Title

Month Year

MSAC application no. XXXX

Assessment report

VERSION CONTROL

DOCUMENT HISTORY

Version Number	Date Changed	Author	Reason for Change
1.1	18-Feb-2016	Sean McCandless	Version control introduced
2.1	9-Mar-2016	Sean McCandless	Alt text added to Version Control Tables Document renamed and printed to Portable Document Format in preparation for publishing Online
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DOCUMENT APPROVAL

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4.0	28-Jul-2017	Sean McCandless	Document Released

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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.
>

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

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

This report was prepared by XXXX from XXXX. Clinical advice was provided by XXXX – who are members of the Health Expert Standing Panel. The report was commissioned by the Australian Government Department of Health. It was edited by XXXX.

The suggested citation for this document is:

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

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BOXES

FIGURES

EXECUTIVE SUMMARY

KEEP EXECUTIVE SUMMARY SHORT – 6 - 8 PAGES FOR A TYPICAL TECHNOLOGY WITH ONE CLINICAL INDICATION.

Main issues for MSAC consideration

- *List the key issues that will impact on MSAC decision-making here.*

- *Keep to less than one page.*

- *This should not be a summary of the evidence or critique, but rather, pointing out where critical uncertainties exist.*

Clearly set out the key aspects and issues that were presented in the main body of the assessment report.

Title of Submission

This <submission-based/contracted> assessment examines the evidence to the support listing of XXXX on the Medicare Benefits Schedule (MBS). The service would be <exclusively> used in the XXX setting for the treatment/management of XXXX. The target population are people with XXXX. <We propose/The applicant has claimed> that the successful listing of the technology in the target population and setting will lead to XXXX.

ALIGNMENT WITH AGREED PICO CONFIRMATION

This < submission-based/contracted> assessment of XXXX addresses <all/most/some/none> of the PICO[1] elements that were pre-specified in the PICO Confirmation that was <submitted to/ratified by> the PICO Advisory SubCommittee (PASC). If deviations from a ratified PICO Confirmation have occurred, please state briefly what has changed and give reasons for the change (including by referring to the relevant section in the main body of the report). If the PICO Confirmation was not ratified by PASC, please state this.

PROPOSED MEDICAL SERVICE

Describe the key features of the intervention.

---

[1] Population, Intervention, Comparator, Outcomes

Indicate whether the intervention is currently funded or reimbursed in private or public setting in Australia for the same or another clinical indication.

PROPOSAL FOR PUBLIC FUNDING

Provide MBS or other public funding descriptors in the table below. Use the proposed item descriptor as set out in the PICO Confirmation. If the PASC process has not been used by the applicant, then please make this clear in the text prior to presenting the proposed MBS item descriptor in the format below.

Table 1   Proposed MBS item descriptor

Category X – XXXXXX
(a)

POPULATION

Briefly describe the population in whom it is proposed the test should be used, and a summary of the frequency (prevalence and/or incidence) of the population or disease in question.

COMPARATOR DETAILS

Briefly describe the main comparator(s) that was agreed in the PICO Confirmation. If there are any additional comparators to those in the agreed PICO Confirmation, please justify their selection.

CLINICAL MANAGEMENT ALGORITHM(S)

Briefly describe how the intervention fits in the overall management of the condition and why it is needed. You might like to refer to the location of the clinical management algorithms in the main body of the report.

KEY DIFFERENCES IN THE DELIVERY OF THE PROPOSED MEDICAL SERVICE AND THE MAIN COMPARATOR

Briefly describe any differences in the delivery/organisation of care associated with the intervention and the main comparator.

CLINICAL CLAIM

Provide information about the clinical claim with respect to the proposed intervention, as set out in the PICO Confirmation. If the applicant has not utilised the PASC process to state the clinical claim, please mention this here.

APPROACH TAKEN TO THE EVIDENCE ASSESSMENT

A systematic review of published <and unpublished> literature was undertaken.

Summarise databases searched and/or time period, key study selection criteria (PICO), methods for selecting studies and critical appraisal methods.

CHARACTERISTICS OF THE EVIDENCE BASE

Describe the number of studies identified, and the quality of them. Identify any serious issues with the studies (design/population/risk of bias/relevance of outcome measures etc) and provide a link to where the information on characteristics can be found in the main document.

RESULTS

Safety

Key points from main body of the report – concentrate on comparative safety, as measured by the patient-relevant outcomes specified in the PICO Confirmation, if these data are available. The emphasis should be on whether there are clinically relevant differences in the reported harms, irrespective of whether the results are statistically significant.

Effectiveness

Key points from main body of the report – concentrate on comparative effectiveness, as measured by the patient-relevant outcomes specified in the PICO Confirmation, if the data are available.

The summary of findings (incorporating no more than seven critical and important outcomes, both benefits and harms) is shown in Table 2.

Table 2   **Balance of clinical benefits and harms of intervention, relative to comparator, and as measured by the <u>critical</u> patient-relevant outcomes in the key studies**

Outcomes (units) Follow-up	Participants (studies)	Quality of evidence (GRADE)[a]	Relative effect (95%CI) <OR/RR/HR and 95% CI> <results of statistical testing and p-value and/or 95% CI>	Risk with control <n with event/N (%)> <mean ± SD>	Risk or risk difference with intervention <RD± NNT/NNH and 95% CI> <mean difference and SD or 95%CI>	<Comments>

[a] GRADE Working Group grades of evidence (Guyatt et al., 2013)

⊕⊕⊕⊕ **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.

<SD=standard deviation; RD=risk difference; NNT=number needed to treat; OR=odds ratio; RR=relative risk; HR=hazard ratio; NNH=number needed to harm.>
Select or add abbreviations as required.
If outcome is continuous, please provide the scale.

On the basis of the benefits and harms reported in the evidence base (summarised above), **it is suggested that, relative to the comparator, the intervention has superior/non-inferior/ inferior safety and superior/non-inferior/ inferior effectiveness.**

TRANSLATION ISSUES

Briefly indicate the key translation issues and pre-modelling studies that were used to adapt the evidence presented in Section B for the purposes of the economic evaluation (eg the economic model that predicts the cost-effectiveness of the new intervention, relative to the agreed comparator, if the intervention is used according to the proposed MBS item descriptor).

If translation of the clinical evidence was not needed or not undertaken, please state this.

ECONOMIC EVALUATION

Based on the evidence supporting the clinical claim, and with reference to Table D.1.2 in the *MSAC Therapeutic Guidelines*, state what type of economic evaluation has been used in the table below eg cost-effectiveness, cost-utility, cost-minimisation, cost-consequences.

If an economic evaluation is not undertaken, please justify this with reference to Table D.1.2 of the *MSAC Therapeutic Guidelines* and do not insert the tables below into this section.

Table 3 Summary of the economic evaluation

Perspective	
Comparator	
Type of economic evaluation	e.g. cost-effectiveness, cost-utility, cost-minimisation, cost-consequences.
Sources of evidence	e.g. systematic review
Time horizon	e.g X years in the model base case
Outcomes	e.g. name or list the outcome/s used in the model eg. LYG and QALYs
Methods used to generate results	e.g. trial-based, cohort expected value analysis, Markov model
<Health states>	Only put in this row if it is relevant to your model
<Cycle length>	Only put in this row if it is relevant to your model
Discount rate	

Software packages used	

See Table D.3.1 in the *MSAC Therapeutic Guidelines.*

Key structural assumptions of the model are:

Two different formats for presenting the findings of the economic evaluation are provided below. Choose which of these is appropriate for the evaluation that has been undertaken. Please delete the inappropriate one and/or incorporate additional summary information, as required.

