*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.**

[Instructional text]

The report template is structured into Sections 1, 2, 3, 4 and 5 to align with the MSAC Guidelines which are available on the MSAC website. Choose which Section 2 and Section 3 of the template are most applicable (see Figure 1).

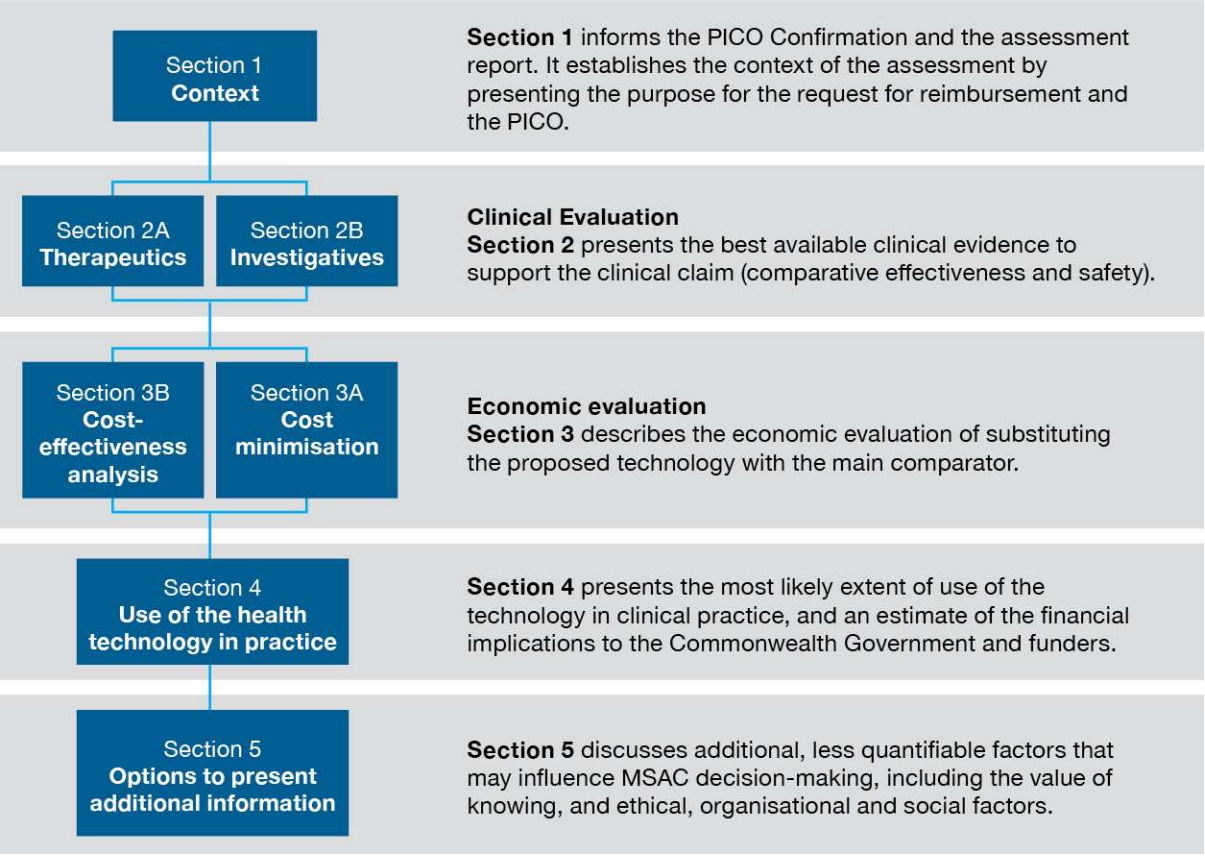


Figure 1 Sections of the template

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]

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.

[Instructional text]

Please keep the Section Break (Odd Page) below to ensure the page numbering remains consistent.

[End instructional text]

Contents

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 non-specified 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.

ADAR Executive Summary

[Instructional text]

An ADAR executive summary aims to provide a brief overview of the key aspects of the PICO, and key results. It is intended that this executive summary is brief and focused. It will be accompanied by another executive summary, generated during an evaluation of the ADAR, which will form the basis of the ESC advice and MSAC public summary document. This PSD-style executive summary is longer and structured. The two executive summaries perform different functions and are not intended to compete.

