

****Title of application***

***Month Year**

[Instructional text] The date should reflect the date the final report is submitted to the Department. [End instructional text]

MSAC application no. *XXXX

Assessment report

[Instructional text]

Notes on the template

This document is the template for a Medical Services Advisory Committee (MSAC) Assessment Report, the objective of which is to synthesise the key information that MSAC needs to inform its deliberations.

A secondary objective is to demonstrate that a high-quality systematic review has been performed. Information requests for this purpose are predominantly in the Appendices.

This template is provided to encourage consistency between assessment reports in the underlying structure of the report, and to guide applicants and assessment groups regarding which pieces of information are most likely to be informative. However, **judgement should be used regarding whether subsections are relevant or not, and the template may be amended as required for an individual topic**. For example, if the assessment report is for a resubmission, only present sections of the report that require amendment based on feedback from MSAC.

It may be necessary to duplicate sections of the template to allow for multiple populations or interventions. Judgement is required in determining the most appropriate structure.

This page provides instructions on how the template should be interpreted. In addition to the instructions below, please be mindful that web accessibility requirements must be met for all documents that are posted on Department of Health websites.

The template includes different coloured text:

- Text written in green represents instructional text, to be deleted prior to finalising the assessment report. The beginning and end of instructional text is also indicated by the words 'Instructional text' and 'End instructional text', respectively.
- Text written in black represents proposed wording, and may contain **highlighted** and asterisked (*) text to indicate that an input is required.
- **Cross-references to Technical Guidance (TG) sections of the *Guidelines for preparing assessments for the Medical Services Advisory Committee* (MSAC Guidelines) are presented in blue and preceded by the words 'Refer to:'. These cross-references are to be deleted prior to finalising the assessment report.**

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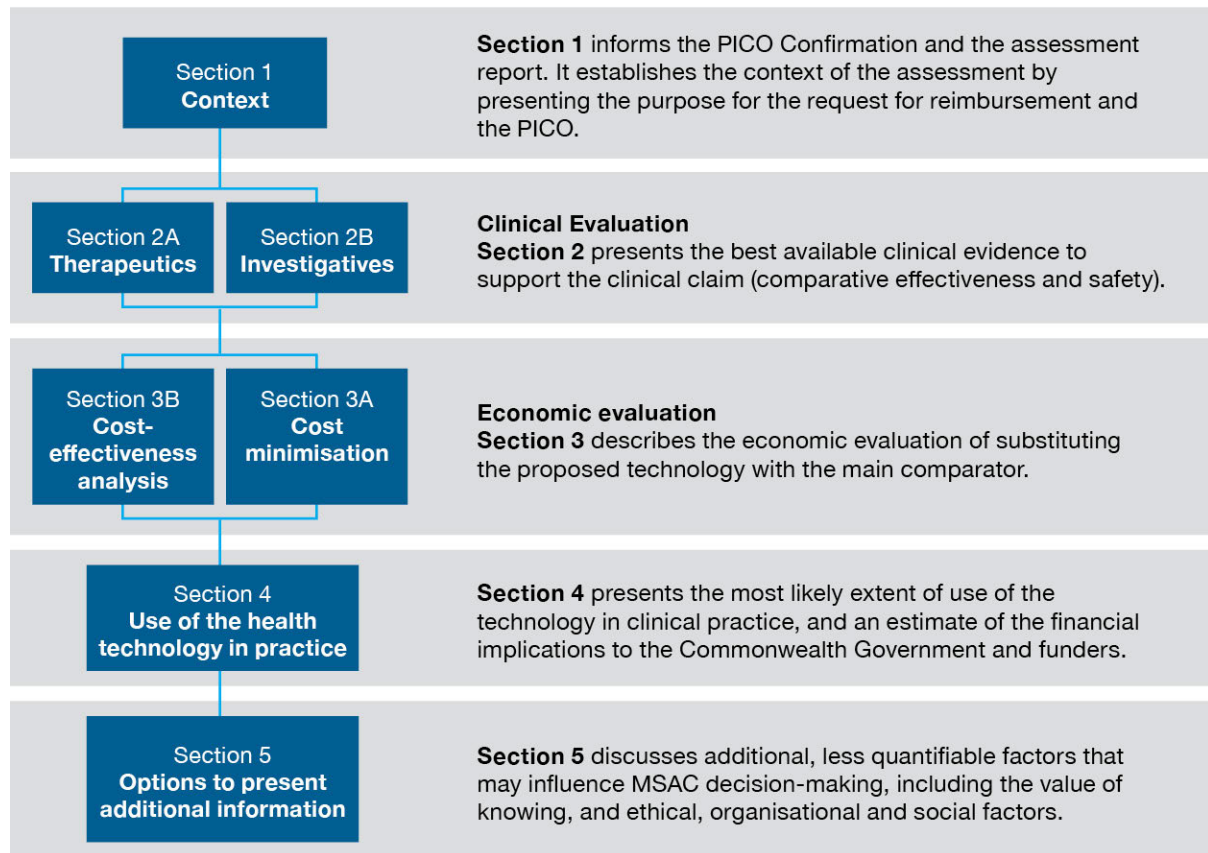


Figure 1 Sections of the template

Assessors should note that not all instructions are relevant to all technologies. This is particularly the case for therapeutic and investigative technologies. Disregard instructions that are not relevant to the type of technology being assessed.

In some places in the template, the instructional text is minimal. For guidance on completing the template, refer to the MSAC Guidelines where recommendations for presentation are provided.

[End instructional text]

[Instructional text] This section of the report is the frontispiece or inside front cover of the report.
[End instructional text]

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The technical information in this document is used by the Medical Services Advisory Committee (MSAC) to inform its deliberations. MSAC is an independent committee 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 through the Medicare Benefits Schedule (MBS) or alternative funding programs/arrangements.

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

This report was prepared by *XXXX from *XXXX. Clinical advice was provided by *XXXX. The report was commissioned by the Australian Government Department of Health. It was edited by *XXXX.

The suggested citation for this document is:

*Lastname FirstInitial, LastName FirstInitial, etc. (*20XX). *Report title. MSAC Application *Number, Assessment Report. Commonwealth of Australia, Canberra, ACT.

[Instructional text]

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Please keep the Section Break (Odd Page) below to ensure the page numbering remains consistent. [End instructional text]

¹ www.inahta.org

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Template style guide

[Instructional text]

General guidance

The assessment report seeks to provide MSAC with relevant information for decision-making. The information that is most relevant is guided by the factors that influence MSAC decision-making (see MSAC Guidelines, Preamble), and includes the comparative effectiveness, safety and cost-effectiveness of the proposed technology. Other factors that may affect the assessment of these measures are also relevant (to the extent that they will affect the interpretation of the measures). Additional factors may include, for example, consumer preferences, equity or implementation issues.

The development of an assessment report will usually result in a large amount of evidence with varying levels of impact on decision-making. For results that are less influential, it may be appropriate to report in the main body of the assessment report that the analysis has been done, and provide the analysis and results in a technical appendix. An example of less influential results might be secondary or nonspecified study outcomes that are consistent with the primary outcomes and other patient-relevant outcomes. For example, objective response rates may be less influential if overall survival and progression-free survival are available, and the direction and magnitude of results for objective response rates are consistent with those presented for overall survival and progression-free survival.

As well as providing the context in which a technology is assessed, an assessment report should present the best evidence to support a decision. This involves presenting the best quality evidence and an interpretation of that evidence alongside mitigating factors, concerns and assumptions. The key issues and concerns that aid the interpretation of the evidence are likely to inform the key issues for MSAC consideration.

In general, the assessment report should provide quantitative and numerical results in tables or figures. It is uninformative to repeat results in text if they are captured in tables.

Present the interpretation of tables and figures in text. An interpretation does not repeat numbers or estimates from tables, but explains their relevance and how the results relate to other findings, and identifies concerns relating to bias, confounding or validity of the results. The interpretation of the results also includes consideration of the applicability of the evidence to the Australian setting.

Executive summary

The executive summary should synthesise the information that is critical for decision-making by MSAC and its sub-committees. Present data in the most logical and succinct way to get the story told. The executive summary will form the basis of the ESC advice and the MSAC public summary document. Deviations from the template instructions are permissible where justified; however, avoid changes to the heading structure used in the executive summary.

Aim to keep the executive summary brief (less than 20–30 pages).

Avoid cross-referencing to the main body of the report. If there is relevant information in the main body, provide a brief summary. For example, do not state that ‘Secondary outcomes are presented in Section 2A.3’. If the results of the secondary outcomes are relevant to the

interpretation of the results in the executive summary, state, for example, 'The results of the secondary outcomes are consistent with those of overall survival and progression-free survival'.

Use references sparingly and insert them as footnotes.

[End instructional text]

DCAR Executive Summary

Application No. *XXXX – Application name (from MSAC website)

Applicant: [*legal name of applicant]

Date of MSAC consideration: MSAC *XXth Meeting, [*meeting date]

Main issues for MSAC consideration

[Instructional text] Provide a high-level summary of the issues that are pivotal for MSAC decision-making. This summary is not intended as stand-alone information, and should only include sufficient information to understand the main issues. Further supporting detail should be included elsewhere in the executive summary. List issues in order of importance. [End instructional text]

Clinical issues:

[Instructional text]

Discuss:

- the appropriateness of any requested MBS item descriptor. For example, is the descriptor consistent with MBS policy and TGA-approved/proposed use, including class?
- the place and timing of the proposed technology in the clinical pathway
- the choice of the main comparator(s)
- the choice of cut-off or diagnostic threshold of the test
- the availability of the clinical utility standard and other suitable test options in Australia
- the reference standard for testing, if available
- caveats arising from the assessment of the primary source(s) of evidence.

[End instructional text]

Economic issues:

[Instructional text]

Discuss:

- the appropriateness of the estimate of the prevalence of the biomarker
- whether or not the economic model appropriately incorporated outcomes and costs for false-positive and false-negative test results
- whether or not the economic model appropriately incorporated any need for retesting and/or rebiopsy
- issues arising from likely actual fees charged over MBS rebate amounts and implications for out-of-pocket payments and the Extended Medicare Safety Net.

[End instructional text]

Financial issues:

[Instructional text]

Discuss:

- the appropriateness of assumptions used to estimate the numbers of eligible patients each year
- whether there are under- or overestimates, and the likely magnitude of these
- the potential for use beyond the population specified by the MBS item descriptor.

[End instructional text]

Other relevant information:

[Instructional text]

Discuss:

- any issues related to the value of knowing. This section is included if the results are likely to affect the interpretation of the key results, or influence MSAC decision-making.
- any other relevant issues that MSAC might wish to take into consideration, for example, equity issues, accessibility issues due to location restrictions, workforce issues, results of clinical trials or studies that are imminent. This section should only be included if considered sufficiently important.

[End instructional text]

1. Purpose of application

[Refer to: MSAC Guidelines TG 1.1 \(Request for public funding\)](#)

[Instructional text] Summarise the purpose of the application using the following format: [End instructional text]

An application requesting [*Medicare Benefits Schedule (MBS) listing OR public funding] of [*intervention name] – e.g. repetitive transcranial magnetic stimulation (rTMS)] for [*indication] – e.g. treatment of antidepressant medication-resistant major depressive disorder (MDD)] was received from the [*legal name of applicant] by the Department of Health.

OR

The codependent application requested:

- Medicare Benefits Schedule (MBS) listing of [*intervention name] – e.g. optical coherence tomography (OCT) for the determination of patient eligibility and for efficacy assessment of a single treatment with ocriplasmin (JETREA®); and
- Pharmaceutical Benefits Scheme (PBS) Authority Required listing of [*medicine name] – e.g. ocriplasmin for the treatment of vitreomacular traction (VMT) including those with full-thickness macular hole (FTMH)].

2. Background

[Instructional text]

Summarise any relevant background to the application, such as prior applications for the same or similar technologies. Example text:

MSAC has not previously considered single-balloon enteroscopy for the investigation of gastrointestinal bleeding.

MBS items 30680, 30682, 30684 and 30686 for double-balloon enteroscopy were introduced on the MBS from 1 July 2007.

[Refer to: MSAC Guidelines TG 4 \(History of MSAC submissions for the health technology\)](#)

If the proposed technology has been previously considered by MSAC (for this or a similar indication), summarise the previous MSAC considerations. Include other relevant MSAC considerations, if informative.

Summarise the key matters of concern from previous considerations using the standard table format below (Table 1) and include hyperlinks to key relevant published PSDs.

[End instructional text]

Table 1 Summary of key matters of concern

Component	Matter of concern	How the current assessment report addresses it
[Identify the relevant section of the previous assessment report, e.g. comparator, clinical claim, economic evaluation]	[Identify matter of concern. Cite paragraph of the MSAC PSD (use abbreviated referencing in tables)]	[*Addressed/Not adequately addressed/not addressed] [Comment and/or cross-reference to where matter is addressed in the executive summary or main body of the report]
Example text: Clinical place in therapy	Example text: MSAC suggested the descriptor should reinforce that psychotherapy must have been previously trialled (PSD, p.2).	Example text: Addressed. Restriction amended to reflect MSAC comments.
Example text: Clinical effectiveness	Example text: MSAC noted there was other available evidence that could be informative on the relative effectiveness that was not presented in the resubmission, including the EUnetHTA 2017 and Ontario Health 2016 reports (PSD, p.3)	Example text: Addressed. The efficacy results from EUnetHTA 2017 are now applied in the economic modelling as this is the more recent of the two reviews requested to be reviewed by MSAC.

EUnetHTA = European Network for Health Technology Assessment; MSAC = Medical Services Advisory Committee; PSD = Public Summary Document. [Define all abbreviations used in the table]

3. Prerequisites to implementation of any funding advice

[Instructional text]

State whether the proposed technology includes a therapeutic good that requires TGA approval. Provide the status of the TGA process (including date or estimated date of inclusion on the ARTG and the relevant ARTG numbers where available).

State any other prerequisites, for example, a quality assurance program for a pathology test, a licensing program for an imaging technology, or a funding arrangement that needs to be established because the proposed technology is not suitable for any current source of public funding. Identify where each such prerequisite is still to be met.

[End instructional text]

4. Proposal for public funding

[Refer to: MSAC Guidelines TG 3 \(Proposed funding arrangements\)](#)

[Instructional text]

State the applicant's post-PASC proposal for public funding.

State whether the proposed technology (or technologies) is new or a variation of an existing technology. If a description of the technology is necessary, this should be brief.

If public funding is sought via the MBS, state whether the proposal intends to use existing MBS items, amend existing MBS items or create new MBS items (or a combination of these options).

For each MBS item, provide its group, descriptor, fee, benefits and explanatory notes. Ensure that amendments are clearly presented (Table 2).

[End instructional text]

Table 2 Presentation of an existing, amended or newly proposed MBS item

Category <*Insert proposed category no.> – <INSERT CATEGORY NAME>
MBS item *XXXX <*Insert intervention name> <*Specify any restrictions on use, e.g. patient characteristics to be satisfied, limits on frequency of use, limits on who can provide the item, or where it can be provided> <*Specify any relevant explanatory notes>
Fee: <*Insert proposed MBS fee>

[Instructional text]

For all funding proposals (MBS and non-MBS applications), describe and explain any restrictions based on clinical indications or prior interventions. Identify any specialty groups who would deliver the proposed technology, and, if relevant, whether the proposed technology should be restricted to any particular specialists or credentialed practitioners. State whether there are requirements of geography, facilities or location of delivery (e.g. limited to a hospital setting or to institutions with specific accreditation or licensing, or requiring specific equipment).

For investigative technologies, include whether the item should be pathologist determinable, or whether it should be limited to approved laboratories.

Provide the proposed fee, and comment on how it compares to existing similar items.

Summarise any key issues with the proposed descriptor (e.g. not consistent with the trial, TGA registration or clinical guidelines).

Examples:

The application proposed that the MBS item numbers for DBE be amended to replace the term 'double balloon enteroscopy' with 'balloon-assisted enteroscopy' so that the same MBS items may be used for either DBE or SBE.

MBS items for capsule endoscopy (CE) also need to be amended to cross-reference balloon enteroscopy (or the MBS item numbers) rather than DBE.

[End instructional text]

5. Population

[Refer to: MSAC Guidelines TG 2.1 \(Population\)](#)

[Instructional text]

State whether there is more than one PICO set (usually required when the proposed technology is used across different populations or for different indications).

For each PICO set (each unique population/indication pair) state whether the proposed technology would be used:

- in place of a current technology (as an alternative or as a replacement)
- in addition to a current technology (before, after, concomitantly or displacement)
- where no current technology is publicly funded (available, but not funded)
- where no current technology is available (e.g. 'best supportive care' or 'watchful waiting')
- in the context of a rare disease or circumstance (e.g. an orphan or minority population).

For each PICO set, summarise where the proposed technology fits into the clinical management algorithm according to the applicant's post-PASC proposal for public funding. The summary should include the patient's clinical pathway up to the point where the proposed technology is appropriate.