< The overall costs and outcomes, and incremental costs and outcomes as calculated for the intervention and comparator in the model, and using the base case assumptions, are shown in the table below.>

Table 4   Title

	Cost	Incremental cost	Effectiveness (QALYs)	Incremental effectiveness	ICER
Intervention					
Comparator					

ICER = Incremental Cost Effectiveness Ratio>

<The modelled results were most sensitive to >

Table 5   Key drivers of the economic model

Description	Method/Value	Impact
e.g. Time horizon	25 years; assumed from 6 month trial duration	High, favours intervention
e.g. Upper 95% CL of the difference in outcomes	$100,000/QALY	High; favours comparator
etc		

<Other key areas of uncertainty were >

ESTIMATED EXTENT OF USE AND FINANCIAL IMPLICATIONS

<An epidemiological approach has been used to estimate the financial implications of the introduction of XXX.>

The financial implications to the MBS resulting from the proposed listing of XXX are summarised in Table 6.

Table 6   Total costs to the MBS associated with XXX

	2015-16	2016-17	2017-18	2018-19	2019-20
Intervention					
Number of services					
Sub-total cost					
<Any co-administered services currently MBS listed>					
Number of services					
Sub-total cost					
Total services					
Total cost					

The summary should primarily focus on the financial implications in terms of MBS rebates. If a service is primarily out-of-hospital, then there will need to be a separate analysis of the financial implications to the safety net.

The ratio of in-hospital vs out-of-hospital service needs to be determined and the 75% vs 85% rebate (or if a GP service, 100% rebate), respectively, proportionately assigned in the costing. The Department is interested in the rebate as the input cost, not the schedule fee.

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

CONSUMER IMPACT SUMMARY

Summarise any feedback received during the public consultation period.

<OTHER RELEVANT CONSIDERATIONS>

This section is reserved for content relating to changes in the organisation of care, social/ethical/legal considerations, specific policy considerations, impact on consumers/patients, access/equity considerations, training/workforce considerations, risk share arrangements etc.. The content of this section is topic-specific; it is, therefore, optional.

ACRONYMS AND ABBREVIATIONS

Add/delete as applicable

Acronym/abbreviation	Meaning
AIHW	Australian Institute of Health and Welfare
ARTG	Australian Register of Therapeutic Goods
CI	confidence interval
HESP	Health Expert Standing Panel
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 A   CONTEXT

In this Section: Establish the context for the assessment report. Describe the proposed medical service, its intended use on the MBS or elsewhere, and the medical services that would be co-delivered or substituted (the medical service likely to be most replaced by health care providers in practice is the 'main comparator').

This <contracted/submission-based> assessment of XXX for the <treatment/management of XXX> is intended for the Medical Services Advisory Committee (MSAC). MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Schedule (MBS) in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

If you are writing a Submission-based Assessment, use the following text:

Name of applicant has provided a systematic review and economic evaluation of XXXXXX in order to inform MSAC's decision-making regarding whether the proposed medical service should be publicly funded.

If you are writing a Contracted Assessment, use the following text:

Name of contracting agency has been commissioned by the Australian Government Department of Health to conduct a systematic literature review and economic evaluation of XXXXXX. This assessment has been undertaken in order to inform MSAC's decision-making regarding whether the proposed medical service should be publicly funded.

<Appendix A provides a list of the people involved in the development of this assessment report, <including clinical expertise sourced from XXX/the Health Expert Standing Panel (HESP).>

Contracted assessors can provide more detail on HESP input here by including the following text:

HESP are a pool of experts collated from various medical fields who have been nominated by their associated professional body or by applicants. HESP members are a panel of the MSAC and are engaged to provide practical, professional advice that directly relates to each application and the service being proposed for the MBS. HESP members are not members of either MSAC or its subcommittees. Their role is limited to providing input and guidance to the assessment groups to ensure that the pathway is clinically relevant and takes into account consumer interests. HESP member's advice is used to inform the deliberations that MSAC presents to the Federal Minister for Health.

<The proposed use of XXXX 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.> <This application is following a fit-for-purpose pathway, therefore a PICO Confirmation outlining the proposed use of XXXX in Australian clinical practice was not presented to/ratified by the PICO Confirmation Advisory SubCommittee (PASC).>

A.1.   ITEMS IN THE AGREED PICO CONFIRMATION

<This <contracted/submission-based> assessment of XXXX addresses <all/most/some/none> of the PICO elements that were pre-specified in the PICO Confirmation <that was ratified by/submitted to> PASC.> If deviations from the PICO Confirmation have occurred, please 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.

A.2.   PROPOSED MEDICAL SERVICE

Provide information about the proposed medical service and the mode of delivery.

Has MSAC previously considered an application requesting listing of this item and/or have any reviews relating to this intervention been conducted? If it has previously been considered, in a few sentences indicate the result of that consideration and main reason for the return of the proposal. What is different with the new SBA/CA?   <Any limitations on how the intervention would be provided or the setting in which the intervention can be provided>

<MARKETING STATUS OF DEVICE / TECHNOLOGY

If the intervention does not require a new device but is instead a procedure or service, this section does not need to be completed. However, information on training/credentialing of service providers should still be mentioned in Section F.

All therapeutic products marketed in Australia require listing on the Australian Register of Therapeutic Goods (ARTG). MSAC will not consider a therapeutic product for reimbursement if the device is not listed on the ARTG. Items on the ARTG that are relevant to this application are shown in Table 7.

Table 7   XXX listed on the ARTG

ARTG no.	Product no.	Product description	Product category	Sponsor

Source: Therapeutic Goods Administration, accessed Day Month Year Link to TGA.gov.au

>

<OTHER INDICATIONS>

<Mention whether the intervention is currently used for other clinical indications in Australia.>

CURRENT FUNDING ARRANGEMENTS

Discuss availability of the intervention in public hospitals and in private hospitals – this might include funding under the MBS, in the research setting, whether reimbursed under private health insurance or currently used through self-pay. Indicate whether the intervention is currently reimbursed in either the private or public setting for the same or another indication. If listed on the MBS provide the item number, descriptor, date listed, review arrangements for interim funded items, etc

A.3.   PROPOSAL FOR PUBLIC FUNDING

The proposed MBS item descriptor is summarised in Table 8.

Provide MBS or other public funding descriptors, as set out in the PICO Confirmation. If there are differences between the proposed descriptor and the PASC ratified item descriptor, those differences should be highlighted and justification provided.

Table 8   Proposed MBS item descriptor

Category X – XXXXXX

A.4.   PROPOSED POPULATION

Identify the main population(s) described in the PICO Confirmation including key inclusion and exclusion criteria.

Include a high level summary of the frequency (prevalence and/or incidence) of the population or disease in question and where relevant the natural history/pathophysiology of the condition of interest.

A.5. COMPARATOR DETAILS

Brief description of the main comparator(s) described in the PICO Confirmation, or if a PICO Confirmation was not produced, then the comparator is the current practice most likely to be replaced or added to by the proposed medical service (refer to clinical management algorithm).

If there are any additional comparator(s) to those in the agreed PICO Confirmation, justify their selection.

Note any limitations on provider or the setting in which the comparator can be provided.

The MBS item descriptor/s for the relevant comparator/s is summarised below.

Table 9   Relevant MBS item for the comparator

Category X – XXXXX
MBS

A.6. CLINICAL MANAGEMENT ALGORITHM(S)

Present the clinical management algorithm that depicts the context of the intended use of the proposed medical service following a listing on the MBS or other public funding (as listed in the PICO Confirmation, if presented to PASC).

Present the corresponding algorithm depicting the current context (as listed in the PICO Confirmation, if presented to PASC).

If possible present the two algorithms next to each other so the differences can be seen easily. Highlight the differences between the two algorithms in the text e.g. change in positioning of a therapy in terms of lines of therapy; expansion/augmentation of the current management options; identification of patients who would now be treated who would previously not have been treated.