The ADAR executive summary is an opportunity for the applicant or stakeholders involved in preparing the assessment report to provide high-level contextual information and a value proposition for the proposed technology in simple language. A brief document that does not include substantial detail (as would be provided in the assessment report) ensures broad engagement across the committees, who in reality are burdened by the quantity of documents that they are required to read for each meeting.

Aim to keep the executive summary brief (2–5 pages).

Suggested items for inclusion in the executive summary are:

- *a description of the technology, the clinical need, a clinical claim and the intended benefits (value proposition)*
- *a summary PICO table (containing the proposed population and indication, the proposed technology and the main comparator) – see Section 1.6 of the template*
- *the proposed funding mechanism (e.g. MBS), the practitioner who requests the service and the practitioner who performs the service*
- *the key evidence and clinical outcomes*
- *the key economic findings*
- *the estimated cost to the funder*
- *other key relevant considerations (such as consumer inputs).*

[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

[Instructional text]

Describe the purpose of the application. Include the following text:

[End instructional text]

This ADAR 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 applicant] has provided a systematic review and economic evaluation of [*proposed technology] to inform MSAC's decision-making regarding whether the proposed health technology should be publicly funded through the [*proposed funding source]. 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]

Insert text here

1.1 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 1).

[End instructional text]

Table 1 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 2), including hyperlinks to the relevant published PSD(s), and discuss how the current assessment report addresses these concerns.

[End instructional text]

Table 2 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]

1.2 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]

1.3 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]

1.4 Intervention

Refer to: MSAC Guidelines TG 2.2 (Intervention)

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

1.5 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]

1.6 Summary of the PICO criteria

[Instructional text]

Provide the PICO criteria from the PICO confirmation, if one was developed (Table 3).

[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 3.

Table 3 PPICO criteria for assessing [*proposed health technology] for [*indication]

Component	Description
Population	
<Prior tests>	
Intervention	

Component	Description
Population	
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]

1.7 Alignment with the PICO confirmation

Refer to: MSAC Guidelines TG 2 (PICO)

[Instructional text]

Include the following text:

[End instructional text]

This ADAR 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]

1.8 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]

1.9 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 4).

Provide the proposed fee and explain how it was derived.

[End instructional text]

Table 4 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 5.

[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 5 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 6, Table 7 and Table 8 show examples of how some outcomes might be presented.

[End instructional text]

Table 6 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 7 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>

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>
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 8 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]

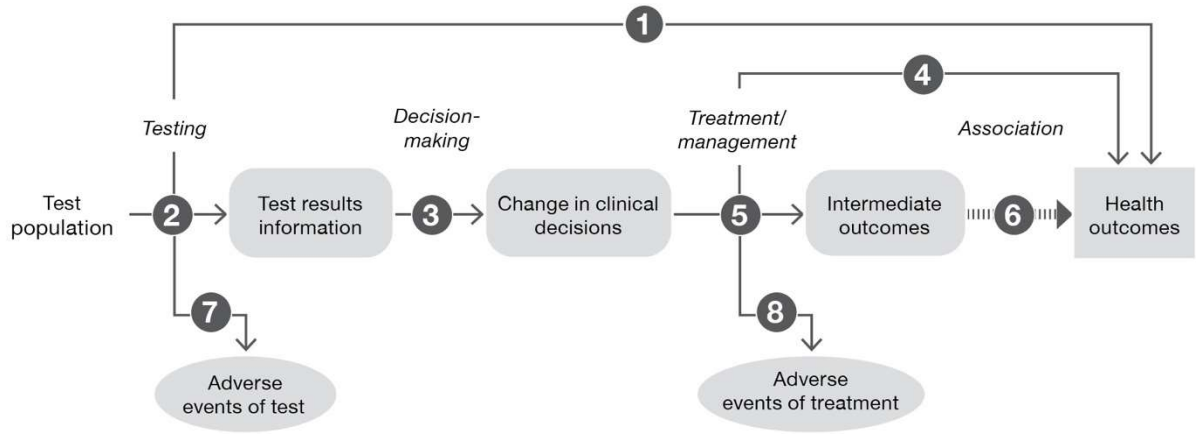


Figure 2 Assessment framework for [*proposed health technology/intervention] for [*indication]