If the use of medical services following the use of the proposed technology will change, summarise the downstream impacts on resource use (e.g. displaced therapies or avoided tests).

State whether the assessment report addresses the requirements of the confirmed PICO.

[End instructional text]

6. Comparator

[Refer to: MSAC Guidelines TG 2.3 \(Comparator\)](#)

[Instructional text]

Describe the comparator as specified by the applicant post-PASC.

State whether the post-PASC comparator is appropriate. If not, what is the preferred comparator and why?

State whether and how the comparator is currently funded (e.g. public or private hospital, MBS, other funding source). If the comparator is MBS listed, provide the MBS item number(s), descriptor(s) and date(s) of listing.

[End instructional text]

7. Characteristics of the evidence base

[Instructional text]

Note. There are no particular TGs in the MSAC Guidelines that request this type of summary. This is the culmination of the methodological appendices (2–5), and the information should be drawn from the study profiles in Appendix B.

Tabulate the primary source(s) of evidence (see Table 3 and Table 4). Indicate which sources provide evidence of safety, effectiveness or both. For each source, identify the type of study (e.g. randomised trials, indirect comparison, nonrandomised studies), the key outcome(s) relevant to the evaluation and the overall risk of bias (relevant to the key outcomes). Indicate which sources have been used in the economic evaluation.

[End instructional text]

Table 3 Key features of the included evidence (example for a therapeutic technology)

References	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
[*proposed intervention vs comparator]						
Jones 2010	225		Low			Not used
Smith 2012	310		High			Not used
Brown 2005	75		Low			Not used
Meta-analysis	410	Included Jones 2010 and Brown 2005; sub-group analysis; assessed overall survival				Survival gain
etc.						
etc.						

DB = double blind; MC = multicentre; OL = open label; OS = overall survival; PFS = progression-free survival; R = randomised. [Define all abbreviations used in the table]

Table 4 Key features of the included evidence (example for an investigative technology)

Criterion	Type of evidence supplied	Extent of evidence supplied			Overall risk of bias in evidence base
Accuracy and performance of the test (cross-sectional accuracy)	[Describe study designs used to assess test accuracy]	<input type="checkbox"/>	k=	n=	[use QUADAS-2 risk of bias tool]
Prognostic evidence (longitudinal accuracy)	[Comparison of outcomes in patients receiving <i>usual care</i> , conditioned on the presence or absence of biomarker-positive status]	<input type="checkbox"/>	k=	n=	[could use QUIPS risk of bias tool]
Change in patient management	[Evidence to show that test result guides decisions about treatment or alters behaviour]	<input type="checkbox"/>	k=	n=	[could use Cochrane risk of bias tool]
Health outcomes	[Evidence to show that the changes in management or behaviour affect health outcomes]	<input type="checkbox"/>	k=	n=	[could use Cochrane risk of bias tool]
Predictive effect (treatment effect variation)	[Comparison of outcomes in patients with and without the biomarker who receive the treatment of interest, or usual care]	<input type="checkbox"/>	k=	n=	[could use Cochrane risk of bias tool]
Other		<input type="checkbox"/>	k=	n=	

k=number of studies, n=number of patients. [Define all abbreviations used in the table]

8. Comparative safety

Refer to: [MSAC Guidelines TG 7 \(Safety of therapeutic technologies\)](#)

Refer to: [MSAC Guidelines TG 14 \(Safety of investigative technologies\)](#)

[Instructional text]

Tabulate the main safety results in a way that permits a comparison of the proposed technology and the main comparator. Safety results relevant for inclusion in the executive summary are those that support or diminish the clinical claim. Usually these will be safety results that are severe (with a substantial impact on patients) or frequent, or where the safety profile of the proposed technology differs from that of the comparator.

For investigative technologies, present the direct harms of the test. Separately summarise the consequent harms of testing (i.e. those mediated through subsequent changes to clinical management).

State key limitations of the evidence and provide an interpretation of their impact on the certainty of the results.

State whether the proposed technology is safer, of similar safety or less safe than clinical management without it.

[End instructional text]

9. Comparative effectiveness

Refer to: [MSAC Guidelines TG 6 \(Effectiveness of therapeutic technologies\)](#)

Refer to: [MSAC Guidelines TG 10 \(Direct from test to health outcomes evidence\)](#)

Refer to: [MSAC Guidelines TG 11 \(Linked evidence – test accuracy\)](#)

Refer to: [MSAC Guidelines TG 12 \(Linked evidence – change in management\)](#)

Refer to: [MSAC Guidelines TG 13 \(Linked evidence – health outcomes\)](#)

[Instructional text]

Tabulate the main effectiveness results in a way that permits a comparison of the proposed technology and the main comparator. Where appropriate, provide meta-analysed results. For time-to-event outcomes, graphical presentations may be informative. Effectiveness results relevant for inclusion in the executive summary are those that are derived using high-quality evidence and which support or diminish the clinical claim. Usually these will be effectiveness results that are most patient relevant, or that reveal similarity or dissimilarity to the main comparator.

The selection of results for the executive summary should provide a clear picture of the comparative effectiveness but not repeat findings. After providing the most important results, it is sufficient to state whether the secondary or alternative outcomes are consistent with the primary outcomes.

Effectiveness results for therapeutic technologies include the primary outcomes of studies, and key secondary patient-relevant outcomes.

Effectiveness results for investigative technologies will depend on the approach taken:

- For direct from test to health outcomes evidence, report patient-relevant outcomes as for therapeutic technologies above. Results should be separated for test-positive and test-negative patients, where possible.
- For a linked evidence approach, briefly report the test accuracy, prevalence and relevant estimates of accuracy as applied to the target Australian population (e.g. positive predictive value, negative predictive value). Present results for change in management. Results for health outcomes are reported in a similar way to outcomes of a therapeutic technology; however, results should be separated by test-positive and test-negative patients. In addition, results for false positives and false negatives may be relevant.

- For the assessment of investigative technologies, discuss the clinical utility (net health benefit or harm) incorporating all of the relevant steps. Where this is uncertain, describe these uncertainties.

State key limitations of the evidence, with reference to the internal validity of the evidence (bias or confounding), the approach to generating the evidence (transitivity for indirect comparisons of studies), translations of the evidence (if surrogate outcomes have been used and translated to patient relevant outcomes), and the applicability of the evidence to the Australian setting. Provide an interpretation of the impact any limitations of the evidence may have had on the certainty of the evidence. Limit the key limitations to those that are most likely to impact the estimates of the results.

Provide a summary of the interpretation of the clinical evidence including the direction of effect, the size of effect and the level of confidence MSAC can have in this evidence.

State whether the proposed technology is more effective, of similar effectiveness or less effective than clinical management without it.

[End instructional text]

Clinical claim

[Refer to: MSAC Guidelines TG 8 \(Interpretation of the therapeutic evidence\)](#)

[Refer to: MSAC Guidelines TG 16 \(Interpretation of the investigative evidence\)](#)

[Instructional text] Summarise whether the evidence supports the clinical claim, and thus whether the presented form of economic evaluation is appropriate and supported. [End instructional text]

10. Economic evaluation

[Instructional text]

State the type of economic analysis.

[Refer to: MSAC Guidelines TG 17 \(Overview and rationale of the economic evaluation\)](#)

Describe the structure of the model and provide a brief overview (tabulated; see Table 5) of the model parameters.

If no economic evaluation was performed, explain why and summarise the alternative approach taken.

[Refer to: MSAC Guidelines TG 26 \(Cost-minimisation approach\)](#)

If the assessment of the proposed technology has taken a cost-minimisation approach, report the costs for the proposed health technology and the comparator. Present the costs separated into direct costs associated with the use of the technology, and downstream costs or cost offsets. Identify where costs are incurred across different funding mechanisms (e.g. private costs, MBS costs, public hospital costs). Summarise uncertainties associated with the cost comparison.

[End instructional text]

Table 5 Summary of the economic evaluation

Component	Description	MSAC Guidelines Reference
Perspective	[*e.g. Health care system perspective]	TG 17.3
Population	[For multi-indication models, specify the different populations (or subgroups) modelled. For example, for testing of heritable diseases, index cases, and adult and child relatives may be modelled]	TG 19
Prior testing	[*specify the tests required to determine the population in the model]	TG 19
Comparator	[*comparator]	TG 17.2
Type(s) of analysis	[*e.g. cost-effectiveness analysis, cost-utility analysis]	TG 17.5
Outcomes	[*e.g. events avoided, life-years gained, quality-adjusted life years]	TG 21
Time horizon	[*e.g. [x] days/months/years in the model base case (vs [y] weeks/years in the key trial(s))]	TG 18.2
Computational method	[*e.g. cohort expected value, Markov, partitioned survival analysis, microsimulation, discrete event simulation]	TG 18.3
Generation of the base case	[*e.g. trial based or modelled. [If modelled, summarise the steps undertaken in the economic analysis]	TG 17.6
Health states	[If a state transition model is used, state the health states included. This could also include decision tree terminal states or events modelled in a discrete event simulation.]	TG 18
Cycle length	[*x days/weeks/months/years]	TG 18.3
Transition probabilities	[Where different data sources are used to inform different transition probabilities, e.g. baseline event rate, treatment effect, secondary transition probabilities, describe the source(s) of each key model input. For investigative technologies, the sources of data used to inform additionally relevant inputs, such as prevalence, accuracy and change in management, should also be summarised. Indicate if the data required translation for use in the economic analysis.]	TG 20
Discount rate	[*e.g. 5% for both costs and outcomes]	TG 17.4
Software	[*e.g. Excel, @RISK, TreeAge Pro]	TG 18.3

[Define all abbreviations used in the table]

Refer to: MSAC Guidelines TG 24 (Results of the base-case economic evaluation)

[Instructional text] If possible, present a stepped economic analysis for the base-case results of the economic evaluation (see Table 6 and Table 7). [End instructional text]

Table 6 Results of the stepped economic analysis (therapeutic example)

Step	[*Proposed health technology]	[*Main comparator]	Increment	ICER
Step 1 – Comparative study data (as presented in Section 2); Setting: [*trial setting]; Time horizon: [*trial follow-up]				
Costs	\$[A]	\$[B]	\$[A – B]	
Outcome 1 (surrogate outcome)	[C]	[D]	[C – D]	\$[A – B]/[C – D]
Step 2 – Study evidence transformed from surrogate to clinical outcome				

Step	[*Proposed health technology]	[*Main comparator]	Increment	ICER
Costs	[\$A]	[\$B]	[\$A – B]	
Outcome 1 (clinical outcome)	[E]	[F]	[E – F]	[\$A – B]/[E – F]
Step 3 – Study evidence transformed to clinical outcome and translated to the Australian population and/or Australian setting (may need multiple steps)				
Costs	[\$A]	[\$B]	[\$A – B]	
Outcome 2	[E]	[F]	[E – F]	[\$A – B]/[E – F]
Step 4 – Study evidence transformed to clinical outcome, translated to the Australian population/setting, and extrapolated to the appropriate time horizon				
Costs	[\$G]	[\$H]	[\$G – H]	
Outcome 2	[I]	[J]	[I – J]	[\$G – H]/[I – J]
Step 5 – Study evidence transformed to clinical outcome, translated to the Australian population/setting, extrapolated and with additional assumptions or modelled information				
Costs	[\$K]	[\$L]	[\$K – L]	
Outcome 2	[M]	[N]	[M – N]	[\$K – L]/[M – N]
Step 6 – Study evidence translated to clinical outcomes, the Australian population/setting, extrapolated, with additional modelling, and transformed into a relevant health outcome (e.g. QALYs)				
Costs	[\$K]	[\$L]	[\$K – L]	
Outcome 3 (QALYs)	[O]	[P]	[O – P]	[\$K – L]/[O – P]

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year. [\[Define all abbreviations used in the table\]](#)

Note: Multiple outcomes may be informative for MSAC decision making-within each step.

Table 7 Results of the stepped economic analysis (investigative example)

Step	[*Proposed health technology]	[*Main comparator]	Increment	ICER
Step 1 – Comparative diagnostic accuracy, as applied to the prevalence in the eligible Australian population Time horizon: time to reach a diagnosis				
Costs	\$[A]	\$[B]	\$[A – B]	
Total correct diagnoses	[C]	[D]	[C – D]	$\frac{[A - B]}{[C - D]}$
Step 2 – Incorporation of repeat or confirmatory testing, which may affect final diagnostic conclusions Time horizon: time to reach a diagnosis				
Costs	\$[E]	\$[F]	\$[E – F]	
Total correct final diagnoses	[G]	[H]	[G – H]	$\frac{[E - F]}{[G - H]}$
Step 3 – Uptake of treatment, or other change in clinical management, by final test result Time horizon: time to treatment allocation decision				
Costs	\$[I]	\$[J]	\$[I – J]	
Appropriate management allocation	[K]	[L]	[K – L]	$\frac{[I - J]}{[K - L]}$
Step 4 – Incorporation of effectiveness of treatment (e.g. survival benefit) translated to the Australian population and/or setting, and extrapolated to the appropriate time horizon (may need multiple steps) Time horizon: appropriate time horizon to capture differences in costs and outcomes due to changes in treatment allocation decisions (e.g. lifetime)				
Costs	\$[M]	\$[N]	\$[M – N]	
Life years gained	[O]	[P]	[O – P]	$\frac{[M - N]}{[O - P]}$
Step 5 – Outcomes transformed into a relevant health outcome (e.g. QALYs)				
Costs	\$[M]	\$[N]	\$[M – N]	
QALYs	[Q]	[R]	[Q – R]	$\frac{[M - N]}{[Q - R]}$

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year. [Define all abbreviations used in the table]

Note: Multiple outcomes may be informative for MSAC decision-making within each step.

Where the proposed health technology is a heritable genetic test, in addition to a table that presents step-wise incorporation of key assumptions regarding change in management due to testing and transformation of outcomes (i.e. Table 7), present a table that explores alternate listing scenarios around the base-case analysis, where testing is limited to, for example, affected cases only, affected cases and their first-degree relatives only, etc. (Table 8).

Table 8 Alternate scenarios exploring which cohorts of relatives are eligible for proposed heritable genetic testing

Parameter	[*Proposed health technology]	[*Main comparator]	Increment	ICER
Affected cases only				
Costs				
QALYs				
No. positive affected cases identified				
No. positive relatives identified				
No. with appropriate management				
Affected cases and first-degree relatives				
Costs				
QALYs				
No. positive affected cases identified				
No. positive relatives identified				
No. with appropriate management				
Affected cases and first- and second-degree relatives				
Costs				
QALYs				
No. positive affected cases identified				
No. positive relatives identified				
No. with appropriate management				

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year. [Define all abbreviations used in the table]

Note: Multiple outcomes may be informative for MSAC decision-making – examples have been presented.

[Instructional text] Present the overall results of the base case (Table 9). [End instructional text]

Table 9 Results of the economic evaluation

Parameter	[*Proposed health technology]	[*Main comparator]	Increment
Costs	\${*}	\${*}	\${*}
Life years	{*value}	{*value}	{*value}
QALYS	{*value}	{*value}	{*value}
Incremental cost per life year gained			\${*} or dominant/dominated
Incremental cost per QALY gained			\${*} or dominant/dominated

QALY = quality-adjusted life year. [Define all abbreviations used in the table]

Refer to: MSAC Guidelines TG 25 (Uncertainty analysis: model inputs and assumptions)

[Instructional text] Present the key drivers of the model that are uncertain (Table 10). Drivers may include inputs and translation issues. Rate the impact on the ICER as high or moderate. Keep the text in the tables brief. If further explanation of the key drivers is required, provide this in text.

[End instructional text]

Table 10 Key drivers of the model

Description	Method/Value	Impact [If relevant per rows below, add:] Base case: \$xx,xxx/QALY gained
Extrapolation	Treatment effect continued beyond [*x]-month trial period for up to [*xx] years OR Point of extrapolation [*before/after] time when observed data became unreliable as a result of [*e.g. small numbers of patients remaining event-free]	<i>High, favours [*proposed technology]</i> [If relevant, consider adding:] <i>Use of [*xx approach] increased the ICER to *\$xx,xxx/QALY gained.</i> [State the base-case ICER in the header row.]
Utilities	High values for model health states taken from [*literature] and no disutility for adverse events	<i>High, favours [*proposed technology]</i> [If relevant, consider adding:] <i>Use of [*xx utilities] increased the ICER to *\$xx,xxx/QALY gained.</i> [State the base-case ICER in the header row.]
etc.		

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year. [Define all abbreviations used in the table]

[Instructional text]

Present key concerns with the economic evaluation. These may be the key drivers of the model. For example:

- If the time horizon is a key issue, consider presenting a trace of ICER over time, but only present this in the executive summary if it will be informative for MSAC decision-making (e.g. consider whether it is the time horizon or the extrapolation that is a key issue).
- If the utilities or costs are a key issue, consider presenting an abbreviated disaggregated costs/outcomes table to show the impact.
- Where relevant, consider including information that highlights inconsistencies or differences between the model and clinical data (e.g. a table comparing the number of events avoided in the model compared with the clinical trial data; graphs with an overlay of the Kaplan–Meier plot and the modelled extrapolations; or disaggregated costs and outcomes).
- Where relevant, describe the extent to which the model includes out-of-pocket expenses.