Indicate whether multiple-listing scenarios are presented.
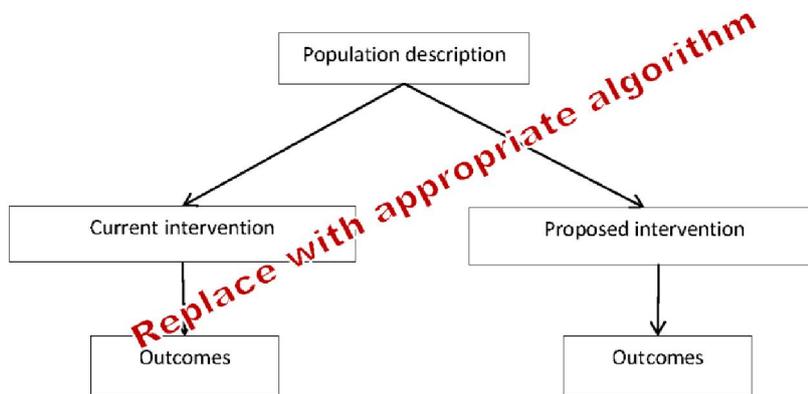
Figure 1 **Clinical management algorithm/s for the proposed new intervention relative to current clinical practice**

A.7. KEY DIFFERENCES IN THE DELIVERY OF THE PROPOSED MEDICAL SERVICE AND THE MAIN COMPARATOR

Describe any differences in the delivery/organisation of care between the intervention and main comparator.

A.8. CLINICAL CLAIM

Provide information about the clinical claim with respect to the proposed medical service, as set out in the PICO Confirmation. If the applicant has not utilised the PASC process to state the clinical claim, please mention this here.

A.9. SUMMARY OF THE PICO

The guiding framework of a PICO Confirmation is recommended by MSAC for each assessment. The PICO Confirmation describes current clinical practice and reflects the likely future practice with the proposed medical service.

The Population, Intervention, Comparator and Outcomes (PICO) that were pre-specified to guide the systematic literature review are presented in Box 1 and Box 2.

Box 1 Criteria for identifying and selecting studies to determine the safety of XXX in patients with XXX

Selection criteria	Description
Population	
Intervention	
Comparator/s	
Outcomes	Critical for decision making:
	Important, but not critical for decision making:
	Low importance for decision making:
Systematic review question	

Box 2 Criteria for identifying and selecting studies to determine the effectiveness of XXX in patients with XXX

Selection criteria	Description
Population	
Intervention	
Comparator/s	
Outcomes	Critical for decision making:
	Important, but not critical for decision making:
	Low importance for decision making:
Systematic review question	

A.10. CONSUMER IMPACT STATEMENT

Summarise the key points received during the public consultation period of the PICO Confirmation.

Section B   Clinical Evaluation

B.1.   Literature Sources and Search Strategies

The medical literature was searched on Date to identify relevant studies <and systematic reviews> published during the period XXX to XXX. Searches were conducted of the databases and sources described in Appendix B. <Attempts were also made to source unpublished or grey literature from XXX> <Search terms are described in Table 10.> If the search terms are comprehensive, they can be included in an Appendix. 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 that it allows it to be replicated. Limits may include the date span of the search and language. Adapt as required for multiple populations etc.

Table 10   Search terms used (literature search platform)

Element of clinical question	Search terms
Population	
Intervention	
Comparator (if applicable)	
Outcomes (if applicable)	
Limits	

B.2.   Results of Literature Search

<A PRISMA flowchart (Figure 2) provides a graphic depiction of the results of the literature search and the application of the study selection criteria (listed in Box 1 and Box 2) (Liberati et al., 2009). >

<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.> Choose one.

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

<Additional pre-specified 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 D. All other studies that met the inclusion criteria are listed in Appendix C.
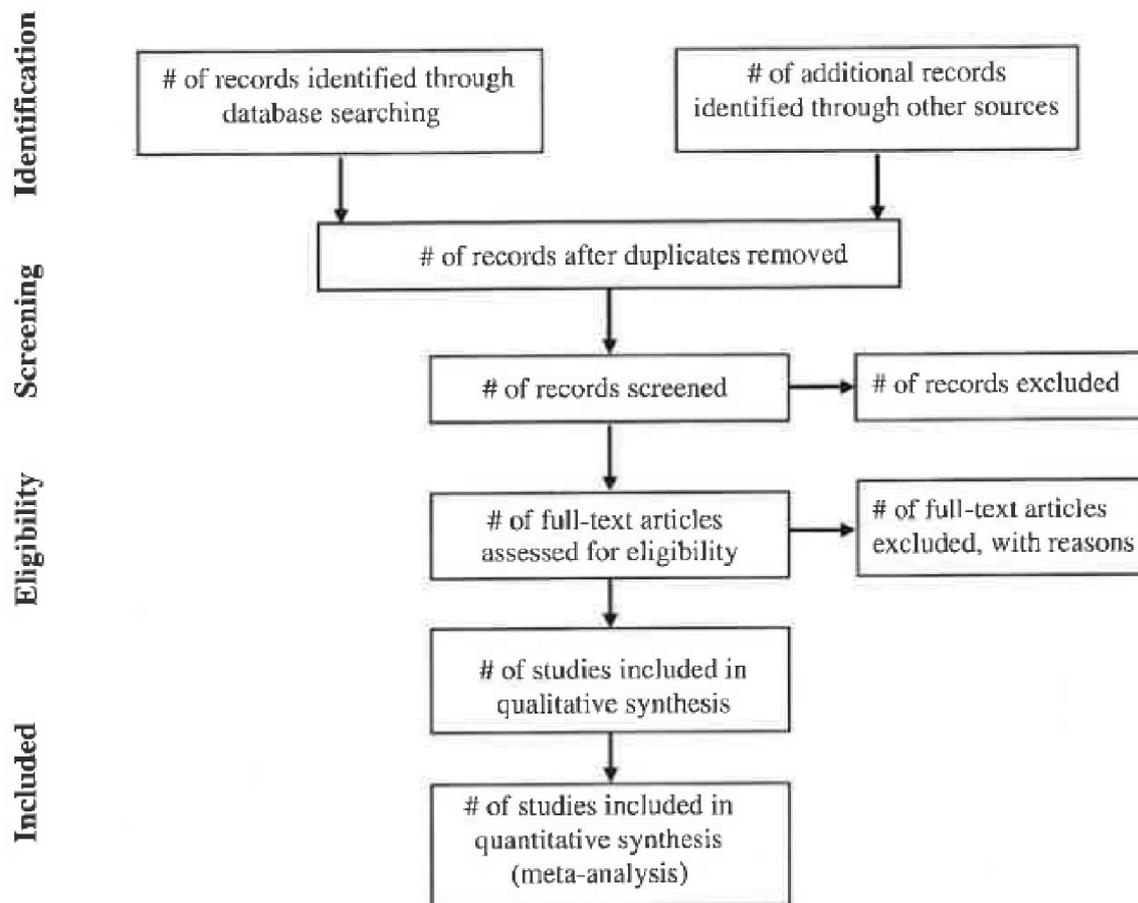
Figure 2   Summary of the process used to identify and select studies for the assessment

This is a picture of a PRISMA flowchart. You will need to construct and adapt these elements for your own search results (i.e. if searches were performed separately for different indications etc, add multiple flowcharts, and adapt as necessary). If you are writing a **contracted assessment** you will then need to save the flowchart as a picture file (TIFF) and copy and paste in, so that web accessibility requirements are met.

A profile of each included study is given in Appendix C. This study profile describes the authors, study ID, publication year, study design <and quality (level of evidence and risk of bias)>, study location, setting, length of follow-up of patients, study population characteristics, description of the intervention, description of the comparator and the relevant outcomes assessed. Study characteristics are also summarised in a shorter format in Section B.4.

APPRAISAL OF THE EVIDENCE

Appraisal of the evidence was conducted in 3 stages:

Stage 1: Appraisal of the risk of bias within individual studies (or systematic reviews) included in the review. <Some risk of bias items were assessed for the study as a whole, while others were assessed at the outcome level>. (Section B.3)

Stage 2: Extraction of the pre-specified outcomes for this assessment, synthesising (meta-analysing or a narrative synthesis) to determine an estimate of effect per outcome, <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. This was done to provide an indication of the confidence in the estimate of effect in the context of Australian clinical practice (Evidence profile tables, Appendix D).