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

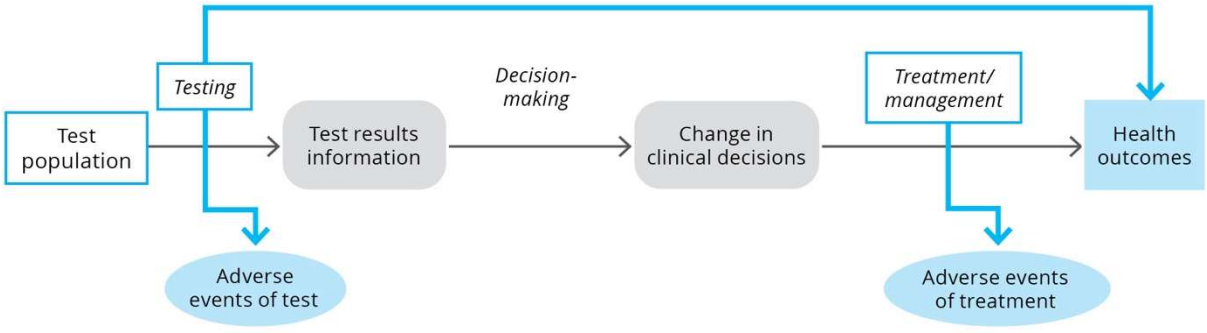
[Instructional text]

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 2Figure 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 9.

[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 9 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 10 and Table 11 show examples of how some outcomes might be presented.

[End instructional text]

Table 10 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 11 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]

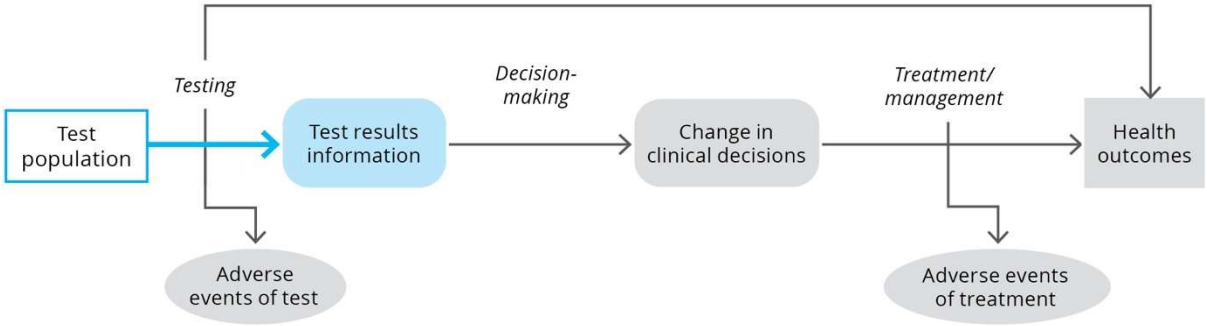
**Outcome 4*

[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 12.

Table 12 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 13.

[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 13). 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 13 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 14).

[End instructional text]

Table 13 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 14 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 standard[1], and Bayes' Theorem was applied.

Table 15 is an example of a 2-by-2 table for diagnostic accuracy data.

Table 15 Diagnostic accuracy data extraction

		Reference standard		
		Disease +	*Disease –*	
Index test	*Test +*	True positive	False positive	Total test positive
Or comparator	*Test –*	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).

[1] 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.

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]