Present and justify key sensitivity analyses (Table 11).

For example: [End instructional text]

The results of key [*univariate/multivariate] sensitivity analyses are summarised below.

[Instructional text] Only present key sensitivity analyses that are pivotal for MSAC decision-making in the executive summary (i.e. concentrate on parameters with which there are issues and which have an impact on the ICER). This table should generally be no more than half a page. A more comprehensive table should be presented in the main body of the assessment report. Consider presenting 1 or 2 realistic multivariate sensitivity analyses that assess the key issues. [End instructional text]

Table 11 Sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER
Base case	\${*}	{*value}	\${*}
Time horizon (base case 30 years)			
20 years	\${*}	{*value}	\${*}
10 years	\${*}	{*value}	\${*}
etc.			

ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year. [Define all abbreviations used in the table]

11. Financial/budgetary impacts

Refer to: MSAC Guidelines TG 27 (Use of the health technology in practice)

[Instructional text] Explain the approach used to estimate the uptake of the proposed technology (e.g. epidemiological approach, market-based approach). [End instructional text]

The financial implications to the [*MBS/other funding source] resulting from the proposed listing of [*proposed health technology] are summarised in Table 12.

[Instructional text] The financial implications are presented over 6 years (Table 12). Amend table content as relevant. [End instructional text]

Table 12 Net financial implications of [*proposed health technology] to the [*relevant funding program]

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated use and cost of the proposed health technology						
Number of people eligible for [*proposed health technology]						
Number of people who receive [*proposed health technology]						
Number of services of [*proposed health technology] (if more than one per person)						
Cost to the [*relevant funding program] (with appropriate copayments excluded)						
Change in use and cost of other health technologies						
Change in use of [*comparator]						
Change in use of [*other affected health technologies]						
Net change in costs to the [*relevant funding program] (with appropriate copayments excluded)						
Net financial impact to the [*relevant funding program]						

[Define all abbreviations used in the table]

[Instructional text]

The summary of financial implications should primarily focus on the implications to the funding sources (e.g. MBS, National Blood Authority).

Present the following (adapted if necessary):

- The average cost of the proposed technology per patient <per year/per course> is: \$X.
- The average frequency of use of the proposed technology is: X <per year/per lifetime>.
- The average out-of-pocket cost per patient <per year/per course> is: \$X.

Note that the out-of-pocket cost per patient includes both the estimated copayments and the additional costs above the funded amount.

If a service is primarily out-of-hospital, a separate analysis of the financial implications to the Extended Medicare Safety Net will be required.

If there is additional relevant information that should be taken into account in the financial implications (e.g. cost impacts on other government health budgets, patient costs), mention these here and be guided by the Department as to what data would be expected.

[End instructional text]

12. Other relevant information

[Refer to: MSAC Guidelines TG 5 \(Approach to assessment\)](#)

[Refer to: MSAC Guidelines TG 28 \(Value of knowing\)](#)

[Instructional text] In addition to a clinical claim relating to health outcomes, investigative technologies may (uncommonly) make a claim of 'value of knowing'. For an investigative technology that results in no, minimal or uncertain change in management, where the key benefit relates to the value of knowing, tabulate the key proposed value of knowing benefits and harms associated with the use of the proposed test ([Refer to: TG 28.2](#)). Key results are those that are quantitative and supported by evidence. [End instructional text]

[Refer to: MSAC Guidelines TG 29 \(Other relevant considerations\)](#)

[Instructional text] Summarise any other relevant factors (e.g. ethical, legal, social, equity) as appropriate, or identify as 'Nil'. [End instructional text]

13. Committee-in-confidence information

[Instructional text] Include Committee-in-confidence information if relevant, or identify as 'Nil'. [End instructional text]

Acronyms and abbreviations

[Instructional text] Add/delete as applicable. [End instructional text]

AIHW	Australian Institute of Health and Welfare
ARTG	Australian Register of Therapeutic Goods
CI	confidence interval
ESC	Evaluation Sub-Committee
HRQoL	health-related quality of life
HTA	health technology assessment
ICER	incremental cost-effectiveness ratio
MBS	Medicare Benefits Schedule
MD	mean difference
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
PASC	PICO Confirmation Advisory Sub-Committee of the MSAC
QALY	quality-adjusted life year
TGA	Therapeutic Goods Administration

Section 1 Context

1.1 Purpose of application

[Instructional text] Describe the purpose of the application. Include the following text: [End instructional text]

This DCAR of [*proposed technology] for the [*treatment/diagnosis/screening/triaging/staging/investigation of XXXX] is intended for the Medical Services Advisory Committee (MSAC).

MSAC appraises medical services, health technologies and health programs for public funding through an assessment of their comparative safety, clinical effectiveness, cost-effectiveness and total cost, using the best available evidence. This includes, but is not limited to, amendments and reviews of existing services funded on the Medicare Benefits Schedule (MBS) or other non-MBS-funded programs (e.g. blood products, screening programs or prostheses referred to the Prostheses List Advisory Committee).

[*Name of contracting agency] has been commissioned by the Australian Government Department of Health to conduct a systematic literature review and economic evaluation of [*proposed technology]. This assessment has been undertaken to inform MSAC's decision-making regarding whether the proposed health technology should be publicly funded. The purpose of this assessment report is to synthesise the information most likely to be useful for committee members. Technical appendices provide assurance of the rigour behind the systematic review and construction of the economic and financial analyses.

The proposed use of [*proposed technology] in Australian clinical practice was outlined in a PICO confirmation that was presented to, and accepted by, the PICO Confirmation Advisory Sub-Committee (PASC). The PICO confirmation was released for public comment on [*Day Month Year].

Refer to: MSAC Guidelines TG 1 (Purpose of application) for more details regarding the purpose of this section

[Instructional text]

Provide a brief summary of the purpose for the application (Refer to: TG 1.1). Information requests in this section are repeated in later sections (e.g. population is reported briefly here, and expanded in Section 1.2 of the template). The purpose of this section is to provide a brief overview of the context of the application. For example:

Homologous recombination deficiency (HRD) testing is used to detect patients likely to respond to poly-ADP-ribose polymerase (PARP) inhibitors in patients with locally advanced or metastatic ovarian cancer. PARP inhibitors interrupt DNA repair and in patients with deficient homologous repair pathways, result in cell death. HRD testing identifies BRCA1 and BRCA2 pathogenic variants, which account for a large proportion of patients with deficient homologous repair pathways. However, HRD testing also identifies other genetic issues that result in deficient homologous repair pathways, which are also susceptible to PARP inhibitors. HRD testing (followed by a PARP inhibitor in eligible patients) results in superior health outcomes (improved overall survival and progression free survival) compared to BRCA1/2 testing.

In a paragraph or two, note the proposed patient population, the clinical need, the clinical claim, and the proposed funding source.

The clinical claim is typically phrased as one of the options below.

- The use of the proposed technology results in superior health outcomes compared to the comparator/standard practice.
- The use of the proposed technology results in noninferior health outcomes compared to the comparator/standard practice.
- The use of the proposed technology results in inferior health outcomes compared to the comparator/standard practice.

Refer to: MSAC Guidelines TG 1.2 for instructions related to developing the clinical claim

For claims that are noninferior, justify the need for the health technology.

[End instructional text]

1.2 Background

Refer to: MSAC Guidelines TG 4 (History of MSAC submissions for the health technology)

[Instructional text]

Summarise any relevant background to the application, such as prior applications for the same or similar technologies. Example text:

MSAC has not previously considered single-balloon enteroscopy for the investigation of gastrointestinal bleeding.

MBS items 30680, 30682, 30684 and 30686 for double-balloon enteroscopy were introduced on the MBS from 1 July 2007.

If this is the second or subsequent time this technology has been assessed for this, or a similar, indication, tabulate the relevant meeting dates (Table 13).

[End instructional text]

Table 13 MSAC application history

Committee	Meeting date(s)
PASC	*add
ESC	*add
MSAC	*add

[Instructional text] Present a summary of the key matters of concern identified in the MSAC public summary document (Table 14), including hyperlinks to the relevant published PSD(s), and discuss how the current assessment report addresses these concerns. [End instructional text]

Table 14 Summary of key matters of concern

Component	Matter of concern	How the current assessment report addresses it
[Identify the relevant section of the previous assessment report, e.g. comparator, clinical claim, economic evaluation]	[Identify matter of concern. Cite paragraph of the MSAC PSD (use abbreviated referencing in tables)]	[*Addressed/Not adequately addressed/not addressed] [Comment and/or cross-reference to where addressed below in the executive summary or main body of the report.]
Example text: Clinical place in therapy	Example text: MSAC suggested the descriptor should reinforce that psychotherapy must have been previously trialled (PSD, p.2)	Example text: Addressed. Restriction amended to reflect MSAC comments.
Example text: Clinical effectiveness	Example text: MSAC noted there was other available evidence which could be informative on the relative effectiveness that was not presented in the resubmission, including the EUnetHTA 2017 and Ontario Health 2016 Reports (PSD, p.3)	Example text: Addressed. The efficacy results from EUnetHTA 2017 are now applied in the economic modelling as this is the more recent of the two reviews requested to be reviewed by MSAC.

EUnetHTA = European Network for Health Technology Assessment; MSAC = Medical Services Advisory Committee; PSD = Public Summary Document. [Define all abbreviations used in the table]

[Instructional text] If this assessment is a resubmission, avoid presenting information in this assessment report if it is not in dispute. Delete sections of the template that are not required.
[End instructional text]

1.3 Prerequisites to implementation of any funding advice

[Instructional text]

State whether the proposed technology includes a therapeutic good that requires TGA approval. Provide the status of the TGA process (including date or estimated date of inclusion on the ARTG and the relevant ARTG numbers where available).

State any other prerequisites, for example, a quality assurance program for a pathology test, a licensing program for an imaging technology, or a funding arrangement that needs to be established because the proposed technology is not suitable for any current source of public funding. Identify where each such prerequisite is still to be met.

[End instructional text]

1.4 Population

[Refer to: MSAC Guidelines TG 2.1](#)

[Instructional text]

Describe the target population(s) likely to use the proposed health technology if it is publicly funded, and estimate the size of the proposed population(s).

If the application has gone through PASC, these details should be able to be derived from the PICO confirmation.

[End instructional text]

1.5 Intervention

Refer to: [MSAC Guidelines TG 2.2 \(Intervention\)](#)

[Instructional text] Describe the proposed health technology. [End instructional text]

1.6 Comparator(s)

Refer to: [See MSAC Guidelines TG 2.3 \(Comparator\)](#)

[Instructional text] Describe what happens in the absence of the proposed health technology. [End instructional text]

1.7 Summary of the PICO criteria

[Instructional text] Provide the PICO criteria from the PICO confirmation, if one was developed (Table 15). [End instructional text]

The Prior tests, Population, Investigation/Index test, Comparator and Outcomes (PPICO) that were prespecified [\[*in the PICO confirmation\]](#) to guide the systematic literature review are presented in Table 15.

Table 15 PPICO criteria for assessing [\[*proposed health technology\]](#) for [\[*indication\]](#)

Component	Description
Population	
<Prior tests>	
Intervention	
Comparator	
Outcomes	Safety: Effectiveness: Health care system outcomes:
Systematic review questions: What is the safety, effectiveness and cost-effectiveness of [*XXXX] compared to [*XXXX] in [*XXXX]?	

[Define all abbreviations used in the table]

[Instructional text] If more extensive PICO criteria and research questions have been developed for the purpose of the systematic review (e.g. for different components of the linked evidence assessment), provide these in an appendix. [End instructional text]

1.8 Alignment with the PICO confirmation

Refer to: [MSAC Guidelines TG 2 \(PICO\)](#)

[Instructional text] Include the following text: [End instructional text]

This ***DCAR** of ***proposed technology** addresses ***all/most/some/none** of the PICO elements that were prespecified in the PICO confirmation ***that was ratified by/submitted to** PASC.

[Instructional text] If deviations from the PICO confirmation have occurred, state briefly what has changed. Has the approach suggested in the PICO confirmation still been addressed, but an alternative approach has been presented? Or has the approach suggested in the PICO confirmation not been addressed and only the alternative approach has been presented? Give reasons for any departure from the PICO confirmation (including by referring to the relevant section in the main body of the report). If a PICO confirmation was not presented to PASC or MSAC Executive, please state this. [End instructional text]

1.9 Clinical management algorithms

Refer to: [MSAC Guidelines TG 2.6 \(Clinical management algorithms\)](#)

[Instructional text]

Provide the clinical management algorithms from the PICO confirmation.

If a PICO confirmation was not developed, see TG 2.6 for instructions on developing clinical management algorithms.

Highlight the differences between the two algorithms in text; for example, any change in positioning of a therapy in terms of lines of therapy; expansion/augmentation of the current management options; or identification of patients who would now be treated who previously would not have been treated. Indicate whether multiple-listing scenarios are presented.

[End instructional text]

1.10 Proposal for public funding

Refer to: [MSAC Guidelines TG 3 \(Proposed funding arrangements\)](#)

[Instructional text]

State and justify the funding arrangement being proposed (i.e. whether a new MBS listing, an amendment to an existing MBS listing, funding for a package of care, or another form of public funding is being sought, and why).

For MBS items, provide the proposed item descriptor (Table 16).

Provide the proposed fee and explain how it was derived.

[End instructional text]

Table 16 Proposed item descriptor for [*proposed technology]

Category <*Insert proposed category no.> – <*INSERT CATEGORY NAME>
MBS item *XXXX <*Insert intervention name> <*Specify any restrictions on use, e.g. patient characteristics to be satisfied, limits on frequency of use, limits on who can provide the item, or where it can be provided> <*Specify any relevant explanatory notes>
Fee: <*insert proposed MBS fee>

Section 2A Clinical evaluation of therapeutic technologies

[Instructional text] Delete Section 2A if assessing an investigative technology. [End instructional text]

2A.1 Methods for undertaking the assessment

Refer to: [MSAC Guidelines Appendices 1 to 5 for details on the methods of the assessment](#)

[Instructional text]

Very briefly, summarise the approach used to derive the clinical evidence for Section 2 of the assessment report, including (but not limited to):

- whether a protocol was registered a priori
- what types of search terms were used
- what limits were placed on the searches
- how many databases were searched.

It is anticipated that the methods for the review would take less than a page to describe.

Provide a full description of the methods in Appendix A.

[End instructional text]

2A.2 Characteristics of the evidence base

Refer to: [MSAC Guidelines Appendix 3 for the assessment of risk of bias of included studies](#)

Refer to: [MSAC Guidelines Appendix 5 for information on extracting relevant study characteristics](#)

[Instructional text] Include the following text: [End instructional text]

A total of ***XX** studies met the inclusion criteria for assessing the safety and effectiveness of ***proposed technology** compared to ***comparator**. Full study profiles and a PRISMA flowchart are presented in Appendix B.

A summary of the key features of the studies on the comparative safety and effectiveness of ***the intervention and comparator(s)** is provided in Table 17.

[Instructional text]

Develop an appropriate way of presenting information on the interventions and/or comparators, and outcomes being tested for these study designs (see example in Table 17). Depending on the number of trials identified, include the key studies only. Keep this section brief, and provide more detail in the study profiles in Appendix B.

Provide information about any study/participant characteristics that are not reported elsewhere, but which are key to interpreting the implications of the evidence. The study/participant characteristics that will be informative for interpreting the results may include those that raise concerns about the internal validity of studies (imbalances across study arms), applicability of the evidence to the Australian setting, or transitivity issues for indirect comparisons. Depending on the volume of studies, tabulate the characteristics of the key studies and compare against the proposed Australian setting.

[End instructional text]

Table 17 Key features of the included evidence comparing [*intervention] with [*comparator]

Trial/Study	N	Study design Risk of bias	Population	Intervention	Comparator	Key outcome(s)	Result used in economic model

[Define all abbreviations used in the table]

[Instructional text]

State the method used to assess risk of bias. It is suggested to use a ‘heat map’ to highlight the deficiencies of the evidence.

Concerns relating to the internal validity or applicability of the evidence may be briefly raised in this section. These concerns should then be more fully discussed in the following sections, alongside the interpretation of results that may be impacted by these concerns.

[End instructional text]

2A.3 Results

[Refer to: MSAC Guidelines TG 6 \(Effectiveness of therapeutic technologies\)](#)

[Refer to: MSAC Guidelines TG 7 \(Safety of therapeutic technologies\)](#)

[Instructional text]

Synthesise the best available evidence that addresses the research questions. Provide tables/figures with results instead of narrative synthesis where possible.

In some circumstances, the evidence will be derived from all included studies. If broad inclusion criteria were used, and a large volume of literature has been identified, then consider presenting comparative studies only, and those at least risk of bias and with the highest applicability. Justify the criteria for selecting studies, and cross-reference to an appendix for a description of the excluded studies.

