that would be referred for second, expert opinion in Australia if an MBS rebate was available? Note that the two proposed Schedule fees are $180 and $370 for second, expert opinions requiring ≤ or >30 minutes of expert pathologist's time, respectively.	1.17% (1.73%)	0.5% [<0.1% to <5%]
11. The study by Azam et al (2002) found that approximately 85% of tissue pathology requests for a second, expert opinion on tissue pathology	76.43%	85.0%

Question	Mean (SD)	Median [Range]
samples were initiated by the pathologist. Does this reflect current referral patterns for non-gynaecological cytopathology in Australia, assuming that all referrals are from the initial pathologist, the clinician who requested the initial pathology, or the clinician in charge of treatment? If no, specify a figure.	(26.10%)	[50% to 100%]
12. If an MBS rebate was available for cytopathology second, expert opinions, what proportion of requests for a second, expert opinion are likely to be initiated by the pathologist (see Question 10 for the proposed MBS fee)?	59.50% (40.96%)	85.0% [1-2% to 100%]
13. It is expected that difficult cytopathology cases would be referred to a pathologist with particular expertise in the condition or type of disease. Due to their expertise, some cases considered difficult by the initial pathologist may be relatively straightforward or 'non-complex' for the expert pathologist. Non-complex cases may be defined as those that take up to 30 minutes for an expert pathologist to review, while 'complex' cases may be defined as cases which involve over 30 minutes of the expert pathologist's time (excluding administrative tasks such as unpacking, accessioning, data entry etc.).	-	-
(a) In your opinion, what proportion of non-gynaecological cytopathology cases that are referred by a pathologist for expert opinion are 'complex', involving over 30 minutes of the expert pathologist's time?	19.29% (18.80%)	10.0% [0% to 50%]
(b) In your opinion, what proportion of non-gynaecological cytopathology cases that are referred by a clinician for expert opinion are 'complex', involving over 30 minutes of the expert pathologist's time?	18.33% (19.15%)	12.5% [0% to 50%]
14. If an MBS rebate was available for pathology second, expert opinions:	-	-
(a) What proportion of non-gynaecological cytopathology cases that are referred by a pathologist for expert opinion would be 'complex', involving over 30 minutes of the expert pathologist's time?	18.57% (19.30%)	10.0% [0% to 50%]
(b) What proportion of non-gynaecological cytopathology cases that are referred by a clinician for expert opinion would be 'complex', involving over 30 minutes of the expert pathologist's time?	18.33% (19.15%)	12.5% [0% to 50%]
15. For second, expert opinion on a cytopathology sample the expert pathologist may conduct ancillary tests (such as immunocytochemical staining) to aid diagnosis. The proportion of cases in which ancillary tests are used may vary between 'non-complex' and 'complex' expert opinions, outlined in Question 13.	-	-
(a) Please estimate the proportion of 'non-complex' second, expert opinions in which ancillary tests (e.g. immunocytochemistry) are used.	10.14% (7.43%)	10.0% [1% to 20%]
(b) Please estimate the proportion of 'complex' second, expert opinions in which ancillary tests (e.g. immunocytochemistry) are used.	30.43% (27.17%)	30% [3% to 80%]
16. If an MBS rebate was available for pathology second, expert opinions and expert pathologists were able to bill the MBS for any ancillary tests	-	-

Question	Mean (SD)	Median [Range]
conducted (regardless of whether or not the initial pathologist had already billed the MBS for the test(s)), please estimate:		
(a) The proportion of 'non-complex' second, expert opinions in which ancillary tests (e.g. immunocytochemistry) would be used.	11.57% (10.11%)	10.0% [1% to 30%]
(b) The proportion of 'complex' second, expert opinions in which ancillary tests (e.g. immunocytochemistry) would be used.	32.14% (27.06%)	30.0% [5% to 80%]

Appendix 6. Additional economic information

Table A6.1 Summary of economic studies identified in the literature search

Author (year)	Population *Setting/Country*	Intervention	Diagnostic accuracy and change in management	Economic evaluation	Results of economic evaluation
Bajaj (2012)	N=922 thyroid FNAC cases referred to institution over a 2-year period. *Long Island Jewish Medical Center in the United States*	Second opinion on outside FNAC specimens for all cases referred to the institution.	122/922 (13%) discordant, 44 major and 78 minor. 75/122 (62%) resulted in change in management: • 33 surgical to medical • 29 medical to surgical • 13 changed surgery type 39/44 (90%) major discrepancies resulted in a change in management, with 28 undergoing surgery. Of those, the second opinion was supported in 25 patients and the original opinion was supported in 3 patients.	CBA in USD. Considers savings due to unnecessary surgery avoided. Excludes potential savings due to: • lost wages • surgical complications • life-long thyroid replacement therapy, with accompanying morbidity • litigation	Total cost of 922 FNAC consultations (assuming Medicare reimbursement $97/consult): $89,434. Potential cost saving for 33 patients that avoided surgery (at an average cost of $31,200/case): $940,166.
Bejarano (2001)	N=124 patients (125 cases) who had undergone a liver biopsy and were referred for treatment over a 2-year period. *University medical centre in the United States*	Second opinion on outside specimens by a hepatopathologist with a hepatologist who shared clinical information. All discordant diagnoses were reviewed by another hepatopathologist.	35/125 (28%) discordant, classified as major (defined as a description or diagnosis that may have resulted in inappropriate management decisions if left unmodified.	Total cost of second opinion in USD.	Direct pathology cost at original institutions: $18,422.45. Second opinion on 125 cases: $8,490.56, including: • $7,332.50 as professional charge by consult pathologists • $1,158.06 for charges relating to generation of additional slides and special stains