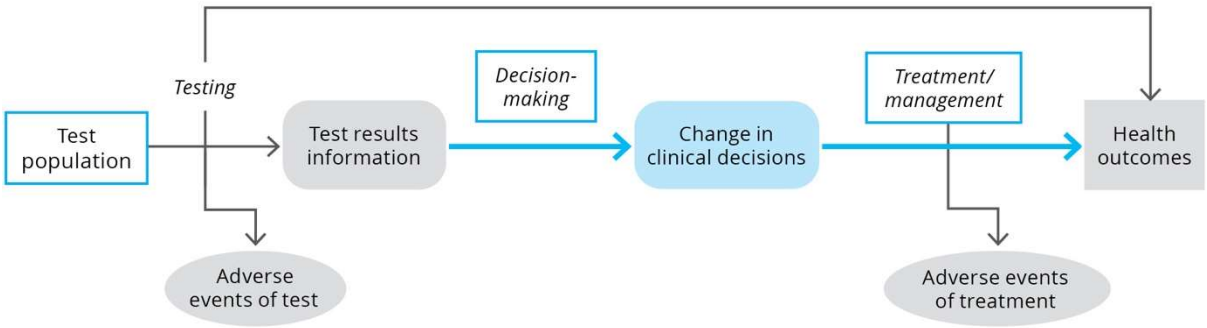
This section reports the direct harms of testing (if required). If a full linked evidence approach is presented, group the safety of the test with the safety associated with downstream changes in management and report this in Section 2B.4 (Linked evidence of health outcomes).

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 16.

[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 16. 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 16, 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 16 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)

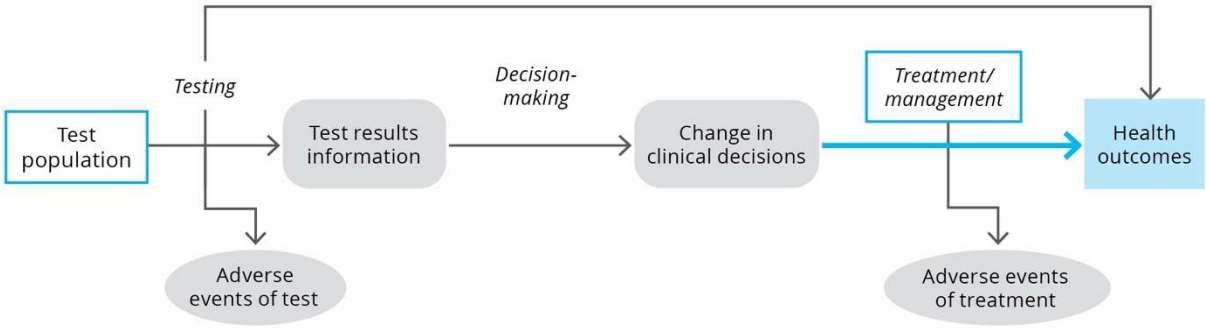
Refer to: MSAC Guidelines Appendix 4 (Certainty of the evidence)

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 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 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 17 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]

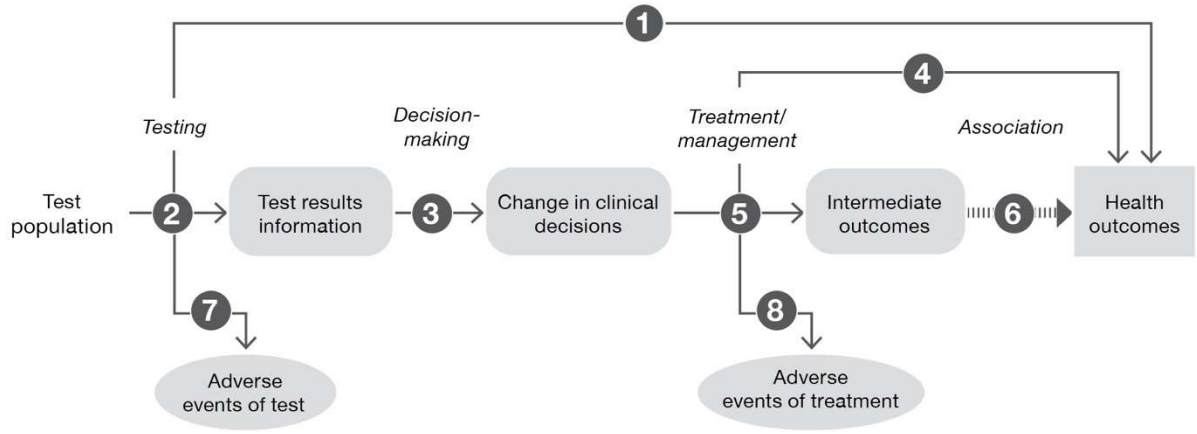


Figure 2 Assessment framework for [*proposed technology/intervention] for [*indication]

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 18 below). Another is as per Table 19.