Present results in descending order of patient relevance.

In order for MSAC to be able to compare the intervention and the comparator, present results for both by outcome measure (i.e. even if a naïve comparison is presented, present the results in

such a way that they can be easily compared, such as tabulation of the proposed technology and the comparator in the same table).

[End instructional text]

***Safety outcome 1**

Refer to: MSAC Guidelines TG 7 (Safety of therapeutic technologies)

[Instructional text] Present evidence of the harms (adverse events) experienced by patients who receive the intervention versus the comparator. Discuss the outcome measure and the results, synthesise how the intervention and the comparator differ on this outcome measure, and discuss how the study design, risk of bias and other factors influence the certainty of the evidence. Consider the applicability of the evidence. [End instructional text]

***Safety outcome 2**

[Instructional text] As above for safety outcome 1. Present evidence for further safety outcomes in the same way. [End instructional text]

***Effectiveness outcome 1**

Refer to: MSAC Guidelines TG 6 (Effectiveness of therapeutic technologies)

[Instructional text]

By outcome measure, discuss the validity of the tools used to measure the outcome, and how a clinically important effect is defined. Discuss whether the analyses presented in the studies were prespecified or post hoc. Discuss the methods you have used (and justification if the method is unusual) to conduct your own statistical analyses for the assessment; for example, calculation of confidence intervals, statistical tests and meta-analyses should be mentioned here.

Present the results for outcome 1. If appropriate, present a pooled estimate or meta-analysis; however, ensure that the influence of individual studies on the pooled estimate can be ascertained. Provide tables/figures with results instead of narrative synthesis where possible. Regardless of the study type (or comparison type, i.e. direct comparison, indirect comparison or naïve indirect comparison), ensure that the incremental difference between the proposed technology and the comparator is presented, where possible.

It is important to ensure that the results from individual studies are reported in addition to pooled estimates. Relevant details of individual study results include:

- the number of patients at risk or providing data to the results
- the number of patients experiencing the event (if appropriate)
- the percentage of patients with the event, and means (standard deviation) or medians (interquartile range) within groups, as appropriate
- confidence intervals (CIs) of the outcomes within groups
- relative and absolute differences between groups, and CIs.

The format of tables for presenting results will need to be adapted to the data available and the type of outcome. Table 18, Table 19 and Table 20 show examples of how some outcomes might be presented.

[End instructional text]

Table 18 Results of [*key patient-relevant outcome] across the [*studies/randomised controlled trials (dichotomous data)]

Study ID	Risk of bias	Intervention <n with event/N (%)>	Comparator <n with event/N (%)>	Absolute difference <RD±NNT/NNH and 95% CI>	Relative difference <OR/RR/HR and 95% CI>
Trial 1					
Trial 2					
etc.					
<Pooled result>				<XX>	<XX>
Chi-square for heterogeneity: Q= , df= , P=	I ² statistic with 95% uncertainty interval =				

[If outcome is continuous, provide the scale]

CI=confidence interval; HR=hazard ratio; NNH=number needed to harm; NNT=number needed to treat; OR=odds ratio; RD=risk difference; RR=relative risk; SD=standard deviation. [Define all abbreviations used in the table]

Table 19 Results of [*key patient-relevant outcome] across the [*studies/randomised controlled trials (continuous data)]

Study ID	Risk of bias	Intervention <mean ± SD>	Comparator <mean ± SD>	Absolute difference <mean difference and SD or 95%CI>	Relative difference <results of statistical testing and p-value and/or 95% CI>
Trial 1					
Trial 2					
etc.					
<Pooled result>				<XX>	<XX>
Chi-square for heterogeneity: Q= , df= , P=	I ² statistic with 95% uncertainty interval =				

[If outcome is continuous, please provide the scale]

CI=confidence interval; SD=standard deviation [Define all abbreviations used in the table]

Table 20 Results of [*key patient-relevant outcome] across the [*before and after studies (continuous data)]

Study ID	Risk of bias	Before Intervention <mean ± SD>	After intervention <mean ± SD>	Change p-value	Clinically important?
Study 1					
Study 2					
etc.					

[If outcome is continuous, please provide the scale]

SD=standard deviation. [Define all abbreviations used in the table]

[Refer to: MSAC Guidelines Appendix 3 \(Risk of bias\)](#)

[Refer to: MSAC Guidelines Appendix 4 \(Certainty of the evidence\)](#)

[Instructional text]

Discuss how the study design, risk of bias and other factors influence the certainty of the evidence.

Discuss uncertainties relating to the results, including heterogeneity across studies, transitivity concerns and applicability to the target population. Reference differences in study and population characteristics presented in Section 2A.2.

[End instructional text]

***Effectiveness outcome 2**

[Instructional text] As above for effectiveness outcome 1. Discuss the outcome measure and the results, synthesise how the intervention and the comparator differ on this outcome measure, and discuss how the study design, risk of bias and other factors influence the certainty of the evidence. Consider the applicability of the evidence. [End instructional text]

***Effectiveness outcome 3**

[Instructional text] As above for effectiveness outcome 1. [End instructional text]

***Effectiveness outcome 4**

[Instructional text] As above for effectiveness outcome 1. Present evidence for further effectiveness outcomes in the same way. [End instructional text]

2A.4 Evidence interpretation

[Refer to: MSAC Guidelines TG 8.1 \(Therapeutic evidence interpretation\)](#)

[Instructional text]

Discuss whether the evidence supports the clinical claim, and the certainty of evidence. A GRADE summary of evidence table may be used in this process.

Provide a summary of the overall evidence base (without repeating evidence from other sections). Consider:

- the level of the evidence, taking account of the directness of the comparison
- the quality of the evidence
- the clinical importance and patient relevance of the effectiveness and safety outcomes
- the statistical precision of the evidence
- the size of the effect
- the consistency of the results across the clinical studies and across subgroups
- the strength or certainty of the evidence
- the applicability of the evidence to the Australian setting
- any other uncertainties in the evidence, including missing outcomes or populations

- other relevant factors that may influence decision-making, particularly implementation and ethical factors.

[End instructional text]

2A.5 Conclusion of the clinical claim

Refer to: MSAC Guidelines TG 8.2 (Conclusion of the clinical claim)

[Instructional text] Include the following text: [End instructional text]

The use of [*proposed health technology] results in [*superior/noninferior/inferior] effectiveness compared with [*comparator].

The use of [*proposed health technology] results in [*superior/noninferior/inferior] safety compared with [*comparator].

Section 2B Clinical evaluation of investigative technologies

[Instructional text] Delete Section 2B if assessing a therapeutic technology. [End instructional text]

Methods for undertaking the assessment

[Refer to: MSAC Guidelines TG 9 \(Assessment framework\)](#)

[Refer to: MSAC Guidelines Appendices 1 to 5 \(methods\)](#)

[Refer to: MSAC Guidelines TG 5 \(Approach to assessment\)](#)

[Instructional text]

Very briefly, summarise the approach used to derive the clinical evidence for Section 2 of the report, including (but not limited to):

- whether a linked or direct evidence approach was used ([Refer to: TG 9](#)) (cross-reference to Section 2B.2 below)
- whether a facilitated/exemplar approach was used (only for genetic tests unless explicitly discussed with the Department; [Refer to: TG 5](#))
- whether a protocol was registered a priori
- what types of search terms were used
- what limits were placed on the searches
- how many databases were searched.

It is anticipated that the methods for the review would take less than a page to describe.

Provide a full description of the methods in Appendix A.

For a linked evidence approach, either present all methods at the beginning of Section 2B, or present the method for each link separately at the beginning of the assessment of that link. Do not present methods in both locations. If a single methods section is presented, clearly separate the methods for each link, where appropriate.

[End instructional text]

Assessment framework

[Refer to: MSAC Guidelines TG 9 \(Assessment framework\)](#)

[Instructional text] Provide the assessment framework and explain which pieces of the framework have been used to link the test population to health outcomes. If the generic framework (Figure 2 below) has been amended to demonstrate the impact of the test, use the amended figure. [End instructional text]

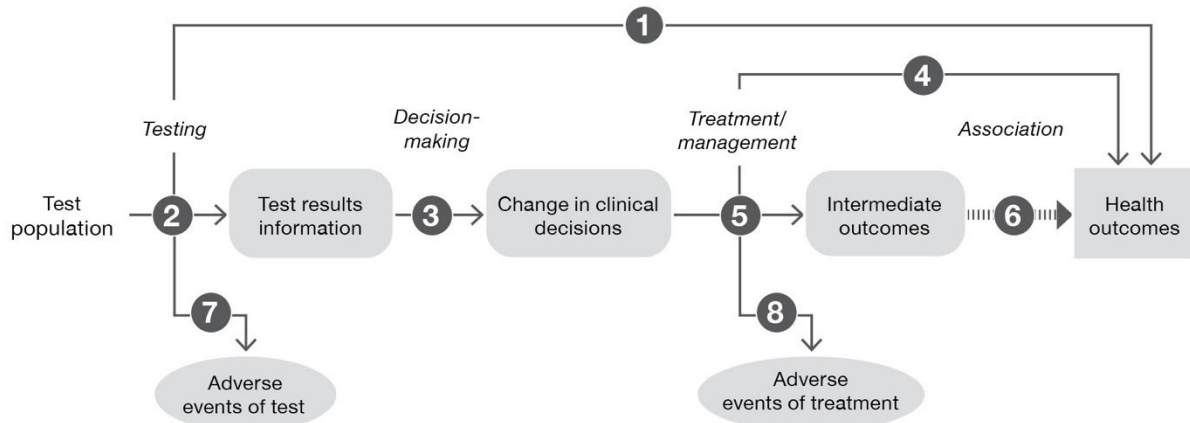


Figure 2 Assessment framework for [proposed health technology/intervention] for [indication]

Figure notes: 1: direct from test to health outcomes evidence; 2: test accuracy; 3: change in diagnosis/treatment/management; 4: influence of the change in management on health outcomes; 5: influence of the change in management on intermediate outcomes; 6: association of intermediate outcomes with health outcomes; 7: adverse events due to testing; 8: adverse events due to treatment

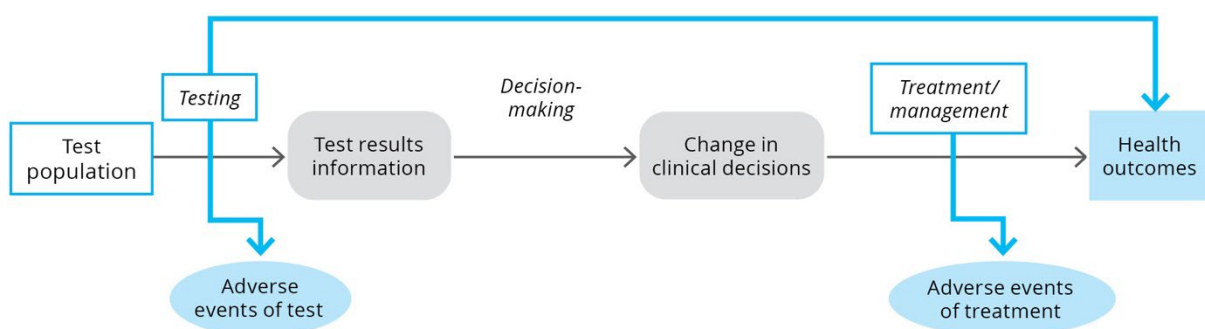
[Instructional text]

Specify which components of the framework have been informed by evidence, and cross-reference to where in the assessment report this information will be found. For example:

No direct test to health outcomes evidence was identified for XXXX. A linked evidence approach was therefore used. Evidence of test accuracy (component 2 in Figure 2) is reported in Section 2B.2. Evidence of the impact of testing on the management of patients (component 3 in Figure 2) is reported in Section 2B.3. Evidence regarding the impact of how the change in management results in health benefits (component 4 in Figure 2) is reported in Section 2B.4.

[End instructional text]

2B.1 Direct from test to health outcomes evidence



2B.1.1 Methods for undertaking the assessment

Refer to: [MSAC Guidelines Appendices 1 to 5 \(methods\)](#)

[Instructional text] If the methods have not already been presented at the beginning of Section 2B above, summarise them here. Delete this section if it is not needed. Note that this section represents the methods for the review, not the methods in the studies. [End instructional text]

2B.1.2 Characteristics of the evidence base

Refer to: MSAC Guidelines Appendix 3 for the assessment of risk of bias of included studies

Refer to: MSAC Guidelines Appendix 5 for information on extracting relevant study characteristics

[Instructional text] Include the following text: [End instructional text]

A total of *XX studies met the inclusion criteria for assessing the direct test to health outcomes evidence of [*proposed technology] compared to [*comparator]. Full study profiles and a PRISMA flowchart are shown in Appendix B.

A summary of the key features of the studies providing direct from test to health outcome evidence for [*the intervention and comparator(s)] is provided in Table 21.

[Instructional text]

Develop an appropriate way of presenting information on the interventions and/or comparators, and outcomes being tested for these study designs (see example in Table 21). Depending on the number of trials identified, include the key studies only. Keep this section brief, and provide more detail in the study profiles in Appendix B.

Provide information about any study/participant characteristics that are not reported elsewhere, but which are key to interpreting the implications of the evidence. The study/participant characteristics that will be informative for interpreting the results may include those that raise concerns about the internal validity of studies (imbalances across study arms), applicability of the evidence to the Australian setting, or transitivity issues for indirect comparisons. Depending on the volume of studies, tabulate the characteristics of the key studies and compare against the proposed Australian setting.

[End instructional text]

Table 21 Key features of the included evidence comparing [*intervention] with [*comparator]

Trial/Study	N	Study design Risk of bias	Population	Intervention	Comparator	Key outcome(s)	Result used in economic model

[Define all abbreviations used in the table]

Refer to: MSAC Guidelines TG 10.4 (Considerations relevant to a direct from test to health outcomes evidence approach)

Refer to: MSAC Guidelines TG 10.5 (Assessment of the applicability of direct from test to health outcomes evidence)

[Instructional text]

Discuss the transitivity and applicability of the direct from test to health outcomes evidence. Explain how additional evidence has been used to address issues with applicability.

Concerns relating to the internal validity or applicability of the evidence may be briefly raised in this section. These concerns should then be more fully discussed in the following sections, alongside the interpretation of the results that may be impacted by these concerns.

A special concern relating to direct from test to health outcomes evidence is whether the proposed test or tests (to be used in Australia) are identical to the clinical utility standard (the test and testing methodology used in the direct from test to health outcomes study). If the proposed test or tests differ (including all components of the test methodology), the assessment report would include an additional test accuracy section that compares the proposed test with the clinical utility standard.

[End instructional text]

2B.1.3 Results

Refer to: MSAC Guidelines TG 10.6 (Presentation of direct from test to health outcomes evidence)

Refer to: MSAC Guidelines TG 14 (Safety of investigative technologies)

Refer to: MSAC Guidelines TG 6 (Effectiveness of therapeutic technologies) and TG 7 (Safety of therapeutic technologies) for further guidance

[Instructional text]

Present the direct from test to health outcomes evidence. Provide tables/figures with results instead of narrative synthesis where possible.

Present results in descending order of patient relevance.

In order for MSAC to be able to compare the intervention and the comparator, present results for both by outcome measure (i.e. even if a naïve comparison is presented, present the results in such a way that they can be easily compared, such as tabulation of the proposed technology and the comparator in the same table).

[End instructional text]

***Safety**

Refer to: MSAC Guidelines TG 14 (Safety of investigative technologies)

[Instructional text]

Present evidence of the harms (adverse events) experienced by patients who receive the proposed test versus the comparative test (standard practice). These harms should include direct test-related harms and harms that are associated with subsequent management decisions. Present outcomes separately for test-positive and test-negative patients.

Discuss how the study design, risk of bias and other factors influence the certainty of the evidence (**Refer to: TG Appendix 3** on risk of bias; **Refer to: TG Appendix 4** on certainty of the

evidence). Consider the applicability of the evidence based on the study characteristics (Refer to: TG 10.5 and TG Appendix 5).

Optionally, report the GRADE of each key outcome.

[End instructional text]

*Outcome 1

[Instructional text]

By outcome measure, discuss the validity of the tools used to measure the outcome, and how a clinically important effect is defined. Discuss whether the analyses presented in the studies were prespecified or post hoc. Discuss the methods you have used (and justification if the method is unusual) to conduct your own statistical analyses for the assessment; for example, calculation of confidence intervals, statistical tests and meta-analyses should be mentioned here.

Provide tables/figures with results instead of narrative synthesis where possible.

It is important to ensure that the results from individual studies are reported in addition to pooled estimates. Relevant details of individual study results include:

- the number of patients at risk or providing data to the results
- the number of patients experiencing the event (if appropriate)
- the percentage of patients with the event, and means (standard deviation) or medians (interquartile range) within groups, as appropriate
- confidence intervals (CIs) of the outcomes within groups
- relative and absolute differences between groups, and CIs.