Stage 4: Integration of this evidence for conclusions about the net clinical benefit of the intervention in the context of Australian clinical practice. (Sections B.6-8)

B.3. RISK OF BIAS ASSESSMENT

Reviewers may choose to use the risk of bias table format in the *MSAC Therapeutic Guidelines*, although it should be noted that not all elements of risk of bias are covered by this format. Alternatives could be the Cochrane risk of bias tool, GRADE approach for assessing the risk of bias, or other tools suitable for RCTs, AMSTAR or PRISMA for systematic reviews, and other validated checklists for non-randomised or observational studies. Whatever the choice, the method of assessing risk of bias should be transparent and justifiable. Please note – if an indirect comparison is presented then the risk of bias assessment of the individual trials/studies would need to be supplemented with an assessment of the exchangeability of the study populations being compared – that is, the results for the common comparator arms should suggest that the populations are similar. For some topics, it may make sense to combine this section with the following section, to reduce duplication.

If following GRADE methodology, some elements of risk of bias will apply to the study as a whole (e.g. 'Allocation concealment'), while others must be assessed at an outcome level or cluster of outcomes (e.g. 'Blinding'). An overall risk of bias should be made for each outcome, across studies.[2]

---

[2] For more information, see Guyatt et al. (2011) 'GRADE guidelines: Rating the quality of evidence – study limitations (risk of bias)'. *Journal of Clinical Epidemiology*, 64, 407 – 415.

B.4. CHARACTERISTICS OF THE EVIDENCE BASE

See Appendix C for details on the individual studies included in the evidence base. A summary is provided in Table 11. Keep this section brief, and provide more detail in the study profiles, in Appendix C. Provide any information about the study/participant characteristics that is not reported elsewhere in B.3-B.5, but which is key to interpreting the implications of the evidence. Comment on the applicability (directness) of the included studies.

Table 11 **Key features of the included evidence comparing intervention with comparator**

Trial/Study	N	Design/ duration	Risk of bias	Patient population	Key outcome(s)	Result used in economic model
Jones 2010	225	R, DB 6 mths	Low		Mortality	Not used
Smith 2012	310	R, OL 3 mths	High		Response rate	Not used
Brown 2005	75	CS, OL 8 mths	Low		QoL	Not used
etc						
etc						
Meta-analysis	410 k=			\<Fixed effect/random effect> model; \<overall pooled> \<and> \<subgroup analyses> presented; heterogeneity analysis \<key outcomes> analysed		Survival gain

\<CC=case control; Coh=cohort; CS=case series; DB=double blind; MC=multi-centre; NR=non-randomised; OL=open label (unblinded); QoL=quality of life; R=randomised; SB=single blind; X=cross-sectional..>

Select or add abbreviations as required.

Note – k=no. of studies included in meta-analysis. If the meta-analysis results are provided or relied upon in preference to the individual study results, then the individual studies do not need to be listed here – although they will need to be discussed in Section B.6.

Note – if you are relying on an indirect comparison, you will need to construct the table differently to indicate the common comparator and the two different trials or sets of trials that are being compared. Risk of bias in that situation must consider the exchangeability of the trial populations.

B.5. OUTCOME MEASURES AND ANALYSIS

See Appendix C for details on the outcomes measured in the included studies, along with the statistical methods used to analyse the results.

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 pre-specified or *post hoc*, and the limitations associated with the latter. Comment on the directness of the outcome measures.

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

B.6.   RESULTS OF THE SYSTEMATIC LITERATURE REVIEW

IS IT SAFE?

Summary – Research question

If multiple indications are being assessed, consider changing the heading to "Is it safe for XXXX" , or provide sub-headings for the different populations.

Concentrate on comparative safety, as measured by the patient-relevant outcomes specified in the PICO Confirmation, if these data are available. The emphasis should be on whether there are clinically relevant differences in the reported harms, irrespective of whether the results are statistically significant.

The type of information needed per pre-specified outcome (from the PICO) is given in the table below. The table can be copied for additional pre-specified outcomes. Additional graphical representations might be helpful. The meta-analysis is optional – it will depend on the available evidence base as to whether a meta-analysis can be conducted. If a meta-analysis is conducted, forest plots should be presented.

For each important outcome, the GRADE approach specifies that the overall quality of the evidence (the confidence in estimates of effect) should be assessed. One domain, the risk of bias, has already been outlined. However, additional domains to be assessed per outcome include inconsistency[3], indirectness of the population, intervention, comparator, outcome or setting relative to the proposed use of the intervention in the Australian setting[4], imprecision[5] and risk of publication bias[6]. The quality of evidence for each important outcome may be determined following the GRADE methodology manually, or produced automatically through recording the quality assessment

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[3] For guidance on assessing inconsistency, see Guyatt et al. (2011). GRADE guidelines: 7. Rating the quality of evidence – inconsistency. *Journal of Clinical Epidemiology*, 64, 1294 – 1302.

[4] For guidance on assessing indirectness, see Guyatt et al. (2011). GRADE guidelines: 8. Rating the quality of evidence – indirectness. *Journal of Clinical Epidemiology*, 64, 1303 – 1310.

[5] For guidance on assessing imprecision, see Guyatt et al. (2011). GRADE guidelines: 6. Rating the quality of evidence –imprecision. *Journal of Clinical Epidemiology*, 64, 1283 – 1293.

[6] For guidance on assessing publication bias, see Guyatt et al. (2011). GRADE guidelines: 5. Rating the quality of evidence –publication bias. *Journal of Clinical Epidemiology*, 64, 1277 – 1282.

domains using the 'Guideline Development Tool'[7]. Statements regarding each critical and important safety outcome could therefore be given a grade. The full evidence profile table (with explanatory footnotes), incorporating all critical and important outcomes, should be included in Appendix D.

The GRADE process also requires the assumed control risk to be determined, as a measure of the typical burden of the disease in the target population (i.e. the Australian population likely to make use of the proposed item number). If there are studies from a directly relevant population in the evidence base, the baseline control risk could be determined from this study or mean baseline risk from a group of studies. Otherwise, assess the baseline risk from relevant observational studies.[8]

HARM 1 ETC

Brief discussion of the evidence base reporting on this outcome, and the results found, with reference to table below. Adapt the table as necessary, depending on the evidence available.

Table 12   Results of key patient-relevant outcome across the studies/randomised controlled trials

Study ID	Risk of bias	Intervention <n with event/N (%)> <mean ± SD>	Comparator <n with event/N (%)> <mean ± SD>	Absolute difference <RD± NNT/NNH and 95% CI> <mean difference and SD or 95%CI>	Relative difference <OR/RR/HR and 95% CI> <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 =>				

Define abbreviations used in the table.
If outcome is continuous, please provide the scale.
Note – in table above SD=standard deviation; RD=risk difference; NNT=number needed to treat; OR=odds ratio; RR=relative risk; HR=hazard ratio; NNH=number needed to harm.

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[7] Guideline Development Tool

[8] For more information on assumed baseline risk, and presenting the results, see Guyatt et al. (2013). GRADE guidelines: 12. Preparing Summary of Findings tables – binary outcomes. *Journal of Clinical Epidemiology* 66, 158 – 172 and Guyatt et al. (2013). GRADE guidelines: 13. Preparing Summary of Findings tables and evidence profiles – continuous outcomes. *Journal of Clinical Epidemiology* 66, 173 – 183.

HARM **2** ETC

Is it effective?

Concentrate on comparative effectiveness, as measured by the patient-relevant critical and important outcomes specified in the PICO Confirmation, if the data are available. The emphasis should be on whether there are clinically relevant differences in the reported results between treatment arms ie statistical significance is important but not sufficient.