[End instructional text]

Table 18 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 19 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	
Overall assessment of the evidence	

[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 20). Include rows as relevant to the model presented.

[End instructional text]

Table 20 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 21). 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 21 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 22, Table 23 and Table 24 below. Adapt as necessary.

[End instructional text]

Table 22 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 – $yk	zk%
	Total	∑$x	∑$y	∑$x – ∑$y	∑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]

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]
	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]
	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 23 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. – $y etc.	z etc
	Total for health state 1	∑$x	∑$y	∑$x – ∑$y	∑z
Health state 2	Resource type 1	$xx1	$yy1	$xx1 – $yy1	zz1
	Resource type k	$xxk	$yyk	$xxk – $yyk	zzk
	Total for health state 2	∑$xx	∑$yy	∑$xx – ∑$yy	∑zz
etc.	etc.	etc.	etc.	etc.	etc.
Total	**–**	**∑$x + ∑$xx etc.**	**∑$y + ∑$yy etc.**	**(∑$x + ∑$xx etc.) – (∑$y + ∑$yy etc.)**	**100**

[Define all abbreviations used in the table]

– = not required

Table 24 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 25). Include rows as relevant to the model presented.

[End instructional text]

Table 25 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 26). Refer to: TG 26.1 Health care resource use and costs.

[End instructional text]

Table 26 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 additional costs or cost offsets associated with the use 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 27).

[End instructional text]

Table 27 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 28), 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 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 28 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)						

Parameter	20XX	20XX	20XX	20XX	20XX	20XX
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

1.

2.

3.

4.

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.

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]

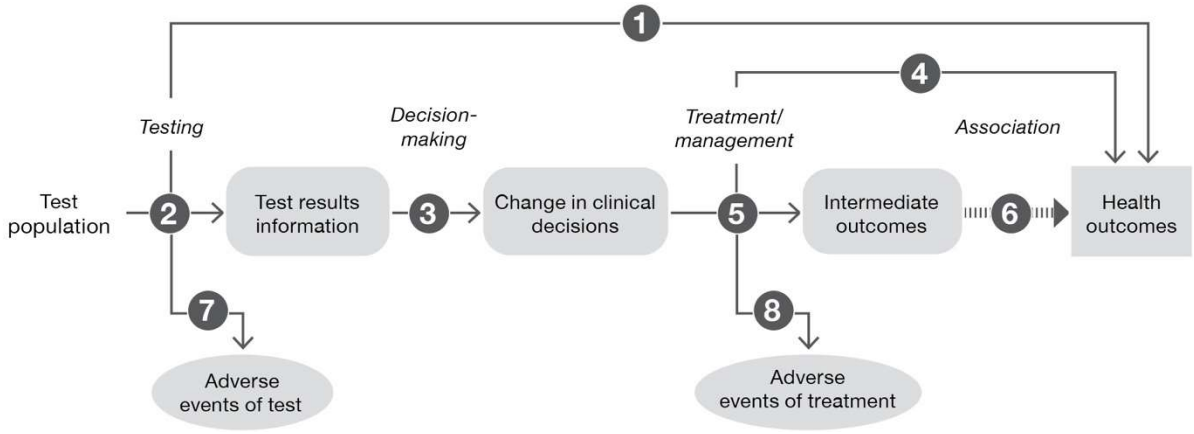


Figure 2 Assessment framework for [*proposed technology/intervention] for [*indication]

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 29) 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 29.

[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 29 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 30 and Table 31) 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 30 and Table 31.

[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 30 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	

Component	Description
<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 31 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 33**Error! Reference source not found.**.

[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 32.>

[Instructional text]

Describe the full search string for at least one database (see Table 32 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 32 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 33). 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 33 Record of search strategies

Source	Date span of search
MEDLINE (via PubMed)	[insert dates]
EMBASE (e.g. Embase.com)	[insert dates]

Source	Date span of search
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[2]

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:

[2] www.who.int/clinical-trials-registry-platform

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>.

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 Evidence profile tables). *[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).