The format of tables for presenting results will need to be adapted to the data available and the type of outcome. Table 22 and Table 23 show examples of how some outcomes might be presented.

[End instructional text]

Table 22 Results of [*key patient-relevant outcome] across the [*studies/randomised controlled trials (dichotomous data)]

Study ID	Risk of bias	Index test strategy <n with event/N (%)>	Comparator <n with event/N (%)>	Absolute difference <RD± NNT/NNH and 95% CI>	Relative difference <OR/RR/HR and 95% CI>
Trial 1					
Trial 2					
etc.					
<Pooled result>				<XX>	<XX>
Chi-square for heterogeneity: Q= , df= , P=	I ² statistic with 95% uncertainty interval =				

[If outcome is continuous, please provide the scale]

CI=confidence interval; HR=hazard ratio; NNH=number needed to harm; NNT=number needed to treat; OR=odds ratio; RD=risk difference; RR=relative risk; SD=standard deviation. [Define all abbreviations used in the table]

Table 23 Results of [*key patient-relevant outcome] across the [*studies/randomised controlled trials (continuous data)]

Study ID	Risk of bias	Index test strategy <mean ± SD>	Comparator <mean ± SD>	Absolute difference <mean difference and SD or 95%CI>	Relative difference <results of statistical testing and p-value and/or 95% CI>
Trial 1					
Trial 2					
etc.					
<Pooled result>				<XX>	<XX>
Chi-square for heterogeneity: Q= , df= , P=	I ² statistic with 95% uncertainty interval =				

[If outcome is continuous, please provide the scale]

CI=confidence interval; SD=standard deviation. [Define all abbreviations used in the table]

Refer to: MSAC Guidelines TG 10.5 (Assessment of the applicability of direct from test to health outcomes evidence)

Refer to: MSAC Guidelines Appendix 3 (Risk of bias)

Refer to: MSAC Guidelines Appendix 4 (Certainty of the evidence)

[Instructional text]

Discuss how the study design, risk of bias and other factors influence the certainty of the evidence (Refer to: TG Appendix 3 on risk of bias; Refer to: TG Appendix 4 on certainty of the evidence).

Discuss uncertainties relating to the results, including heterogeneity across studies, transitivity concerns and applicability to the target population. Reference differences in study and population characteristics presented in Section 2B.1.2.

[End instructional text]

*Outcome 2

[Instructional text] As above for outcome 1. Discuss the outcome measure and the results, synthesise how the intervention and the comparator differ on this outcome measure, and discuss how the study design, risk of bias and other factors influence the certainty of the evidence. Consider the applicability of the evidence. [End instructional text]

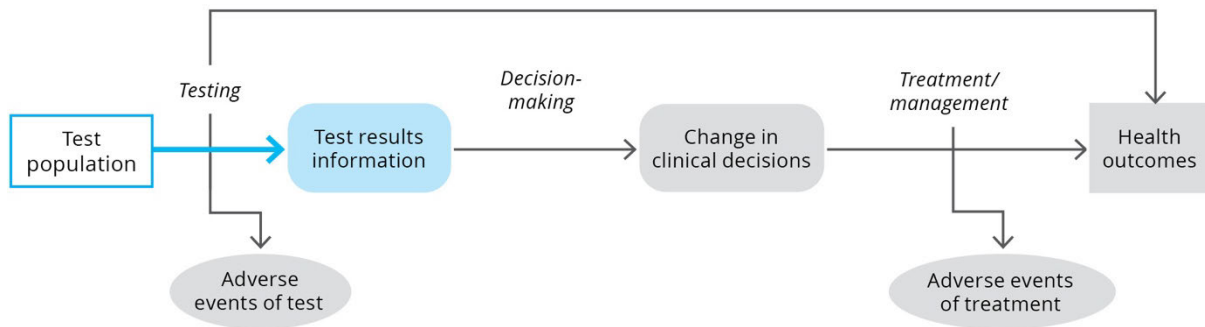
*Outcome 3

[Instructional text] As above for outcome 1. [End instructional text]

*Outcome 4

[Instructional text] As above for outcome 1. Present evidence for further outcomes in the same way. [End instructional text]

2B.2 Linked evidence of test accuracy



[Instructional text] A single investigative technology may have multiple purposes, and provides different forms of information. Use this section to present the test accuracy results relevant to the proposed purpose (and add additional sections if it is claimed that a test provides more than one type of information). For example, if a test is to be used for diagnosis as well as prognosis, separate these results. [End instructional text]

2B.2.1 Methods for undertaking the assessment

[Instructional text] If the methods have not already been presented at the beginning of Section 2B above, summarise them here. Delete this section if it is not needed. Note that this section represents the methods for the review, not the methods in the studies. [End instructional text]

2B.2.2 Reference standard/clinical utility standard

[Refer to: MSAC Guidelines TG 11 \(Linked evidence – test accuracy\)](#)

[Instructional text]

Describe the reference standard(s) (if using a linked evidence approach). [Refer to: TG 11.2 \(Key concepts\)](#) for details.

An example is provided in Table 24.

Table 24 Example reference standards to determine the accuracy of genetic testing for cardiac arrhythmias

Type of test information	Reference standard
Diagnostic (cross-sectional accuracy)	Sanger sequencing (for accuracy of identifying the variants) Clinical diagnosis (for accuracy of diagnosing the condition)
Prognostic (longitudinal accuracy)	Cardiac events over follow-up (adjusting for treatment) Clinical outcomes subsequent to diagnosis
Predictive (longitudinal accuracy)	Cardiac events over follow-up, considering differential response to treatment (benefits or harms) Response to treatment

[Define all abbreviations used in the table]

If the assessment involves direct from test to health outcomes evidence (common for codependent assessments), provide a description of the clinical utility standard.

[End instructional text]

Refer to: MSAC Guidelines TG 11.2 (Key concepts)

2B.2.3 Characteristics of the evidence base

Refer to: MSAC Guidelines Appendix 3 for the assessment of risk of bias of included studies

Refer to: MSAC Guidelines Appendix 5 for information on extracting relevant study characteristics

[Instructional text] Include the following text: [End instructional text]

A total of *XX studies met the inclusion criteria for assessing the test accuracy of [*proposed technology] compared to [*comparator]. Full study profiles and a PRISMA flowchart are presented in Appendix B.

A summary of the key features of the studies on test accuracy of [*the intervention and comparator(s)] is provided in Table 25.

[Instructional text]

Develop an appropriate way of presenting information on the interventions and/or comparators, and outcomes being tested for these study designs (see example in Table 25). Depending on the number of trials identified, include the key studies only. Keep this section brief, and provide more detail in the study profiles in Appendix B.

Provide information about any study/participant characteristics that are not reported elsewhere, but which are key to interpreting the implications of the evidence. If the risk of bias can be easily summarised in Table 25 this may be sufficient. If not, tabulate or graph the risk of bias separately. For studies of cross-sectional test accuracy (e.g. for triaging, diagnosis, staging), QUADAS 2 is an example of an appropriate checklist (Table 26).

[End instructional text]

Table 25 Key features of the included test accuracy evidence comparing [*intervention] with [*comparator] against [*reference standard/clinical utility standard]

Trial/Study	N	Study design Risk of bias	Population	Intervention	Comparator	Key outcome(s)	Result used in economic model
						[*sensitivity/specificity compared to reference standard]	
						[*predicting risk of recurrence]	
						[*predicting response to treatment]	

[Define all abbreviations used in the table]

Table 26 Risk of bias of test accuracy studies (using QUADAS 2 checklist)

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	Patient selection	Index test	Reference standard/ clinical utility standard	Flow and timing	Patient selection	Index test	Reference standard/ clinical utility standard

Low risk High risk Unclear risk

Refer to: MSAC Guidelines TG 11.4 (Cross-sectional accuracy)

[Instructional text] Discuss the transitivity and applicability of the test accuracy evidence. Explain how additional evidence has been used to address issues with applicability (e.g. deriving the positive predictive value and negative predictive value by applying an appropriate prevalence value to the sensitivity and specificity data). [End instructional text]

2B.2.4 Results

Refer to: MSAC Guidelines TG 11.4 (Cross-sectional accuracy)

Refer to: MSAC Guidelines TG 11.9 (Prevalence of the disease or biomarker in the PICO population)

[Instructional text]

The presentation of the direct harms of testing (compared with the comparator) may be relevant to include in the linked evidence of test accuracy section if this is the only section of the linked evidence approach that has been used. This circumstance may arise when there is direct from test to health outcomes evidence for a clinical utility standard and the test or tests to be used in Australia are different. If the test logically has the same level of risk (e.g. both the clinical utility standard and the proposed test require a biopsy, or both use the same imaging process), then it may be reasonable to conclude that the direct harms from the test are similar.

If a full linked evidence approach is required (where evidence for change in management and health outcomes is presented), provide the direct harms of the test in the health outcomes section along with harms of downstream consequences of test classification.

Downstream harms associated with the test (compared with the comparator) are related to the treatments or changes in management that arise following the classification of the patient. Present harms for both test-positive and test-negative patients. In addition, harms relating to the false classification (false positive or false negative) are relevant to address. These harms can be discussed in the 'Linked evidence of health outcomes' section of the template.

Report the prevalence of the disease and/or the biomarker

[End instructional text]

***Cross-sectional accuracy**

[Instructional text]

Use this section to present, for example, diagnostic information against a non-clinical reference standard.

Discuss the outcome measures used. For example:

To assess the diagnostic accuracy of the proposed test, studies were only included if they provided data that could be extracted into a classic 2-by-2 table, in which the results of the index test or the comparator were cross-classified against the results of the reference standard², and Bayes' Theorem was applied.

Table 27 is an example of a 2-by-2 table for diagnostic accuracy data.

² Armitage, P, Berry, G & Matthews, JNS 2002, *Statistical methods in medical research*, fourth edn, Blackwell Science, Oxford.

Deeks, JJ 2001, 'Systematic reviews of evaluations of diagnostic and screening tests', in M Egger, G Davey Smith & DG Altman (eds), *Systematic reviews in healthcare: meta-analysis in context*, second edn, BMJ Publishing Group, London, pp. 248–282.

Table 27 Diagnostic accuracy data extraction

		Reference standard		
		<i>Disease +</i>	<i>Disease –</i>	
Index test	<i>Test +</i>	True positive	False positive	Total test positive
Or comparator	<i>Test –</i>	False negative	True negative	Total test negative
		Total with disease	Total without disease	

The key measures of cross-sectional accuracy of interest to MSAC are sensitivity and specificity, but other outcomes may be reported, such as likelihood ratios, receiver operating characteristic (ROC) curves and the diagnostic odds ratio (DOR).

Comment on whether the measurement of outcomes in the included studies was likely to be accurate, discuss the validity of the measurement tools used, and make it clear how you are interpreting a clinically important effect for these outcomes. Discuss whether the statistical analyses presented in the studies were prespecified or post hoc, and the limitations associated with the latter.

Refer to: MSAC Guidelines Appendix 7 (Test accuracy measures) for guidance on analysis of test accuracy, including meta-analysis

Discuss the methods you have used (and justification if the method is unusual) to conduct your own statistical analyses for the assessment; for example, calculation of confidence intervals, statistical tests and meta-analyses should be mentioned here.

If no reference standard is available, then diagnostic yield may be relevant to include.

Provide tables/figures with results instead of narrative synthesis where possible.

Present an estimate of test accuracy as applied to the estimate of Australian prevalence, for example, positive and negative predictive values.

Refer to: MSAC Guidelines Appendix 3 (Risk of bias)

Refer to: MSAC Guidelines Appendix 4 (Certainty of the evidence)

Discuss how the study design, risk of bias and other factors influence the certainty of the evidence.

Refer to: MSAC Guidelines TG 11.4 (Cross-sectional accuracy)

Refer to: MSAC Guidelines Appendix 4 (Certainty of the evidence)

Refer to: MSAC Guidelines Appendix 5 (Study characteristics)

Consider the applicability of the evidence based on the study characteristics (Refer to: TG 10.5 and TG Appendix 5). Optionally, report the GRADE of each key outcome.

If evidence used in other parts of the assessment (such as direct from test to health outcomes, or change in management) reports on a study test not used in Australia, assess the comparative accuracy of the proposed test and the study tests. Concordance should be presented using a

2-by-2 table so that the nature of the discordant results is clear. For guidance on concordance, Refer to: TG 11.5.

Additional considerations relevant to this section include:

- cascade testing for heritable diseases (Refer to: TG 11.7)
- test reliability (Refer to: TG 11.8)
- prevalence of the disease or biomarker (Refer to: TG 11.9).

[End instructional text]

***Longitudinal accuracy**

[Instructional text]

Discuss the outcome measures.

For prognosis, report on how well the test performs (compared to the comparator) at predicting health outcomes. Refer to: TG 11.4 for more details.

For predictive accuracy, report on how well the test performs (compared to the comparator) at predicting response to treatment. Refer to: TG 11.4 for more details.

Discuss how the study design, risk of bias, and other factors influence the certainty of the evidence (Refer to: TG Appendix 3 on risk of bias; Refer to: TG Appendix 4 on certainty of the evidence). Consider the applicability of the evidence based on the study characteristics (Refer to: TG 10.5 and TG Appendix 5). Optionally, report the GRADE of each key outcome.

[End instructional text]

***Outcome 3**

[Instructional text] As for either cross-sectional or longitudinal outcomes, described above. [End instructional text]

***Outcome 4**

[Instructional text] As for either cross-sectional or longitudinal outcomes, described above. [End instructional text]

***Safety of the test**

[Instructional text]

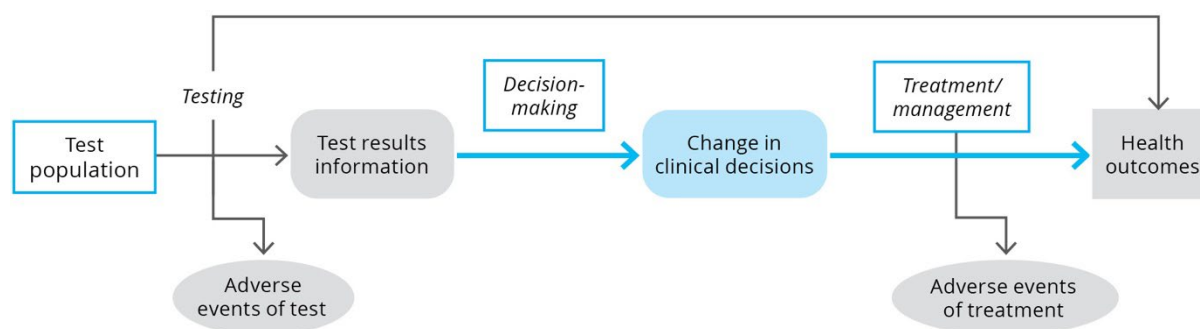
This section reports the direct harms of testing (if required). If a full linked evidence approach is presented, group the safety of the test with the safety associated with downstream changes in management and report this in Section 2B.4 (Linked evidence of health outcomes).

Refer to: MSAC Guidelines TG 15 (Special cases)

Additional guidance is provided for screening (including cascade testing), monitoring, multifactorial algorithms or codependent technologies.

[End instructional text]

2B.3 Linked evidence of change in management



2B.3.1 Methods for undertaking the assessment

[Instructional text] If the methods have not already been presented at the beginning of Section 2B above, summarise them here. Delete this section if it is not needed. Note that this section represents the methods for the review, not the methods in the studies. [End instructional text]

2B.3.2 Characteristics of the evidence base

Refer to: [MSAC Guidelines TG 12.2 \(Change in management evidence\)](#) and [TG 12.3 \(Change in management study designs\)](#) for guidance on different components of change in management and different study types

[Instructional text] Include the following text: [End instructional text]

A total of *XX studies met the inclusion criteria for assessing change in management following [*the proposed technology/intervention] compared to [*comparator]. Full study profiles and a PRISMA flowchart are shown in Appendix B.

A summary of the key features of the change in management evidence for [*the intervention and comparator(s)] is provided in Table 28.

[Instructional text]

Develop an appropriate way of presenting information on the interventions and/or comparators, and outcomes being tested for these study designs (see example in Table 28). Depending on the number of trials identified, include the key studies only. Keep this section brief, and provide more detail in the study profiles in Appendix B.

Provide information about any study/participant characteristics that are not reported elsewhere, but which are key to interpreting the implications of the evidence.

Tabulate or graph the risk of bias. If a summary of risk of bias per study is easy to add to Table 28, it may be included there. Assess change in management studies as per therapeutic studies (rather than using a checklist designed for test accuracy studies).

[End instructional text]

Table 28 Key features of the included change in management evidence comparing [*intervention] with [*comparator]

Trial/Study	N	Study design Risk of bias	Population	Intervention	Comparator	Key outcome(s)	Result used in economic model

[Define all abbreviations used in the table]

2B.3.3 Results

[Refer to: MSAC Guidelines TG 12.4 \(Considerations relevant to change in management\)](#)

[Refer to: MSAC Guidelines TG 12.6 \(Presentation of change in management evidence\)](#)

[Instructional text]

Present results showing the extent to which management changes (and the nature of the change) in a circumstance where the proposed test is available compared with when it is not available (i.e. a comparator test or usual practice is applied). Report change in management for both test-positive and test-negative patients.