Author (year)	Population *Setting/Country*	Intervention	Diagnostic accuracy and change in management	Economic evaluation	Results of economic evaluation
Chan (1999)	Retrospective review of N=569 specimens from 498 patients referred for gynaecologic oncology treatment over a 5-year period. *University hospital in Hong Kong*	Routine second opinion of cervical biopsy and cytologic specimens by gynaecologic pathologists, with findings discussed at fortnightly conferences with the gynaecologic oncology team prior to treatment planning. Consultation error determined by comparison with subsequent pathologic diagnosis and clinical follow-up.	108/569 (19%) discordant, 37/569 (6.5%) major (defined as leading to a change in therapy or clinical evaluation). Rate drops to 4.2% if changes in extent and grading not taken into account. Treatment changes involved: 17 surgery alteration, 6 chemotherapy alteration, 3 added radiotherapy, 3 cancelled radiotherapy. When compared with final diagnoses, there were 5 discrepant cases, none of which resulted in alteration of clinical care; in 3 cases the original pathology diagnosis was more correct than second opinion; in 2 cases both original and second opinion were incorrect.	Cost of finding a major discrepancy with therapeutic or prognostic implications, in HKD and USD.	Total cost of review of 569 specimens from 498 patients (assuming $142/consultation): US$70,870. Cost of finding a discrepancy: US$656 Cost of finding a major discrepancy: $1,915. Each review cost the patient a delay of treatment: mean 4.6 days (median 2 days). It excluded specimen types that do not require second opinion (cervical biopsy specimens in patients with gross tumours and cervical/vaginal smears), cost of finding a major discrepancy: $1,430.
Coblentz (2001)	N=97 patients (131 TUR or biopsies) with a diagnosis of urothelial carcinoma of the bladder referred for treatment over a 3-year period. *Academic urology department in the United States*	Second opinion on all outside specimens prior to surgery. Slides initially reviewed by any one of six general surgical pathologists, without preparation of new slides or special stains. All discordant diagnoses were re-reviewed in a blinded manner by an expert genitourinary pathologist.	24/131 (18%) discordant. 19/24 (78%) had adequate pathologic material for re-review by expert pathologist who confirmed second opinion diagnosis in all cases. 5 repeat TUR procedures were recommended for inadequate staging. One TUR was avoided due to patient proceeding directly to cystectomy. 5 radical cystectomies avoided. One cystectomy was recommended on pathology review.	CEA in USD. Excludes potential savings due to: • morbidity • pain • quality of life • 2-3% perioperative mortality rate for radical cystectomy	Total cost of pathologic review of 131 cases (assuming $120/case for second opinion): $15,720. Total cost of 4 additional TUR (assuming average cost of TUR for bladder tumour is $14,907): $59,628. Total cost of 4 fewer radical cystectomies (assuming average cost of radical cystectomy is $40,381): $161,524. Total savings generated by pathology second opinion: $86,176. $658 per TUR reviewed. $888 per patient reviewed. $1310 per patient to identify significant therapeutic changes in 12 patients.