Summary – Research question

The type of information needed per pre-specified outcome (from the PICO) is given in the table below. The table can be copied for additional pre-specified outcomes. Additional graphical representations might be helpful. The meta-analysis is optional – it will depend on the available evidence base as to whether a meta-analysis can be conducted. If a meta-analysis is conducted, forest plots should be presented. Adapt as necessary, depending on the evidence available.

As outlined in the safety section above, GRADE methodology recommends assessing inconsistency[9], indirectness of the population, intervention, comparator, outcome or setting relative to the proposed use of the intervention in the Australian setting[10], imprecision[11] and risk of publication bias[12] for all the critical and important health outcomes. These details are put into the evidence profile tables in Appendix D, and summarised in B.8, the Interpretation of the Clinical Evidence (summary of findings table). For the purposes of these tables, the assumed control or baseline risk should also be specified[13].

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[9] For guidance on assessing inconsistency, see Guyatt et al. (2011). GRADE guidelines: 7. Rating the quality of evidence – inconsistency. *Journal of Clinical Epidemiology*, 64, 1294 – 1302.

[10] For guidance on assessing indirectness, see Guyatt et al. (2011). GRADE guidelines: 8. Rating the quality of evidence – indirectness. *Journal of Clinical Epidemiology*, 64, 1303 – 1310.

[11] For guidance on assessing imprecision, see Guyatt et al. (2011). GRADE guidelines: 6. Rating the quality of evidence –imprecision. *Journal of Clinical Epidemiology*, 64, 1283 – 1293.

[12] For guidance on assessing publication bias, see Guyatt et al. (2011). GRADE guidelines: 5. Rating the quality of evidence –publication bias. *Journal of Clinical Epidemiology*, 64, 1277 – 1282.

[13] For more information on assumed baseline risk, and presenting the results, see Guyatt et al. (2013). GRADE guidelines: 12. Preparing Summary of Findings tables – binary outcomes. *Journal of Clinical Epidemiology* 66,

EFFECTIVENESS OUTCOME 1 ETC

Brief discussion of the evidence base reporting on this outcome, and the results found, with reference to table below.

Table 13   Results of key patient-relevant outcome across the studies/randomised controlled trials

Study ID	Risk of bias	Intervention <n with event/N (%)> <mean ± SD>	Comparator <n with event/N (%)> <mean ± SD>	Absolute difference <RD± NNT/NNH and 95% CI> <mean difference and SD or 95%CI>	Relative difference <OR/RR/HR and 95% CI> <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 =>				

<SD=standard deviation; RD=risk difference; NNT=number needed to treat; OR=odds ratio; RR=relative risk; HR=hazard ratio; NNH=number needed to harm.>
Select or add abbreviations as required.
If outcome is continuous, please provide the scale.

EFFECTIVENESS OUTCOME 2 ETC

B.7.   EXTENDED ASSESSMENT OF HARMS

This section allows for post-market surveillance/unpublished data on harms to be included if it is relevant to the assessment being undertaken. This might include data captured in administrative data sets, registry data, and recalls by regulatory agencies and from industry. This section is supposed to complement on the earlier safety section rather than replicate it, and is important for detecting rare adverse outcomes that might occur in the long term. Where these complementary data are from non-comparative sources, an overall comparative conclusion should be drawn.

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158 – 172 and Guyatt et al. (2013). GRADE guidelines: 13. Preparing Summary of Findings tables and evidence profiles – continuous outcomes. *Journal of Clinical Epidemiology* 66, 173 – 183.

B.8. INTERPRETATION OF THE CLINICAL EVIDENCE

It is important to classify the therapeutic profile of the proposed therapeutic medical service in relation to its main comparator (i.e. whether it is therapeutically superior, inferior or equivalent to the comparator).

On the basis of the evidence profile (summarised in Table 14), **it is suggested that, relative to the comparator, the intervention has superior/non-inferior/uncertain/inferior safety and superior/non-inferior/uncertain/inferior effectiveness.**

You might like to discuss here how you came to the conclusions above.

The table below is based on the GRADE evidence profile, with a couple of minor modifications. GRADE recommends incorporating 7 or fewer of the most important patient-relevant outcomes (desirable and undesirable), to provide a succinct, easily digestible presentation of the confidence in effect estimates (quality of evidence) and magnitude of effects. If no evidence is identified on critical outcomes, these could also be listed in the table.

Where a meta-analysis is not able to be done to arrive at a summary estimate of effect for each critical patient relevant outcome, it is suggested that the results from one or more of the better quality studies is presented and that the range of effects in these studies, with/without calculation of a median effect, is provided.

Please consult the paper by Guyatt et al 2013 (see reference list - the paper is freely available) for information on how to interpret findings. Please note, though, that the overall confidence in effect estimates rating across outcomes (ie which would relate to the overall clinical claim in this instance) is usually based on the critical outcome that provides the lowest confidence in the effect estimates.

The table below is one example of how a summary of findings table may look, but it may be adapted to suit the evidence. The things to include are: 1) a list of all important outcomes, both desirable and undesirable; 2) a measure of the typical burden of these outcomes (e.g. control group, estimated risk); 3) a measure of the risk in the intervention group or, alternatively or in addition, a measure of the difference between risks with and without intervention; 4) the relative magnitude of effect; 5) the number of participants and studies addressing these outcomes; 6) a rating of the overall confidence in effect estimates for each outcome (which may vary by outcome); and possibly; 7) comments. The summary of findings table is a simplified version of the evidence profile table, which is located in Appendix D.

Table 14   Balance of clinical benefits and harms of intervention, relative to comparator, and as measured by the critical patient-relevant outcomes in the key studies

Outcomes (units) Follow-up	Participants (studies)	Quality of evidence (GRADE)	Relative effect (95%CI)	Risk with control	Risk or risk difference with intervention	<Comments>

[a] GRADE Working Group grades of evidence (Guyatt et al., 2013)

⊕⊕⊕⊕ **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.

SECTION C   TRANSLATION ISSUES

Where **consistency, indirectness** of outcome measures (i.e. surrogate outcomes)**, indirectness** of setting or target population (**applicability**) **or other considerations have impacted on the confidence in the estimates (ie very low to moderate quality)** in Table 14**Error! Reference source not found.** above, please indicate in Section C below how the data are translated for use in the economic model (if an economic model is produced).

For example, if **consistency** was poor (eg high heterogeneity in a meta-analysis), a subgroup analysis may be undertaken or referred to in Section C and then modelled in Section D. According to the *MSAC Therapeutics Guidelines*, this would be classified as an Applicability Translation Issue. Example tables and approaches are suggested in the *Guidelines*.

If the **directness** (applicability) of the evidence to the target Australian population is poor, because the people participating in the studies (in the evidence base) were different, then Section C may require a description of the baseline risk in the Australian population which - in the model - can then be multiplied by the relative treatment effects reported in the evidence base. This is also classified as an Applicability Translation Issue in the *MSAC Therapeutic Guidelines*. If, however, the generalisability of the evidence to the Australian population is poor because the trial follow-up was not representative of the use of the intervention in practice (ie an "**other consideration**"), then this is an Extrapolation Translation Issue according to the *MSAC Therapeutic Guidelines*.

If the **directness** (applicability) of the evidence is poor in terms of the healthcare context, then Section C would need to provide a list and unit costs of the healthcare resource usage likely in the Australian setting. This is an Applicability Translation Issue according to the *MSAC Therapeutic Guidelines*.

If the outcomes used are **indirect** (eg the use of surrogate or intermediate outcomes) then this will require translation for use in the economic model eg transformation of the surrogate or intermediate outcomes in order to estimate clinically relevant outcomes such as QALYs. This would be a Transformation Issue according to the *MSAC Therapeutic Guidelines*.

Briefly indicate the key translation issues and pre-modelling studies that are used to adapt the evidence presented in Section B for the purposes of the economic evaluation (eg the model that predicts the cost-effectiveness if the new intervention is used according to the proposed MBS item descriptor). Please read Section C of the *MSAC Therapeutic Guidelines* for guidance on how to address each type of translation issue.

If translation of the clinical evidence is not needed or not undertaken, please state this.