Change in management is usually a categorical outcome (often dichotomous). Present the results in a similar way as for a therapeutic technology. Meta-analyse if appropriate. Discuss the outcome measures (how change in management was measured) and any limitations with these measures.

Provide tables/figures with results instead of narrative synthesis where possible.

[Refer to: MSAC Guidelines TG 12.5 \(Assessment of the applicability of change in management evidence\)](#)

Discuss reasons for variation in clinical management in patients with similar test results. Discuss whether the change in management may be confounded by factors other than the test results.

Discuss the applicability of the change in management evidence to the Australian setting. Where the evidence for change in management is partially applicable to the Australian setting, explore, where possible, the variation in management across subgroups, or present supplementary evidence to support the generalisability of the study results across settings.

[Refer to: MSAC Guidelines Appendix 3 \(Risk of bias\)](#)

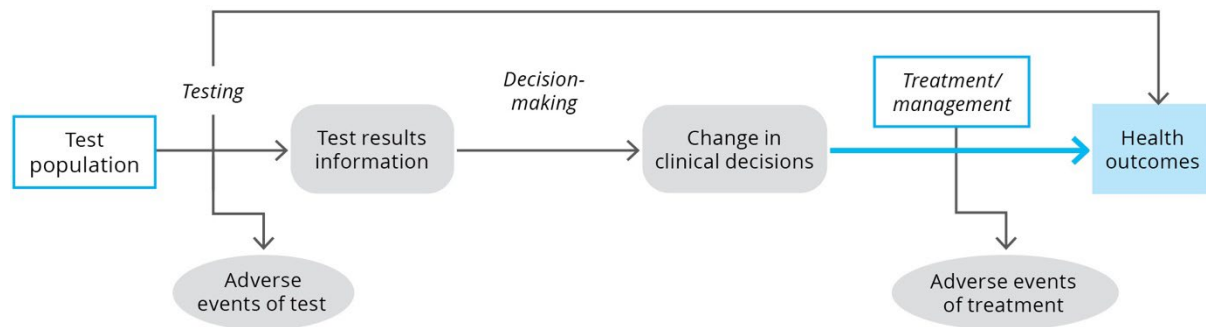
[Refer to: MSAC Guidelines Appendix 4 \(Certainty of the evidence\)](#)

Discuss how the study design, risk of bias and other factors influence the certainty of the evidence. Optionally, report the GRADE of each key outcome.

If there are gaps in the evidence base regarding what happens on the basis of test results, justify why it may be logical to assume that a change in management happens (e.g. a change in diagnosis should result in a different treatment, based on clinical practice guidelines).

[End instructional text]

2B.4 Linked evidence of health outcomes



2B.4.1 Methods for undertaking the assessment

Refer to: [MSAC Guidelines Appendices 1 to 5 \(methods\)](#)

[Instructional text]

If the methods have not already been presented at the beginning of Section 2B above, summarise them here. Delete this section if it is not needed. Note that this section represents the methods for the review, not the methods in the studies.

Health outcomes evidence (that has not been included under direct test to health outcomes evidence) will often require separate literature searches, as studies related to the health outcomes resulting from change in management will not necessarily mention the test of interest.

[End instructional text]

2B.4.2 Characteristics of the evidence base

Refer to: [MSAC Guidelines TG 13.2 \(Therapeutic effectiveness evidence\)](#) and [TG 13.3 \(Therapeutic effectiveness study designs\)](#) for guidance on different components of health outcomes evidence and different study types

[Instructional text] Include the following text: [End instructional text]

A total of *XX studies met the inclusion criteria for assessing evidence on health outcomes resulting from change in management due to [*proposed technology compared to comparator]. Full study profiles and a PRISMA flowchart are presented in Appendix B.

A summary of the key features of the studies providing health outcome evidence is provided in Table 29.

[Instructional text]

Develop an appropriate way of presenting information on the interventions and/or comparators, and outcomes being tested for these study designs (see example in Table 29). Depending on the

number of trials identified, include the key studies only. Keep this section brief, and provide more detail in the study profiles in Appendix B.

Provide information about any study/participant characteristics that are not reported elsewhere, but which are key to interpreting the implications of the evidence. The study/participant characteristics that will be informative for interpreting the results may include those that raise concerns about the internal validity of studies (imbalances across study arms), applicability of the evidence to the Australian setting, or transitivity issues for indirect comparisons. Depending on the volume of studies, tabulate the characteristics of the key studies and compare against the proposed Australian setting.

[End instructional text]

Table 29 Key features of the included health outcomes evidence comparing [*intervention] with [*comparator]

Trial/Study	N	Study design Risk of bias	Population	Intervention	Comparator	Key outcome(s)	Result used in economic model

[Define all abbreviations used in the table]

[Instructional text] The assessment of linked evidence of health outcomes is similar to that for therapeutic technologies. Choose an appropriate risk of bias tool. Tabulate or graph the risk of bias. If a summary of risk of bias per study is easy to add to Table 29 it may be included there.
[End instructional text]

2B.4.3 Results

[Refer to: MSAC Guidelines TG 13.4 \(Considerations relevant to linked evidence of health outcomes\)](#)

[Refer to: MSAC Guidelines TG 13.5 \(Assessment of the applicability of health outcome gains evidence\)](#)

[Refer to: MSAC Guidelines TG 13.6 \(Presentation of health outcome gains evidence\)](#)

[Instructional text]

This section should explicitly be linked to the changes in management reported in Section 2B.3, and should include consideration of the results of the test accuracy reported in Section 2B.2.

The method of presenting this section will vary greatly depending on the impact that the test has on the management of patients. Provide tables/figures with results instead of narrative synthesis where possible.

Explain how evidence for each of the management pathways has been constructed (e.g. treatment for test-positive patients was derived from study X, standard care for test-negative patients was derived from study Y).

Clearly identify when outcomes for one group are based on a relative treatment effect compared to another group (e.g. an RCT of a treatment vs standard care), and when the evidence is derived from different sources (e.g. indirect comparison or single arm studies).

Present the evidence for health outcome gains (for each different management pathway) in the same way as presenting evidence for a therapeutic technology (i.e. describe the literature search and any subsequent searches for supplementary evidence to explore uncertainties in the evidence, risk of bias and trial characteristics, present the results, and meta-analyse if appropriate).

When presenting the results, provide an assessment of the outcomes relating to the change in management (e.g. if a test results in 20% of patients receiving Treatment A instead of Treatment B, a comparison of Treatment A vs Treatment B is appropriate).

Determine the implications of treatment of test-positive patients (true positives and false positives), the implications of nontreatment (or alternative treatment) for test-negative patients (true negatives and false negatives), and prognostic or further clinical evidence if required.

If possible, provide the net health benefit expected (accounting for the health gains and losses associated with the use of the proposed test vs the comparator test).

Clearly describe the assumptions required to generalise evidence across groups (e.g. the treatment effect is assumed to be the same for patients who test positive using both the comparator test and the proposed test).

Present evidence to support the generalisability of the evidence across different populations. Discuss implications of a risk of change in the spectrum of disease, or differences in prognosis associated with a biomarker. Explain the outcomes for misclassified patients (false negatives and false positives).

If appropriate, discuss concerns relating to overdiagnosis (or improved prognosis due to increases in the 'sensitivity' of the test).

Refer to: MSAC Guidelines TG 13.5 (Assessment of the applicability of health outcome gains evidence)

Discuss the applicability of the health outcome gains evidence to the target Australian setting. Include the impact of applicability issues identified at the test accuracy step or the change in management step. Explore the impact of applicability in subgroup analyses.

Refer to: MSAC Guidelines Appendix 3 (Risk of bias)

Refer to: MSAC Guidelines Appendix 4 (Certainty of the evidence)

Present a summary of the quality and certainty of the body of evidence.

Refer to: MSAC Guidelines TG 14 (Safety of investigative technologies)

Present the safety of the test (direct) and the safety implications of downstream changes in management.

[End instructional text]

2B.5 Conclusion

2B.5.1 Evidence interpretation

Refer to: [MSAC Guidelines TG 16.1 \(Investigative evidence interpretation\)](#)

[Instructional text]

This section describes the impact that testing has on health outcomes. If good quality and applicable direct from test to health outcomes evidence is available, this will be simple. However, in most cases, this will require synthesis of evidence across the linkages, and outlining of the key uncertainties.

It may assist to refer to Figure 2 (repeated below for convenience) when describing which components of the linked evidence approach were supported by evidence.

[End instructional text]

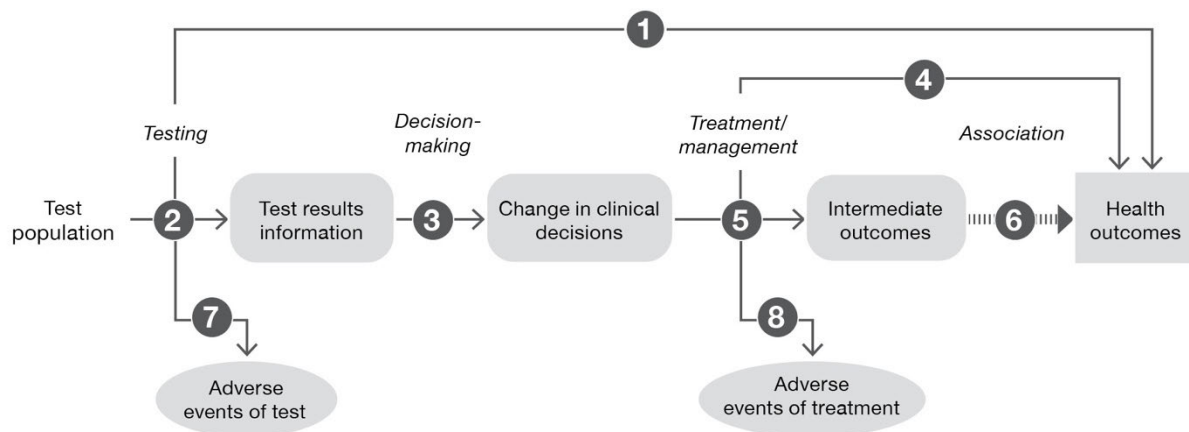


Figure 2 Assessment framework for [*proposed technology/intervention] for [*indication]

Figure notes: 1: direct from test to health outcomes evidence; 2: test accuracy; 3: change in diagnosis/treatment/management; 4: influence of the change in management on health outcomes; 5: influence of the change in management on intermediate outcomes; 6: association of intermediate outcomes with health outcomes; 7: adverse events due to testing; 8: adverse events due to treatment

[Instructional text] Present a table of the key uncertainties for each evidentiary step, and an overall assessment of the quality and certainty of the evidence. One method of doing this is to adapt a GRADE summary of findings table (see example in Table 30 below). Another is as per Table 31. [End instructional text]

Table 30 Example summary of findings table for important outcomes of population 1 (index patients)

Section in report	Outcomes	Participants and studies	Results	Interpretation	Quality of evidence using GRADE
2B.1 Direct from test to health outcomes evidence	Quality of life	n=628 k=3 studies, (1 before-and-after case series; 2 qualitative)			⊕⊖⊖⊖ N/A for qualitative
2B.2 Test accuracy	Sensitivity and specificity of genetic testing for detecting variants	n=47 k=2 diagnostic accuracy studies			⊕⊕⊕⊖
2B.3 Change in management	Change in clinical diagnosis	n=178 k=3 before-and-after case series			⊕⊖⊖⊖
	Change in lifestyle modification recommendations	n=1454 k=3 retrospective cohorts			⊕⊖⊖⊖
	Difference in treatments received	n=3390 k=5 retrospective cohorts			⊕⊖⊖⊖
2B.4 Therapeutic effectiveness	Treatment effectiveness	n=4327 k=9 retrospective cohort studies			⊕⊖⊖⊖

[Define all abbreviations used in the table]

⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect.

⊕⊕⊕⊖ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

⊕⊕⊖⊖ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

⊕⊖⊖⊖ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Table 31 Synthesis of the evidence and evidence gaps linking the investigative technology and health outcomes

Evidence component of the assessment	Interpretation and key uncertainties
Test accuracy	
Change in management	
Health outcomes	
Safety of the test	
Safety of the treatment	
<i>Overall assessment of the evidence</i>	

[Define all abbreviations used in the table]

[Instructional text] For a linked evidence approach, a summary of the overall evidence base includes the synthesis of the main findings and concerns for each step of the approach. This section is intended to discuss the clinical utility of the test (which is the net benefits and harms associated with the use of the test compared with the comparator). Do not repeat evidence from previous sections. The synthesis reports whether the presented evidence is adequate to reach a conclusion of benefits and harms, and whether the magnitude of benefits and harms identified in the evidence is likely to be realised in the Australian setting. [End instructional text]

2B.5.2 Conclusion of the clinical claim

Refer to: MSAC Guidelines TG 16.2 (Conclusion of clinical utility)

[Instructional text] Include the following text: [End instructional text]

The use of [*proposed health technology] results in [*superior/noninferior/inferior] effectiveness compared with [*comparator].

The use of [*proposed health technology] results in [*superior/noninferior/inferior] safety compared with [*comparator].

[Instructional text] If the key benefit of testing is not to influence health, but for the value of knowing, cross-reference to Section 5. [End instructional text]

Section 3A Cost-effectiveness analysis

[Instructional text]

The presentation of information relating to the economic analysis should be adequate to explain how the analysis was constructed. Justifications for the inputs and assumptions may be brief in the main body of the report, with evidence supporting the justification presented in an appendix. Inputs and assumptions that have a major impact on the model predictions may be discussed at length in the main body.

Section 3 of the assessment report template requires authors to refer to the MSAC Guidelines for instruction on the most relevant or appropriate information to provide. High-level information requests are included in the template; however, presentation of additional relevant information may be necessary in response to guidance provided in the MSAC Guidelines.

[End instructional text]

3A.1 Overview and rationale of the economic evaluation

Refer to: MSAC Guidelines TG 17.2 (The assessment question addressed by the economic evaluation)

[Instructional text] State the funding question the economic evaluation aims to address, in the context of the results of the clinical evaluation. [End instructional text]

Refer to: MSAC Guidelines TG 17.5 (Type of economic evaluation)

[Instructional text] Describe the type of economic evaluation used. [End instructional text]

3A.2 Methods

3A.2.1 Summary table

Refer to: MSAC Guidelines TG 17.2 (The assessment question addressed by the economic evaluation)

[Instructional text] Present a summary table of the key components of the economic evaluation (example in Table 32). Include rows as relevant to the model presented. [End instructional text]

Table 32 Summary of the economic evaluation

Component	Description	MSAC Guidelines Reference
Perspective	[*e.g. Health care system perspective]	TG 17.3
Population	[For multi-indication models, specify the different populations (or subgroups) modelled. For example, for testing of heritable diseases, index cases, and adult and child relatives may be modelled]	TG 19
Prior testing	[*specify the tests required to determine the population in the model]	TG 19
Comparator	[*comparator]	TG 17.2
Type(s) of analysis	[*e.g. cost-effectiveness analysis, cost-utility analysis]	TG 17.5
Outcomes	[*e.g. events avoided, life-years gained, quality-adjusted life years]	TG 21
Time horizon	[*e.g. [x] days/months/years in the model base case (vs [y] weeks/years in the key trial(s))]	TG 18.2
Computational method	[*e.g. cohort expected value, Markov, partitioned survival analysis, microsimulation, discrete event simulation]	TG 18.3
Generation of the base case	[*e.g. trial based or modelled. [If modelled, summarise the steps undertaken in the economic analysis]	TG 17.6
Health states	[If a state transition model is used, state the health states included. This could also include decision tree terminal states or events modelled in a discrete event simulation.]	TG 18
Cycle length	[*x days/weeks/months/years]	TG 18.3
Transition probabilities	[Where different data sources are used to inform different transition probabilities, e.g. baseline event rate, treatment effect, secondary transition probabilities, describe the source(s) of each key model input. For investigative technologies, the sources of data used to inform additionally relevant inputs, such as prevalence, accuracy and change in management, should also be summarised. Indicate if the data required translation for use in the economic analysis.]	TG 20
Discount rate	[*e.g. 5% for both costs and outcomes]	TG 17.4
Software	[*e.g. Excel, @RISK, TreeAge Pro]	TG 18.3

[Define all abbreviations used in the table]

3A.2.2 Structure of the economic evaluation

Refer to: MSAC Guidelines TG 18 (Model development process)

[Instructional text]

Summarise the model structure, including figure(s).

Describe assumptions incorporated into the model structure.