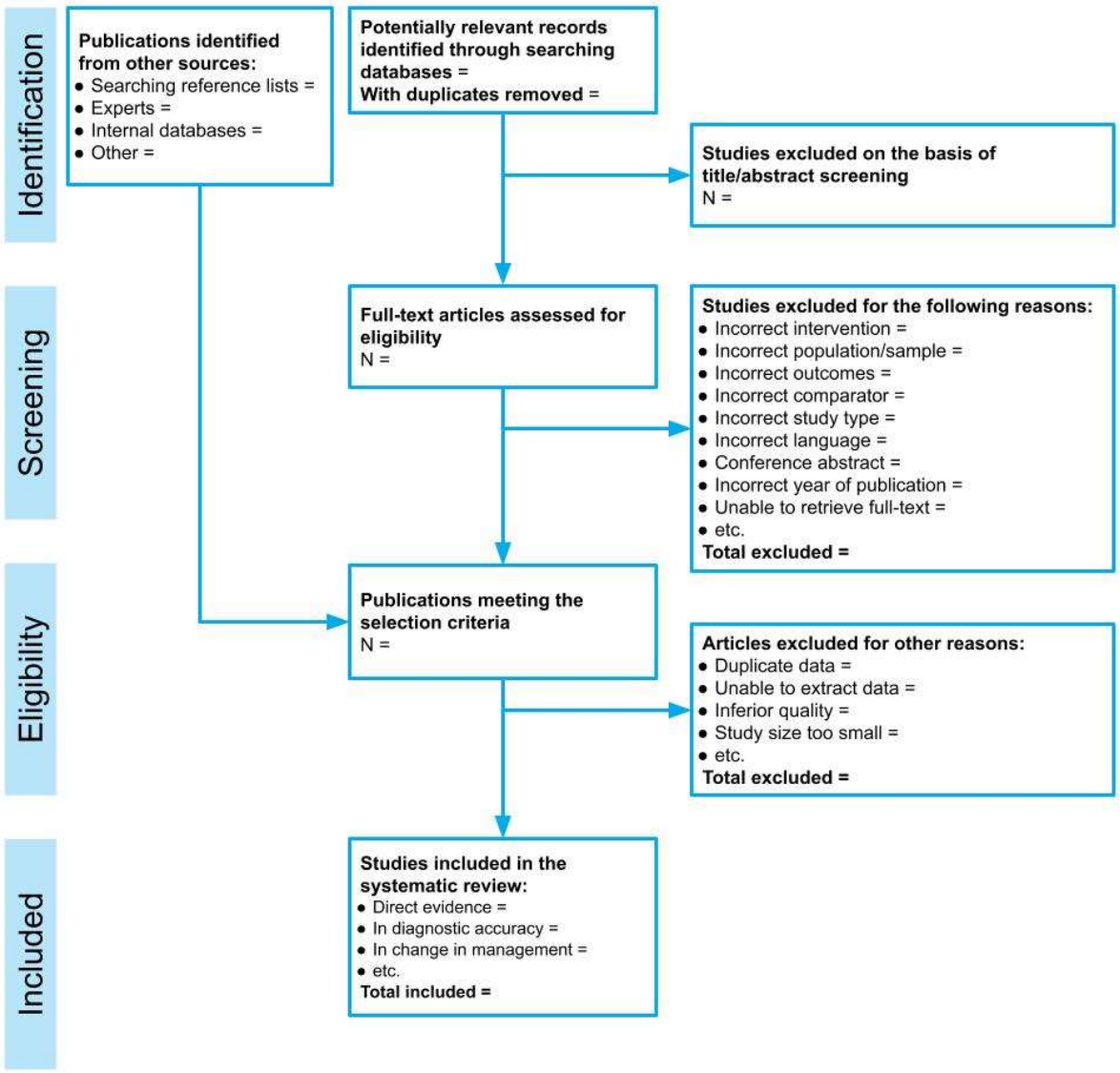
Appendix B Studies included in the systematic review

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 (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. 2009[3]; Moher et al. 2009[4])

[3] 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.

[4] 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.

Study profiles of included studies

[Instructional text]

Provide a study profile for every included study (Table 34). 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]

Table 34 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 35).

[End instructional text]

Table 35 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:			

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:			
		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]