C.1. OVERVIEW

Provide an overview of the model to be used in Section D, and explain where the evidence in Section B needs to be translated in order to fit the model.

C.2. APPLICABILITY TRANSLATION ISSUES

Define application issues: Describe any ways in which the participants and circumstances of use in the studies presented in Section B differ from the proposed population for treatment (including the baseline risk of participants and circumstances of use).

Present and justify a focused analytical plan (which specifies details of data, sources, methods and analyses) to address each applicability issue identified. Convert each defined applicability issue into a succinct question that can be addressed in a pre-modelling study.

Present the results of each pre-modelling study undertaken to address each applicability issue specified. Estimate the comparative treatment effect as results for the proposed investigative medical service; its main comparator; and the increment with its 95% confidence interval.

Discuss the results of each pre-modelling study and explain how they will be used in the economic evaluation (Section D).

C.3. EXTRAPOLATION TRANSLATION ISSUES

Define extrapolation issues: State whether there is a need to extrapolate the outcomes reported in the clinical evaluation beyond the study horizon.

Present and justify a focused analytical plan (which specifies details of data, sources, methods and analyses) to address each extrapolation issue identified. Convert each defined extrapolation issue into a succinct question that can be addressed in a pre-modelling study.

Present the results of each pre-modelling study undertaken to address each extrapolation issue specified. Estimate the comparative treatment effect as results for the proposed investigative medical service; its main comparator; and the increment with its 95% confidence interval.

Discuss the results of each pre-modelling study and explain how they will be used in the economic evaluation (Section D).

C.4.   TRANSFORMATION ISSUES

Define transformation issues: State whether there is a need to transform the nature of the outcomes measured in the clinical evaluation (i.e. taking a surrogate or intermediate endpoint, and transforming it to a QALY or equivalent).

Present and justify a focused analytical plan (which specifies details of data, sources, methods and analyses) to address each transformation issue identified. Convert each defined transformation issue into a succinct question that can be addressed in a pre-modelling study.

Present the results of each pre-modelling study undertaken to address each transformation issue specified. Estimate the comparative treatment effect as results for the proposed investigative medical service; its main comparator; and the increment with its 95% confidence interval.

Discuss the results of each pre-modelling study and explain how they will be used in the economic evaluation (Section D).

C.5.   ANY OTHER TRANSLATION ISSUES

Define any other translation issues: State whether there is any other need to translate from the clinical evaluation.

Present and justify a focused analytical plan (which specifies details of data, sources, methods and analyses) to address each translation issue identified. Convert each defined translation issue into a succinct question that can be addressed in a pre-modelling study.

Present the results of each pre-modelling study undertaken to address each translation issue specified. Estimate the comparative treatment effect as results for the proposed investigative medical service; its main comparator; and the increment with its 95% confidence interval.

Discuss the results of each pre-modelling study and explain how they will be used in the economic evaluation (Section D).

C.6.   RELATIONSHIP OF EACH PRE-MODELLING STUDY TO THE ECONOMIC EVALUATION

Provide a summary from Sub-section C2, C3, C4 and C5 and their uses in response to Section D.

Table 15   Example of summary of results of pre-modelling studies and their uses in the economic evaluation

Section	Pre-modelling study	Results used in Section D	Cross-reference	Results used in Subsection D.6	Cross-reference
Applicability					
	Study 1				
	Study 2				
Extrapolation					
	Study 3				
Transformation					
	Study 4				
Other					
	Study 5				

SECTION D ECONOMIC EVALUATION

D.1. OVERVIEW

The clinical evaluation suggested that, relative to the comparator, the intervention has superior/non-inferior/uncertain/inferior safety and superior/non-inferior/uncertain/inferior effectiveness based on the evidence profile given in Table 14. Table 16 sets out the framework that was used to classify the clinical evidence in Section B so that a decision could be made about the type of economic analysis to undertake (if any) in this Section.

Table 16 **Classification of the comparative effectiveness and safety of the proposed therapeutic medical service compared with its main comparator and guide to the suitable type of economic evaluation**

Comparative safety	Comparative effectiveness			
	Inferior	Uncertain[a]	Non-inferior[b]	Superior
Inferior	Health forgone: need other supportive factors	Health forgone possible: need other supportive factors	Health forgone: need other supportive factors	? Likely CUA
Uncertain[a]	Health forgone possible: need other supportive factors	?	?	? Likely CEA/CUA
Non-inferior[b]	Health forgone: need other supportive factors	?	CMA	CEA/CUA
Superior	? Likely CUA	? Likely CEA/CUA	CEA/CUA	CEA/CUA

CEA=cost-effectiveness analysis; CMA=cost-minimisation analysis; CUA=cost-utility analysis

? = reflect uncertainties and any identified health trade-offs in the economic evaluation, as a minimum in a cost-consequences analysis

[a] 'Uncertainty' covers concepts such as inadequate minimisation of important sources of bias, lack of statistical significance in an underpowered trial, detecting clinically unimportant therapeutic differences, inconsistent results across trials, and trade-offs within the comparative effectiveness and/or the comparative safety considerations

[b] An adequate assessment of 'non-inferiority' is the preferred basis for demonstrating equivalence

It was therefore decided that a XXXX analysis would be undertaken for the economic evaluation.

An economic evaluation should be presented in all assessment reports to be considered by MSAC except when a service is indisputably demonstrated to be associated with net clinical harms to patients (as it is unlikely that MSAC will recommend government subsidy of the service).

State whether the base case of the economic evaluation is generated by:

- a trial-based economic evaluation (i.e. based on randomised controlled trials presented in section B)

- a stepped economic evaluation (i.e. derived from randomised controlled trials presented in Section B using variables reported in Section C of the assessment report)

- a modelled economic evaluation based on an indirect comparison of randomised trials or non-randomised studies.

D.2. POPULATIONS AND SETTINGS

Describe and justify the demographic and patient characteristics of the population included in the economic evaluation.

Describe and justify the circumstances in which the proposed medical service and main comparator are used in the economic evaluation.

Assess the consistency of the demographic and patient characteristics and of the specified circumstances of use across the study populations, the population in the economic evaluation and the population for whom listing is sought.

D.3. STRUCTURE AND RATIONALE OF THE ECONOMIC EVALUATION

A summary of the key characteristics of the economic evaluation is given in Table 17.

Table 17   Summary of the economic evaluation

Perspective	
Comparator	
Type of economic evaluation	e.g. cost-effectiveness, cost-utility, cost-minimisation, cost-consequences.
Sources of evidence	e.g. Systematic review
Time horizon	e.g X years in the model base case
Outcomes	e.g. Name or list the outcome/s used in the model eg. LYG and QALYs
Methods used to generate results	e.g. trial-based, cohort expected value analysis, Markov model
<Health states>	Only put in this row, if it is relevant to your model
<Cycle length>	Only put in this row, if it is relevant to your model
Discount rate	
Software packages used	

See Table D.3.1 in the *MSAC Therapeutic Guidelines*.

LITERATURE REVIEW

A search of the literature should be conducted for published cost-effectiveness analyses of the proposed service.

STRUCTURE OF THE ECONOMIC EVALUATION

Specify the name and version of any software package used to conduct the economic evaluation.

The description of the economic evaluation should include:

• a statement defining in detail the therapy options for which costs and outcomes are estimated in the economic evaluation

• a description of each of the types of event and health states possible in the economic evaluation, together with a justification of the selection of each health state for inclusion in the evaluation and a justification for those that were considered potentially suitable but that were excluded to avoid excessive complexity (if relevant)

• a description of the relationships and interactions between the various events and health states possible in the economic evaluation (including, where relevant for a state transition model, a detailed description of all possible transitions between the health states)

• a description of all assumptions made in the construction of the economic evaluation

• a decision tree diagram summarising the structure of the economic evaluation

The structure of the economic evaluation is shown in Figure 3.