[End instructional text]

Model structuring process

[Instructional text]

Include:

- Model conceptualisation (including literature review)
- Computational methods
- Other structural assumptions

[End instructional text]

Input data (high-level summary of sources of data used in the model)

[Instructional text]

This is a brief table providing the inputs and source of the inputs for the model (see Table 33). No discussion of the inputs is required at this step (this is covered in subsequent sections). Identify which inputs are sourced from the clinical evidence presented in Section 2.

Briefly describe additional methods used to identify data for input parameters (e.g. key clinical study, literature review).

[End instructional text]

Table 33 Summary of the inputs used in the economic evaluation

Parameter	Value	Source
[*e.g. Transition probabilities]		
[*e.g. Utilities]		
Costs		

[Define all abbreviations used in the table]

3A.2.3 Model population and setting

[Refer to: MSAC Guidelines TG 19 \(Population and setting\)](#)

[Instructional text] Describe the population that enters the model and setting of use. Discuss applicability issues and translation studies associated with the population/setting. [End instructional text]

3A.2.4 Model transition probabilities, variables and extrapolation

[Refer to: MSAC Guidelines TG 20 \(Model transition probabilities, variables and extrapolation\)](#)

[Instructional text]

Discuss concerns relating to the transition probabilities. Summarise the extrapolation process (if applicable).

If there are multiple sources of inputs, present the alternative values and their sources, along with a justification of the choice of input used in the base case. State which alternative inputs were used in sensitivity analyses.

[End instructional text]

3A.2.5 Health outcomes

[Refer to: MSAC Guidelines TG 21 \(Health outcomes\)](#)

[Instructional text]

Describe the derivation of the health outcomes used in the model. Describe and justify required translations (if applicable). State and justify any assumptions.

If there are multiple sources of inputs, present the alternative values and their sources, along with a justification of the choice of input used in the base case. State which alternative inputs were used in sensitivity analyses.

[End instructional text]

3A.2.6 Health care resource use and costs

[Refer to: MSAC Guidelines TG 22 \(Health care resource use and costs\)](#)

[Instructional text]

Describe the derivation of the costs used in the model. State and justify any assumptions.

If there are multiple sources of inputs, present the alternative values and their sources, along with a justification of the choice of input used in the base case. State which alternative inputs were used in sensitivity analyses.

[End instructional text]

3A.2.7 Model validation

[Refer to: MSAC Guidelines TG 23 \(Model validation\)](#)

[Instructional text] Present a summary of the approaches used to validate the model results. [End instructional text]

Operational validation of the economic model

Other validation techniques

3A.3 Results

3A.3.1 Base-case analysis

[Refer to: MSAC Guidelines TG 24 \(Results of the base-case economic evaluation\)](#)

Intervention costs per patient

Refer to: MSAC Guidelines TG 24.1 (Intervention costs per patient)

Stepped presentation of results

Refer to: MSAC Guidelines TG 24.2 (Stepped presentation of results)

Disaggregated and aggregated base-case results

Refer to: MSAC Guidelines TG 24.3 (Disaggregated and aggregated base-case results)

[Instructional text] Example of results disaggregated by health care resources and health outcomes are presented in Table 34, Table 35 and Table 36 below. Adapt as necessary. [End instructional text]

Table 34 Health care resource items: disaggregated summary of cost impacts in the economic evaluation

Type of resource item	Subtype of resource item	Costs ^a for proposed health technology	Costs ^a for main comparator	Incremental cost ^a	% of total incremental cost ^a
Health technologies	Type of health technology				
	Health state 1	\$x1	\$y1	\$x1 – \$y1	z1%
	etc.	\$xk	\$yk	\$xk – \$yk	zk%
	Total	$\sum \$x$	$\sum \$y$	$\sum \$x - \sum \y	$\sum z\%$
Medicines	PBS medicine	[as above]	[as above]	[as above]	[as above]
	Health state 1	[add]	[add]	[add]	[add]
	Health state 2	[add]	[add]	[add]	[add]
	etc.	[add]	[add]	[add]	[add]
	Total	[add]	[add]	[add]	[add]
	Non-PBS medicine	[add]	[add]	[add]	[add]
	Health state 1	[add]	[add]	[add]	[add]
	Health state 2	[add]	[add]	[add]	[add]
	etc.	[add]	[add]	[add]	[add]
	Total	[add]	[add]	[add]	[add]
Hospital services	Hospital admission	[add]	[add]	[add]	[add]
	Health state 1	[add]	[add]	[add]	[add]
	etc.	[add]	[add]	[add]	[add]

Type of resource item	Subtype of resource item	Costs ^a for proposed health technology	Costs ^a for main comparator	Incremental cost ^a	% of total incremental cost ^a
	Total	[add]	[add]	[add]	[add]
Residential care	ACFI category	A\$x	A\$y	\$x – \$y	z%
	Total	A\$x	A\$y	\$x – \$y	100%

ACFI = Aged Care Funding Instrument; PBS = Pharmaceutical Benefits Scheme. [Define all abbreviations used in the table]
a [Indicate clearly whether cost values are discounted costs (use of discounted costs is appropriate).]

Table 35 List of health states and disaggregated summary of cost impacts included in the economic evaluation

Health state in model	Resource use by health state (modelled)	Proposed health technology costs	Main comparator costs	Incremental cost	Total incremental cost (%)
Health state 1	Resource type 1	\$x1	\$y1	\$x1 – \$y1	z1
	Resource type 2	\$x2	\$y2	\$x2 – \$y2	z2
	etc.	\$x etc.	\$y etc.	\$x etc. – \$y etc.	z etc
	Total for health state 1	$\sum \$x$	$\sum \$y$	$\sum \$x - \sum \y	$\sum z$
Health state 2	Resource type 1	\$xx1	\$yy1	\$xx1 – \$yy1	zz1
	Resource type k	\$xxk	\$yyk	\$xxk – \$yyk	zzk
	Total for health state 2	$\sum \$xx$	$\sum \$yy$	$\sum \$xx - \sum \yy	$\sum zz$
etc.	etc.	etc.	etc.	etc.	
Total	–	$\sum \$x + \sum \xx etc.	$\sum \$y + \sum \yy etc.	$(\sum \$x + \sum \$xx \text{ etc.}) -$ $(\sum \$y + \sum \$yy \text{ etc.})$	100

[Define all abbreviations used in the table]

– = not required

Table 36 List of health states and disaggregated summary of health outcomes included in the economic evaluation

Health state in model	Outcome for proposed health technology	Outcome for main comparator	Incremental outcome	Total incremental outcome (%)
Health state 1	x1	y1	x1 – y1	z1
Health state 2	x2	y2	x2 – y2	z2
etc.	[x etc.]	[y etc.]	[x etc. – y etc.]	[z etc.]
Total	x	y	x – y	100

[Define all abbreviations used in the table]

Summary of base-case results

[Refer to: MSAC Guidelines TG 24.4 \(Summary of base-case results\)](#)

[Instructional text] Comment on the base-case results, in the context of clinical and economic uncertainties. [End instructional text]

[Refer to: MSAC Guidelines TG 24.5 \(Alternative listing scenarios\)](#)

[Instructional text] If relevant, provide the results of alternative listing scenarios (additional base-case results where the proposed technology is used in additional or different populations). [End instructional text]

3A.3.2 Uncertainty analysis: model inputs, structure and assumptions

[Refer to: MSAC Guidelines TG 24.5 \(Alternative listing scenarios\)](#)

Scenario analyses

[Refer to: MSAC Guidelines TG 25 \(Uncertainty analysis: model inputs, structure and assumptions\)](#)

[Instructional text] Identify uncertainties requiring scenario analyses and present the results of alternative scenarios. [End instructional text]

Sensitivity analyses

[Refer to: MSAC Guidelines TG 25 \(Uncertainty analysis: model inputs and assumptions\)](#)

[Instructional text]

Present the results of key univariate analyses, including assumption analyses and structural sensitivity analyses.

Present the results of multivariate analyses (and probabilistic sensitivity analyses if performed).

[End instructional text]

3A.4 Conclusions

[Instructional text] Summarise the key findings of the economic analysis, and list the key uncertainties. [End instructional text]

Section 3B Cost-minimisation

Refer to: [MSAC Guidelines TG 26 \(Cost-minimisation approach\)](#)

3B.1 Overview

[Instructional text] Justify the use of a cost-minimisation approach in the context of the results of the clinical evaluation. [End instructional text]

3B.2 Methods

Summary table

[Instructional text] Present a summary table of the key components of the approach (see Table 37). Include rows as relevant to the model presented. [End instructional text]

Table 37 Summary of the economic evaluation

Component	Description
Therapeutic claim: effectiveness	Based on evidence presented in Section 2, effectiveness is assumed to be [*noninferior/superior]
Therapeutic claim: safety	Based on evidence presented in Section 2, safety is assumed to be [*noninferior/superior]
Evidence base	[*direct randomised trials/indirect comparison of randomised trials/comparisons based on nonrandomised studies]
Direct health technology costs	[*lower/equivalent/higher]; [*cost of proposed health technology] vs [*cost of comparator] [For therapeutic health technologies, costs are per patient per course for an acute or self-limited therapy, or per patient per year for a chronic or continuing therapy]
Other costs or cost offsets	[*Yes/No] [If yes, add brief description – e.g. adverse effect–related costs, monitoring costs, administration costs]

[Define all abbreviations used in the table]

Health care resource use and costs

[Instructional text] Present a summary table of the health care resources included in the cost-minimisation approach (see Table 38). Refer to: [TG 26.1 Health care resource use and costs](#). [End instructional text]

Table 38 Summary of the costs included in the cost-minimisation approach

Parameter	Value	Source
Direct health technology costs		
Additional costs and/or cost offsets		

[Define all abbreviations used in the table]

Direct health technology costs

[Instructional text] Present the per patient per course, or per patient per year costs of the proposed health technology. [End instructional text]

Additional costs and/or cost offsets

[Instructional text] Present additional costs or cost offsets associated with the use of the proposed health technology. [End instructional text]

3B.3 Results

[Refer to: MSAC Guidelines TG 26.2 \(Results\)](#)

[Instructional text] Present the results of the cost-minimisation approach. [End instructional text]

3B.4 Conclusions

[Instructional text] Summarise the key findings of the cost-minimisation approach, and list the key uncertainties. [End instructional text]

Section 4 Use of the health technology in practice

[Instructional text] Identify the relevant funding program for the proposed health technology. This will be the initial perspective for which the net changes in use and financial implications will be identified (i.e. Sections 4.2 to 4.4). [End instructional text]

4.1 Justification of the selection of approach and data sources

Refer to: [MSAC Guidelines Section 4 \(Use of the health technology in practice\)](#)

[Instructional text] State the approach used (i.e. epidemiological or market-share) to estimate the financial implications of funding the proposed health technology. [End instructional text]

Refer to: [MSAC Guidelines TG 27.1 \(Selection of data sources used to estimate the financial impact of the proposed health technology\)](#)

[Instructional text] Present a table summarising the data sources and how they are used in estimating the financial impact of the proposed health technology (Table 39). [End instructional text]

Table 39 Data sources and parameter values applied in the utilisation and financial estimates

Data	Source and value	Justification

[Define all abbreviations used in the table]

4.2 Estimation of use and financial impact of the proposed health technology

Refer to: [MSAC Guidelines TG 27.2 \(Estimation of use and financial impact of the proposed health technology\)](#)

[Instructional text] Present the estimated use and financial impact of the proposed technology. The presentation of estimates is relevant to the approach taken (epidemiological approach or market share approach). [End instructional text]

4.3 Estimation of changes in use and financial impact of other health technologies

Refer to: MSAC Guidelines TG 27.3 (Estimation of changes in use and financial impact of other health technologies)

[Instructional text] Present the estimated change in the use of other health technologies, and financial impact of this change. If the proposed funding source is the MBS, consider presenting financial results in financial years. [End instructional text]

4.4 Net financial impact to the [*relevant funding program]

Refer to: MSAC Guidelines TG 27.4 (Estimation of the net financial impact)

[Instructional text] Present a table summarising the net financial implications for the relevant funding program over 6 years (Table 40), accounting for the estimated cost of the proposed health technology (Refer to: TG 27.2), the increased usage of other health technologies, and cost offsets for substituted health technologies with a likely reduction in usage (Refer to: TG 27.3). If the proposed funding source is the MBS, consider presenting the net financial implications in financial years. In this case the table should present the year as “FY 20XX-XX” rather than “20XX”. [End instructional text]

Table 40 Net financial implications of [*proposed health technology] to the [*relevant funding program]

Parameter	20XX	20XX	20XX	20XX	20XX	20XX
Estimated use and cost of the proposed health technology						
Number of people eligible for [*proposed health technology]						
Number of people who receive [*proposed health technology]						
Number of services of [*proposed health technology] (if more than one per person)						
Cost to the [*relevant funding program] (with appropriate copayments excluded)						
Change in use and cost of other health technologies						
Change in use of [*comparator]						
Change in use of [*other affected health technologies]						
Net change in costs to the [*relevant funding program] (with appropriate copayments excluded)						
Net financial impact to the [*relevant funding program]						

[Define all abbreviations used in the table]

4.5 Net financial impact to other health budgets

Refer to: [MSAC Guidelines TG 27.4 \(Estimation of the net financial impact\)](#)

[Instructional text] If not captured in response to Section 4.4, present the net financial impact to the Commonwealth health budget.

Discuss the financial impact on other sources of health funding, including private health insurance, patient out-of-pocket expenses and state government budgets. [End instructional text]

4.6 Identification, estimation and reduction of uncertainty in the financial estimates

Refer to: [MSAC Guidelines TG 27.5 \(Identification, estimation and reduction of uncertainty in the financial estimates\)](#)

[Instructional text]

Identify possible sources of uncertainty associated with the use of the technology. These may include increased usage within the proposed population or usage beyond the proposed indication.

Provide analyses to test the impact of the uncertainties.

[End instructional text]

Section 5 Other relevant information

[Instructional text]

Although MSAC's Terms of Reference are to evaluate the strength of evidence about the comparative safety, effectiveness, cost-effectiveness and total cost of the health technology, other aspects outside of these elements may be influential in MSAC's decision-making. This section is optional (unless PASC have specifically requested something be addressed).

Add headings to this section as relevant (e.g. value of knowing, ethical analysis).

Refer to: MSAC Guidelines TG 28 (Value of knowing)

For investigative technologies, where the clinical claim has been accompanied by a claim of 'value of knowing', present the results of an assessment of value of knowing.

The assessment should include the source of the evidence, a discussion of the certainty of the evidence, and how the benefits and harms associated with value of knowing may be beneficial for decision-making.

Refer to: MSAC Guidelines TG 29 (Other relevant considerations)

Other considerations that are relevant to decision-making include those that are unique to the proposed technology (and are unlikely to have been considered by MSAC in the past), those that may have an impact on the estimates of the clinical and economic results or how they should be interpreted, or those that have been included in the ratified PICO confirmation for further assessment.

[End instructional text]

References

Appendix A Systematic review methods

[Instructional text] For therapeutic technologies, use the following section: [End instructional text]

Research questions

A systematic review has been performed to answer the following questions:

[Instructional text]

State the review questions, for example:

What is the comparative safety, effectiveness and cost-effectiveness of XXXX versus XXXX for treating XXXX in patients with XXXX.

[End instructional text]

[Instructional text] For investigative therapies, use the following section: [End instructional text]

Method of assessment and research questions

[Instructional text]

Describe any exemplar/facilitated relationships within the assessment (Refer to: TG 5)

Provide the assessment framework (Figure 2, repeated below for convenience) (Refer to: TG 9) and explain the research questions that were used to assess the link between the test population and health outcomes. If the generic figure below has been amended to demonstrate the impact of the test, use the more assessment-specific figure.

[End instructional text]

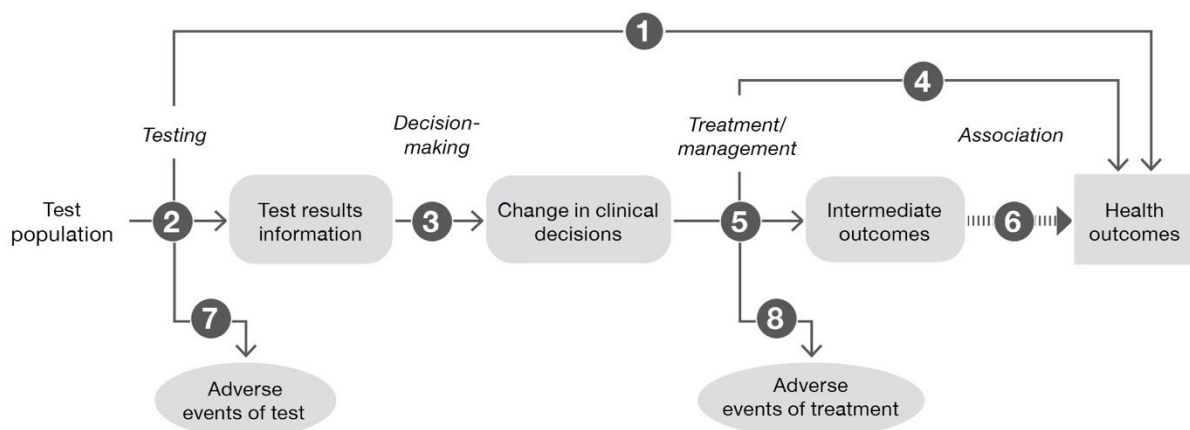


Figure 2 Assessment framework for [proposed technology/intervention] for [indication]

Figure notes: 1: direct from test to health outcomes evidence; 2: test accuracy; 3: change in diagnosis/treatment/management; 4: influence of the change in management on health outcomes; 5: influence of the change in management on intermediate outcomes; 6: association of intermediate outcomes with health outcomes; 7: adverse events due to testing; 8: adverse events due to treatment

Systematic review questions

[Instructional text] Amend the questions below to suit. Not all questions may be required. (Refer to: TG 9 and Appendix 1) [End instructional text]

DIRECT FROM TEST TO HEALTH OUTCOMES EVIDENCE

1. Does the use of the test strategy in place of the current test strategy (comparator) result in the claimed superior health outcomes?
 - a. If there are multiple tests in clinical practice likely to be able to utilise the same funding arrangements, are these tests concordant with the proposed test and/or clinical utility standard?