Author (year)	Population *Setting/Country*	Intervention	Diagnostic accuracy and change in management	Economic evaluation	Results of economic evaluation
Epstein (1996)	N=535 consecutive men referred over a 12-month period for radical prostatectomy after needle biopsy initially diagnosed as adenocarcinoma. *John Hopkins Hospital in the United States*	Mandatory review program. Second opinion on all outside biopsies prior to surgery. Slides initially reviewed by any one of six general surgical pathologists. All discordant diagnoses were reviewed in consultation with a second surgical pathologist. Authors acknowledge that findings do not reflect second 'expert' opinion.	528/535 (98.7%) concordant; confirmed on subsequent surgery. 7/535 discordant (5/7 were originally from teaching hospitals); 1/7 shown to have adenocarcinoma on subsequent biopsy (i.e. second opinion incorrect); 4/7 confirmed benign on subsequent biopsy; no repeat biopsy for 2/7.	CBA in USD, including direct healthcare costs only. Excludes potential savings in: • lost wages • potential litigation • cost of work-up for surgery (e.g. radiology) • cost of treating side effects of surgery (incontinence and impotence)	Total cost of reviewing all 535 biopsies was $44,883, includes: • $42,800 for slide review ($80/review) • $783 for IHC (n=7) • $1,300 for repeat TRUS and biopsy (n=4) Cost saved due to cancellation of surgery (includes hospitalisation, anaesthesia, pathology and surgery) for 6 men was $85,686, includes: • $60,728 for 4 non-Medicare patients • $24,958 for 2 Medicare patients Second opinion prior to surgery saved $1.91 per dollar spent.
Safrin (1993)[13]	N=5,397 surgical pathology cases over a 1-year period. *Alvarado Hospital Medical Center in the United States*	Surgical pathology quality assurance system in which a second (internal) pathologist routinely reviews all surgical pathology cases before release of the report.	14/5397 (25.9%) discrepancies of potential clinical significance were detected by the second observer. In 7/14 of these cases, the error would have resulted in a different clinical intervention than actually occurred.	Cost of finding a major discrepancy.	Routine review added an estimated $7 to the cost of each case, or $2,700 for each discrepancy of potential clinical significance.
Santoso (1998)	Retrospective review of N=720 gynaecological patients referred to the institution for care over an 8-year period. *Tertiary care hospital in the United States*	Second opinion by a gynaecologic pathologist. All discrepancies were re-reviewed by a gynaecologic pathologist, a gynaecologist, and three gynaecologic oncologists.	119/720 discordant, including 15/720 (2%) major (defined as a diagnostic difference that led to an altered clinical intervention) and 104/720 (14%) minor. The 15 major discrepancies resulted in: 6 surgeries cancelled, 2 surgeries modified, 1 adjuvant radiation treatment added, 1 chemotherapy treatment modified, 5 adjuvant chemotherapy treatments cancelled.	Cost of finding a major discrepancy with therapeutic implications, in USD.	Total cost of pathology review of 720 cases (assuming $150/case): $108,000. Cost of identifying each major discrepancy that would result in altered clinical intervention: $7,200.

[13] Safrin RE, Bark CJ. Surgical pathology sign-out. Routine review of every case by a second pathologist. Am J Surg Pathol. 1993;17(11):1190-2.

Author (year)	Population *Setting/Country*	Intervention	Diagnostic accuracy and change in management	Economic evaluation	Results of economic evaluation
Selman (1999)	Retrospective review of N=297 gynaecologic oncologic histopathologic cases referred to the institution for treatment over a 12-month period. *Ohio State University Medical Center in the United States*	Routine second opinion by one of three pathologists with a particular interest in gynaecologic pathology. Rare, unusual or uncertain cases were reviewed by two gynaecologic pathologists.	50/297 (17%) discordant, including 14/297 (4.7%) with major therapeutic or prognostic implications (7 malignant or low malignant to benign, 3 malignant to low malignant potential, 2 change in tumour type, 2 change from superficially invasive to invasive). In 4 cases, surgery was cancelled (including 2 hysterectomies) and surgery was modified in 3 cases. In 3 cases adjuvant treatment was cancelled and in 2 cases adjuvant treatment was added.	Cost of finding a major discrepancy with therapeutic or prognostic implications, in USD.	Total cost of pathology review of 295 cases (assuming $133/specimen): $39,235. Average cost of finding each major discrepancy: $2,802.
Wurzer (1998)	N=538 patients with a biopsy diagnosis of adenocarcinoma who were referred for management over a 4-year period. *Fox Chance Cancer Centre in the United States*	Routine second opinion of prostate biopsies conducted by a single pathologist who is a specialist in prostate pathology. Seven other pathologists specialising in cancer-related pathology reviewed the remainder of the outside biopsy specimens.	212/538 (39.4%) changes in Gleason score, including 128 (23.8%) upgrading and 84 (15.6%) downgrading. 3 cases where adenocarcinoma was not confirmed on second opinion. 26 cases (5%) required treatment modification: 17 required modification of treatment volume or doses, 6 changed from adjuvant hormonal therapy to no hormonal therapy, 3 changed from no hormonal to adjuvant hormonal therapy.	CEA in USD. Excludes potential savings due to: • morbidity • lost productivity • litigation	Charge for second opinion: $251. Reimbursement for second opinion: $104. Total cost of review of 538 cases (assuming reimbursement fee for second opinion is $104): $55,952. Cost saved for 3 avoided courses of radiation therapy for prostate carcinoma (assuming $12,399 reimbursed per course): $37,197. Cost saved for 3 avoided 1-year courses of adjuvant hormonal therapy (assuming $882 reimbursed per monthly injection): $31,752. Total savings generated by pathology review: $12,997.

Abbreviations: CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; FNAC, fine needle aspiration cytology; HKD, Hong Kong dollar; IHC, immunohistochemistry; TRUS, transrectal ultrasound; TUR, transurethral resection; USD, United States dollar

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