If you are writing a **contracted assessment** you will need to save the decision analytic or state transition diagram as a picture file (TIFF) and copy and paste in, so that web accessibility requirements are met.

Figure 3   Decision analytic structure of the economic evaluation.

Assumptions incorporated into the model structure:

Justify the economic evaluation characteristics summarised in Table 17

D.4. INPUTS TO THE ECONOMIC EVALUATION

• Present, as a minimum, the following information for each variable used in the economic evaluation:

  – name (and definition, as necessary)

  – quantity in natural units (as appropriate; for example, this is not applicable for unit costs)

  – source.

• Identify and list the direct health care resource items for which there would be a change in use associated with substituting the proposed medical service for the main comparator and define each in terms of natural units.

• Estimate the present value of direct health care resource costs and health outcomes.

• Discuss the implications for the economic evaluation of any important deficiencies in the available evidence base.

• Summarise this information in a table for each type of variable and provide further details of calculations, as necessary.

D.5. RESULTS OF THE ECONOMIC EVALUATION

• Present the cost per patient per course if the proposed medical service is for acute or self-limited therapy, or the cost per patient per year if the proposed medical service is for chronic or continuing therapy.

• Present the remaining results of the economic evaluation first in a disaggregated form, then in increasingly aggregated forms. Use discounting as appropriate.

• Present the appropriately aggregated and discounted results separately for outcomes and costs, and separately for the proposed medical service and its main comparator.

- Present separate estimates of the incremental cost and the incremental effectiveness of substituting the proposed medical service for the main comparator.

- For cost-effectiveness and cost-utility analyses, present the incremental cost-effectiveness ratio as the incremental cost of achieving each extra unit of outcome with the proposed medical service substituted for the main comparator (the base case of the economic evaluation).

- Draw a conclusion from the base-case economic evaluation that reflects the degree of uncertainty around the presented incremental cost-effectiveness ratios.

Two different formats for presenting the findings of the economic evaluation are provided below. Choose which of these is appropriate for the evaluation that has been undertaken. Please delete the inappropriate one and/or incorporate additional summary information, as required.

<INCREMENTAL COSTS AND EFFECTIVENESS

The overall costs and outcomes, and incremental costs and outcomes as calculated for the intervention and comparator in the model, with the base case assumptions, are shown in the table below.

Table 18   Title

	Cost	Incremental cost	Effectiveness (QALYs)	Incremental effectiveness	ICER
Intervention					
Comparator					

ICER = Incremental Cost Effectiveness Ratio>

<STEPPED ECONOMIC EVALUATION

The results of a stepped analysis of the base case economic evaluation are given in the tables below.

<Table 19   Implications for the base case economic evaluation of applying the results of the clinical evaluation (Step 1 then Step 2)

Population and circumstances of use	As defined in trial(s) using ITT population	As defined by the requested restriction[a]
Costs		
Costs of therapy involving the proposed medical service	(Trial-based)	(Trial-based)[b]

Population and circumstances of use	As defined in trial(s) using ITT population	As defined by the requested restriction[a]
Costs of therapy involving the main comparator	(Trial-based)	(Trial-based)[b]
Incremental costs	(Trial-based)	(Trial-based)[b]
For each trial-based outcome relied on in the economic evaluation before any extrapolation and/or transformation		
Extent of outcomes with the proposed medical service		
Extent of outcomes with the main comparator		
Incremental effectiveness (with 95% CI)	(From Subsection B.6)	(From Subsection C.4)
ICER (cost/XXX)	**XXX** **(Step 1)**	**XXX** **(Step 2)**

CI=confidence interval; ICER=incremental cost-effectiveness ratio; ITT=intention to treat >

[a] If there is no need to apply the results of the clinical evaluation, the data in this column should be identical to the data in the adjacent column reporting the incremental impacts using the results for the study/trial's ITT population.

[b] Justify any variation in estimate of incremental costs from the trial-based costing.

Subsections refer to the *MSAC Therapeutic Guidelines*.

<Table 20 **Implications for the base case economic evaluation of extrapolating and transforming the results of the clinical evaluation (Step 3)**

	Incremental costs	Incremental effectiveness	Incremental cost-effectiveness
For each trial-based outcome relied on in the economic evaluation without further modification	(From corresponding row of Step 2 in Table ES.5)	(From corresponding row of Step 2 in Table ES.5)	(From corresponding row of Step 2 in Table ES.5)
For any trial-based outcome relied on in the economic evaluation *with any **extrapolation** from the time horizon of the trial(s) **only***	(Based on corresponding extrapolation of duration of treatment, if any)	(From Subsection C.4 if extrapolation is required)	**(Alternative Step 3a)**
For any important outcome *generated for or by the economic evaluation* from the trial-based outcome(s) ('***transformation of nature of outcome*** *only*)	(Include here any modelled increases in the provision of some resources and any modelled offsetting decreases of others)	(From Subsection C.4 if possible, or if this approach is used, explain why a presentation here is not possible)	**(Alternative Step 3a)**
For the final outcome relied on in the economic evaluation *generated as a valuation of the trial-based outcome(s)* ('***value transformation*** *only*)	(Should not change from Step 2 because nature of outcome does not change)	(From Subsection C.4 if possible, or if this approach is used, explain why a presentation here is not possible)	**(Alternative Step 3a)**
For the final outcome relied on in the economic evaluation ***combining*** *any* **extrapolation** *from the time horizon of the trial(s)* **with** *any* **transformation** *of the trial-based outcome(s)*			**(Completed Step 3 and expected base case)** **XXX** **(Step 3)**

>

Subsections refer to the *MSAC Therapeutic Guidelines*.

D.6.   SENSITIVITY ANALYSES

• Present univariate (one-way) sensitivity analyses on all variables using plausible extremes of values, and justify the selection of those extreme values.

• Tabulate all univariate sensitivity analyses alongside the base case.

• Present multivariate sensitivity analyses combining variables shown to be sensitive in the univariate analyses.

• Examine and present the sensitivity of the results of the economic analysis to any changes in assumptions concerning the structure of the modelled economic evaluation that are important but uncertain

The modelled results were most sensitive to >

Table 21   Key drivers of the economic model

Description	Method/Value	Impact
e.g. Time horizon	25 years; assumed from 6 month trial duration	High, favours intervention
e.g. Upper 95% CL of the difference in outcomes	$100,000/QALY	High; favours comparator
etc		

SECTION E   FINANCIAL IMPLICATIONS

E.1.   JUSTIFICATION OF THE SELECTION OF SOURCES OF DATA

Where data are available (published or unpublished) from one or more types of data sources:

– summarise the methods used to obtain the data

– present the relevant main results

– interpret the findings

– discuss the limitations (including the representativeness of the results) and biases of the method adopted.

Where data are obtained via one or more studies commissioned for the assessment report:

– describe the gap in the information to be addressed by the commissioned analysis

– summarise the methods used to obtain and analyse the data

– present the relevant main results

– interpret the findings

– discuss the limitations (including the representativeness of the results) and biases of the method adopted.

<An epidemiological approach has been used to estimate the financial implications of the introduction of XXX.>

E.2.   USE AND COSTS OF XXX

Estimate the number of patients with the medical condition targeted by the proposed medical service, the number who would be eligible for the requested restriction and the number of patients likely to use the proposed medical service.

Estimate the number of times the proposed medical service is delivered in each year over five years (disaggregated into proportions for MBS-funding, and by beneficiary type).

Estimate the costs for each form of the proposed medical service in each year over five years.

Aggregate these cost calculations for the proposed medical service overall in each year over five years.

E.3. CHANGES IN USE AND COST OF OTHER MEDICAL SERVICES

Identify the other MBS-funded medical services that are likely to be affected by listing the proposed medical service.

For each proposed medical service, estimate the extent of change in the number of times the proposed medical service is delivered each year over five years (disaggregated into proportions for the MBS and by beneficiary type).

Aggregate both these cost calculations for the other affected medical services in each year over five years.