LINKED EVIDENCE

2. How does the information from the proposed test differ from that of the comparator? What is the concordance of the findings from the proposed test relative to the comparator? What is the accuracy of the proposed test (against a relevant reference standard) compared with the comparator?
 - a. If there are multiple tests in clinical practice likely to be able to utilise the same funding arrangements, are these tests concordant with the proposed test and/or clinical utility standard?
3. Does the availability of new information from the proposed test lead to a change in management of the patient (compared to the information gained from the comparator)?
4. Do the differences in the management derived from the proposed test, relative to the comparator (e.g. differences in treatment/intervention), result in the claimed health outcomes?
5. Do the differences in the management derived from the proposed test, relative to the comparator (e.g. differences in treatment/intervention), result in the claimed surrogate outcomes?
 - a. Has the treatment/management been provided to a population with the same spectrum of disease that the proposed test identifies? Is it biologically plausible that the treatment/management will be as effective in the population with this spectrum of disease? [Instructional text] **There is some concern when the proposed test detects more patients than the comparator as the treatment effect evidence may be based on a more narrowly defined (usually higher risk) positive population where expected benefits may be greater.** [Instructional text]
6. Is the observed change in surrogate outcomes associated with a concomitant change in the claimed health outcomes, and how strong is the association?
7. What are the adverse events associated with the proposed test strategy and the comparative test strategy?
8. What are the adverse events associated with the treatments/interventions that lead from the management decisions informed by the test and by the comparator?

Development of a research protocol

[Instructional text] Include the following text: [End instructional text]

Prior to the start of the systematic review, a research protocol was developed, based on the PICO confirmation ratified by the PICO Advisory Sub-Committee of MSAC. The research protocol was registered with the international prospective register of systematic reviews (PROSPERO) with the registration number ***CRDXXXXXXXXX**.

PICO criteria

[Instructional text]

Provide the PICO criteria from the PICO confirmation, if one was developed.

For technologies with direct from test to health outcomes evidence, present PICO criteria in a table (see Table 41) and include the following text: [End instructional text]

The Prior tests, Population, Investigation/Index test, Comparator and Outcomes (PPICO) that were prespecified to guide the systematic literature review for direct evidence are presented in Table 41.

[Instructional text] The direct effectiveness of the test should consider the health impact that the investigation and associated interventions has on the patient. This is also called the ‘clinical utility’ of the test. [End instructional text]

Table 41 PPICO criteria for assessing [*proposed health technology] for [*indication] (direct from test to health outcomes evidence)

Component	Description
Population	
<*Prior tests>	
Intervention	
Comparator	
Outcomes	Safety: Effectiveness: Health care system outcomes:
Systematic review questions: What is the safety, effectiveness and cost-effectiveness of [*XXXX] compared to [*XXXX] in [*XXXX]?	

[Define all abbreviations used in the table]

[Instructional text] For investigative tests with linked evidence, present PICO criteria in tables (see Table 42 and Table 43) and include the following text: [End instructional text]

The Population, Prior tests, Investigation/Index test, Comparator and Outcomes (PPICO) that were prespecified to guide the systematic literature review for a linked evidence approach are presented in Table 42 and Table 43.

[Instructional text]

Please note that there may be multiple reference standards; for example, for a genetic test, a reference standard of full gene sequencing may be the appropriate reference standard for test accuracy for determining the presence of variants, whereas future health outcomes may be the reference standard for prognosis.

If there is key evidence linking the test to health outcomes (e.g. when it is used as a companion diagnostic), compare the tests most likely to be used in Australia against this clinical utility standard.

[End instructional text]

Table 42 PPICO criteria for assessing [*proposed health technology] for [*indication] (linked evidence for test accuracy and change in management)

Component	Description
Population	
<Prior tests>	
Intervention	
Comparator	
<Reference standard (for test accuracy)>	
<Clinical utility standard>	
Outcomes	Test accuracy: Change in management:
Systematic review questions:	

[Define all abbreviations used in the table]

Table 43 PPICO criteria for assessing [*proposed health technology] for [*indication] (linked evidence for impact of change in management on health outcomes)

Component	Description
Population	
Prior tests	
Intervention	
Comparator	
Outcomes	Health outcomes:
Systematic review questions:	

[Define all abbreviations used in the table]

Literature sources and search strategies

[Instructional text] Describe the literature search strategy including search terms used, and databases and sources searched. Include the following text: [End instructional text]

The medical literature was searched on *Date to identify relevant studies [*and systematic reviews] published during the period *Date to *Date. Searches were conducted of the databases and sources described in Table 45.

[Instructional text] Include the following statements if appropriate: [End instructional text]

<Attempts were also made to source unpublished or grey literature from *XXX>

<Search terms are described in Table 44.>

[Instructional text]

Describe the full search string for at least one database (see Table 44 for an example of possible structure). It is restrictive to search the literature by including search terms concerning the comparator and/or outcomes; however, in circumstances where the literature is very extensive, this might be reasonable. There should be sufficient detail in the search strategy to allow it to be replicated. Limits should include the date span of the search and the language. Adapt as required for multiple populations etc.

A single set of searches may be appropriate for all studies that include the new test (i.e. direct evidence of effectiveness, harms, test accuracy and whether there is a change in patient management from the new test). If the final step of a linked evidence approach is to be used (assessing the effectiveness of patient management changes), an additional set of searches may be required.

Please note, it is important for MSAC to be able to compare the intervention against the comparator. If no comparative evidence is identified, then noncomparative literature must be sought for both the intervention and comparator.

[End instructional text]

Table 44 Search terms used (*literature search platform)

Category	Description	Search terms
Study design (if justified)	[*insert description of category]	[*e.g. Cochrane Highly Sensitive Search Strategies for identifying randomised trials in MEDLINE, or MeSH and text word terms for nonrandomised study designs]
Population	[*insert description of category]	[*include MeSH terms, text words and synonyms for the target population/disease/condition]
Intervention	[*insert description of category]	[*include known proprietary and nonproprietary names, MeSH terms]
Comparator	[*insert description of category]	[*include known proprietary and nonproprietary names, MeSH terms]

MeSH = medical subject headings. [Define all abbreviations used in the table]

Refer to: MSAC Guidelines Appendix 2 for more guidance on search strategies

[Instructional text]

Provide a record of search strategies used (Table 45). Add or delete sources as required. As a minimum, search the published literature, registers of randomised trials, any unpublished studies the applicant may have on file, and reference lists of all relevant articles that are obtained (backward citation searching).

[End instructional text]

Table 45 Record of search strategies

Source	Date span of search
MEDLINE (via PubMed)	[insert dates]
EMBASE (e.g. Embase.com)	[insert dates]
Cochrane Library ^a	[insert dates]
ClinicalTrials.gov	[insert dates]
International Clinical Trials Registry Platform ^b	[insert dates]
Australian Clinical Trials Registry	[insert dates]
INAHTA HTA database	[insert dates]
Prospective Register of Systematic Reviews (PROSPERO)	[insert dates]
Internal registries	[insert dates]
Other (state other sources ^c)	[insert dates]

a Includes the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials

b [International Clinical Trials Registry Platform](#)³

c [Report on the details of supplementary searches, including manual checking of the references in retrieved papers, searches of the TGA dossier and searches of grey literature]

Study selection

[Instructional text] Include appropriate statements to describe study selection. For example: [End instructional text]

<Studies were selected ***independently by two reviewers/by a single reviewer with a random sample receiving independent assessment by a second reviewer/by a single reviewer.**>

[Instructional text] Choose one. [End instructional text]

<Disagreements regarding study selection were resolved by a third independent reviewer.>

<Additional prespecified criteria for excluding studies included: ***XXXX**>

Studies that could not be retrieved, or that met the inclusion criteria but contained insufficient or inadequate data for inclusion are listed as excluded studies in Appendix C. All other studies that met the inclusion criteria are listed in Appendix B.

Appraisal of the evidence

[Instructional text] Describe the process for appraisal of the evidence as follows: [End instructional text]

Appraisal of the evidence was conducted in 4 stages:

Stage 1: Appraisal of the risk of bias within individual studies (or systematic reviews) included in the review. <Some risk of bias items were assessed for the study as a whole, while others were assessed at the outcome level>.

³ www.who.int/clinical-trials-registry-platform

Stage 2: Appraisal of the precision, size of effect and clinical importance of the results reported in the evidence base as they relate to the prespecified primary outcomes for this assessment <and determining the assumed baseline risk>.

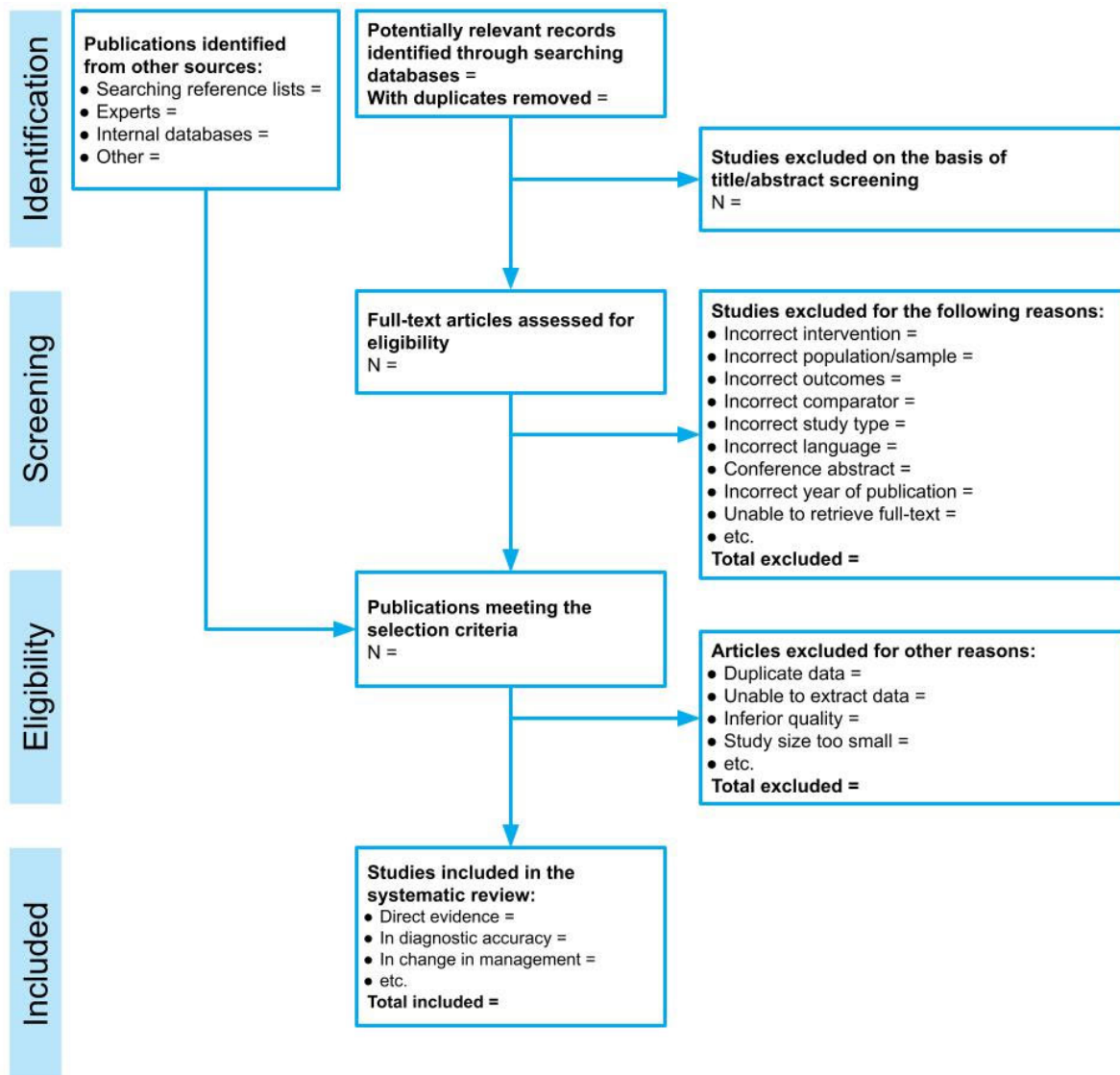
Stage 3: Rating the overall quality of the evidence per outcome, across studies, based on the study limitations (risk of bias), imprecision, inconsistency of results, indirectness of evidence and the likelihood of publication bias (evidence profile tables, Appendix D). [Instructional text] The use of GRADE for this step is optional. [End instructional text]

Stage 4: Integration of this evidence (across outcomes) for conclusions about the net clinical benefit of the test and associated interventions in the context of Australian clinical practice. (Section 2A.5 or 2B.5 in the assessment report).

Appendix B Studies included in the systematic review

PRISMA flowchart of included studies

[Instructional text] A PRISMA flowchart (Figure 3) provides a graphic depiction of the results of the literature search and the application of the study selection criteria (listed in Table 15) (Liberati et al., 2009). Revise figure to suit. [End instructional text]



[Define all abbreviations used in the figure]

Figure 3 Adapted PRISMA flowchart for presenting screening of studies for MSAC assessment reports (Liberati et al. 2009⁴; Moher et al. 2009⁵)

Study profiles of included studies

[Instructional text] Provide a study profile for every included study (Table 46). Amend the table as required, and add additional tables if it assists clarity (e.g. for different types of outcomes, or populations). [End instructional text]

⁴ Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology*. 2009;62(10):e1-e34.

⁵ Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Journal of clinical epidemiology*. 2009;62(10):1006-12.

Table 46 Study profiles for studies included in the systematic review

Study details Country Funding source Conflicts of interest	Study design/ NHMRC level of evidence Quality appraisal	Study population	Inclusion criteria Exclusion criteria	Intervention Comparator	Outcomes
			Inclusion: Exclusion:	Intervention Comparator	

[Define all abbreviations used in the table]

Appendix C Excluded studies

[Instructional text] Provide reasons for exclusion of any studies that were excluded for reasons other than not meeting the inclusion criteria (e.g. duplicated data, unable to extract data, quality inferior to included studies, foreign language article, unable to retrieve in time, study size too small). [End instructional text]

Appendix D Evidence profile tables

[Instructional text] Use of GRADE is optional; however, it is important to find some way of discussing how factors such as the risk of bias, inconsistency, applicability of the population/intervention/comparator or outcomes, imprecision and size of effect influence the level of confidence MSAC may have in basing recommendations on the available evidence. One way to summarise these elements is to use a GRADE table (see Table 47). [End instructional text]

Table 47 Summary of findings table for important outcomes of [*population XXXX]

Question: Patient or population: Intervention: Comparator:						
Section in report	Aim/outcomes	Participants and studies	Quality of evidence	Results	Interpretation	GRADE
		n= k=	Risk of bias: Inconsistency: Indirectness: Imprecision: Publication bias: Other:			
		n= k=	Risk of bias: Inconsistency: Indirectness: Imprecision: Publication bias: Other:			
		n= k=	Risk of bias: Inconsistency: Indirectness: Imprecision: Publication bias: Other:			
		n= k=	Risk of bias: Inconsistency: Indirectness: Imprecision: Publication bias:			

Question: Patient or population: Intervention: Comparator:						
Section in report	Aim/outcomes	Participants and studies	Quality of evidence	Results	Interpretation	GRADE
			Other:			
		n= k=	Risk of bias: Inconsistency: Indirectness: Imprecision: Publication bias: Other:			

[Define all abbreviations used in the table]

⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect.

⊕⊕⊕⊖ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

⊕⊕⊖⊖ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

⊕⊖⊖⊖ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Appendix E Economic evaluation supporting evidence and additional analyses

[Instructional text] Add any supporting evidence and additional analyses performed to supplement the information presented in the main body of the assessment. These might include complex analyses or calculations used to transform inputs, or the presentation of sensitivity analyses that have only minor effects on the base-case ICER. [End instructional text]