E.4. FINANCIAL IMPLICATIONS FOR THE MBS

Estimate the net financial implications for the MBS in each year over five years by subtracting the net cost offsets for both the aggregated estimates calculated in Subsection E.3 from the corresponding estimates calculated in Subsection E.2.

The financial implications to the MBS resulting from the proposed listing of XXX are summarised in Table 22.

Table 22   Total costs to the MBS associated with XXX

	2015-16	2016-17	2017-18	2018-19	2019-20
Intervention					
Number of services					
Sub-total cost					
<Any co-administered services currently MBS listed>					
Number of services					
Sub-total cost					
Total services					
Total cost					

This section should primarily focus on the financial implications in terms of MBS rebates. If a service is primarily out-of-hospital, then there will need to be a separate analysis of the financial

implications to the safety net. The ratio of in-hospital vs out-of-hospital needs to be determined and the 75% vs 85% rebate (or if a GP service, 100% rebate), respectively, proportionately assigned in the costing. The Department is interested in the rebate as the input cost, not the schedule fee.

E.5.   FINANCIAL IMPLICATIONS FOR GOVERNMENT HEALTH BUDGETS

Implementing an MSAC recommendation might have financial implications for other parts of the Australian Government's health budget. It might also have implications for state and territory Government health budgets, including public hospitals.

THE BROADER IMPACT ON THE MBS

The MBS includes a number of elements that are not expected to be estimated. This includes the cost of safety nets and incentives. Where possible, additional information should be provided that will allow the Department to assess these factors.

OTHER GOVERNMENT IMPACTS

Other Australian Government agencies are typically impacted by the implementation of new and amended medical services.

If relevant, estimate the extent of the net change in the number of PBS prescriptions processed by Medicare Australia for payment (and, where appropriate, the net change in the number of authorisations by Medicare Australia) in each year over five years.

STATE AND TERRITORY GOVERNMENT HEALTH BUDGETS

Identify and justify any financial implications for state and territory Government health budgets, such as for public hospitals (including inpatient admissions, emergency department visits and outpatient clinic visits). In presenting the calculations, follow the approach taken above to estimate first the numbers, in their natural units, of the disaggregated resources provided or freed.

There is controversy about valuing freed hospital resources in Government health budgets because, in the Australian public hospital system, the freed resources are typically redeployed to improve the health of the next available patient rather than being realised as financial cost reductions.

Provide further justification to support any claim for financial cost offsets from any reduction in the need to provide a public hospital resource. For example, provide a basis for concluding that the expected change is large enough that a resulting change in the provision of the resource would become a viable option for hospital management or other appropriate decision makers.

Another option could be to exclude the fixed costs from the marginal costs of the identified hospital resource type (the opportunity cost value used in assessment report section D is the full average cost of each resource, which represents its maximum value assuming an infinite time horizon to manage health care resources). Apply the justified unit cost to each type of resource to estimate the net financial implications for each type, and aggregate the newly identified financial implications in each year over five years.

E.6. IDENTIFICATION, ESTIMATION AND REDUCTION OF UNCERTAINTY

• In each step of the calculations, assess the sources of uncertainty and distinguish the type and degree of uncertainty in utilisation and financial estimates.

• Where possible, explain the nature of each uncertainty and its impact on the overall estimates.

• Estimate the level of the uncertainly and propose ways to reduce it.

E.4 and E.6 may be integrated, as needed, so the sensitivity analyses are presented immediately after the base calculations estimated in E.4.

SECTION F   OTHER RELEVANT CONSIDERATIONS

This section is reserved for content relating to changes in the organisation of care, social/ethical/legal considerations, specific policy considerations, impact on consumers/patients, access/equity considerations, training/workforce considerations, risk share arrangements etc.

Discussion of key trials that are ongoing and due to report results shortly could also be discussed here.

The content of this section is topic-specific; it is, therefore, optional.

<Appendix A   Clinical Experts and Assessment Group

This Appendix is only relevant for contracted assessments. Delete for submission-based assessments and re-label the subsequent Appendices.

<HEALTH EXPERT STANDING PANEL (HESP) (IF ALLOCATED)

Member   Expertise or affiliation

<CLINICAL EXPERT

Name   Expertise

ASSESSMENT GROUP

XXXX

Name   Position

Noted conflicts of interest

There were no conflicts of interest.>

APPENDIX B   SEARCH STRATEGIES

BIBLIOGRAPHIC DATABASES

Electronic database	Time period searched
Embase Note – Embase.com and the previous 12 months of PubMed would be more comprehensive as Embase.com includes both Embase and Medline entries and PubMed includes unindexed (pre-Medline) entries	
Medline	
The Cochrane Library (CDSR, Central, DARE, HTA, HEED)	

Add rows if needed

ADDITIONAL SOURCES OF LITERATURE (INCLUDING WEBSITES)

Source	Location
Australian Clinical Trials Registry	
National Institutes of Health	

Add rows if needed

APPENDIX C STUDIES INCLUDED IN THE SYSTEMATIC REVIEW

Profiles of studies on XXXX included in the systematic literature review

Authors Study ID Publication Year	Study design/ duration	Level of evidence[a] and risk of bias assessment[b]	Location Setting Length of follow-up	Study population characteristics Eg N, age, gender, co-morbidities, disease description and severity, baseline function	Description of Intervention <including duration of treatment>	Description of Comparator <including duration of treatment>	Relevant outcomes assessed (ie related to outcomes specified in PICO)	Measurement of outcomes and methods of analysis

<study design characteristics such as CC=case control; Coh=cohort; CS=case series; DB=double blind; MC=multi-centre; NR=non-randomised; OL=open label (unblinded); R=randomised; SB=single blind; X=cross-sectional etc>

[a] source: see NHMRC hierarchy of evidence http://www.biomedcentral.com/1471-2288/9/34; [b] risk of bias as it relates to primary outcomes of the systematic review

APPENDIX D   EVIDENCE PROFILE TABLES

In order to follow GRADE methodology, the full evidence profile tables should be included (with footnotes), per comparison, including all the critical and important outcomes. If no evidence for critical outcomes were identified, a row in the table could be included with a comment that no data were found. Two examples of how an evidence profile table may be formatted are shown below in Table 23 and Table 24 (choose the most appropriate and amend as required). These data are condensed into a 'Summary of findings' table, to be included in the main body of the report.

Table 23   Evidence profile table example 1 for intervention compared to comparator for population

Outcome (units, follow-up)	No. of studies and study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (e.g. publication bias)	No. of patients in intervention arm	No. of patients in comparator arm	Relative effect (95%CI)	Absolute effect (95%CI)	Quality	Importance
e.g. Outcome 1 (6 months)												
Outcome 1 (12 months)												
Outcome 2												

Table 24   Evidence profile table example 2 for ==intervention== compared to ==comparator== for ==population==

Outcome (units, follow-up)	No. of participants, No. of studies and study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (e.g. publication bias)	Quality	Study events rates (%) Risk with ==comparator==	Study events rates (%) Risk with ==intervention==	Relative effect (95%CI)	Anticipated absolute risk with ==comparator==	Anticipated absolute risk with ==intervention==
e.g. Outcome 1 (6 months)	e.g. n=215 k=3 RCTs											

APPENDIX E   EXCLUDED STUDIES

Please restrict this list to studies that may potentially be considered eligible for inclusion based on the PICO criteria, but are subsequently excluded (i.e. due to containing duplicate information, in another language and not being a higher level of evidence than available in English, being unable to extract the data etc).

REFERENCES

Guyatt, G, Oxman, AD, Sultan, S, Brozek, J, Glasziou, P, Alonso-Coello, P, Atkins, D, Kunz, R, Montori, V, Jaeschke, R, Rind, D, Dahm, P, Akl, EA, Meerpohl, J, Vist, G, Berliner, E, Norris, S, Falck-Ytter, Y & Schunemann, HJ 2013, 'GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes', *J Clin Epidemiol*, vol. 66, no. 2, Feb, pp. 151-157.