Australian Government
National Health and Medical Research Council

NHMRC

Using a GRADE Evidence to Decision framework for *Health Coverage* decisions

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Prepared by NHMRC for the Department of Health and Aged Care

Purpose

The purpose of this document is:

(1) To provide the Department of Health and Aged Care (the Department) with an overview of the GRADE[1] Evidence to Decision frameworks utilised by National Health and Medical Research Council (NHMRC) when considering and providing judgement on evidence-based decisions and recommendations.
(2) To inform the Department about how an evidence to decision framework could be adopted alongside the NHMRC commissioned evidence evaluations, to inform decisions for the Natural Therapies Review[2].

Background

What is GRADE and why use a GRADE Evidence to Decision framework?

GRADE is an internationally recognised framework used to assess the certainty of evidence (in systematic reviews) and develop recommendations or decisions in guidelines or decisions based on evidence[1]. The aim of GRADE is to improve transparency and consistency in reporting and decision making. GRADE is recommended by NHMRC for development of evidence-based products, such as guidelines. GRADE is used by the Australian Technical Advisory Group on Immunisation (ATAGI) to develop recommendations for the Australian Immunisation Handbook[3]. **Figure 1** (below) provides an overview of the GRADE Evidence to Decision approach for coverage decisions.

For the Natural Therapies Review, independent evidence reviewers, commissioned by NHMRC, are using GRADE to assess certainty of evidence for each of the 16 natural therapy's evidence evaluation reports.

Research in many fields has shown that there are key aspects of the way studies are designed, run and analysed which affect how certain a reviewer can be that the results reported in studies are accurate. The GRADE process to assess certainty of evidence (see **figure 1**, '*Rate certainty of evidence*') formalises which aspects of the methods and results of studies to look at. Certainty of evidence is sometimes also referred to as the quality or strength of the evidence. A rating of

[1] GRADE: *Grading of Recommendations, Assessment, Development and Evaluation.* Detailed information about GRADE is available at www.gradeworkinggroup.org

[2] Department of Health and Aged Care: Natural Therapies Review 2019-20. Available at: https://www.health.gov.au/health-topics/private-health-insurance/private-health-insurance-reforms/natural-therapies-review-2019-20

[3] Development of the Immunisation Handbook https://immunisationhandbook.health.gov.au/contents/about-the-handbook/development-of-the-handbook

Example evidence to decision processes for Influenza are available at https://www.ncirs.org.au/our-work/australian-immunisation-handbook/influenza-grade-assessments

certainty is given for each critical or important outcome, describing it as high, moderate, low or very low certainty.

- **High certainty** – means the authors have a lot of confidence that the true effect is like the estimated effect
- **Moderate certainty** – means that the true effect is probably close to the estimated effect
- **Low certainty** – means the true effect might be markedly different from the estimated effect
- **Very low certainty** - means the true effect is probably markedly different from the estimated effect.

For more information about assessing the certainty of evidence using GRADE, refer to NHMRC's Guidelines for Guidelines module '*Assessing certainty of evidence'* at: https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence.

In addition to assessing the certainty of evidence of outcomes across studies, GRADE has developed a series of evidence to decision frameworks to help decision makers consider additional factors, alongside the GRADE assessment of certainty of evidence, to inform decisions.

Evidence to decision frameworks (see **table 1** below) provide a list of questions for decision makers to work through to reach a recommendation or decision and record the steps to reach it, which include:

- assessing the evidence for benefits and harms (desirable and undesirable effects)
- assessing how confident (or certain) a decision maker can be that the reported effects in the evidence are correct (overall certainty of the evidence)
- the resources which would be needed to implement a decision
- the acceptability of the decision to users
- the equity and feasibility of the proposed decision.

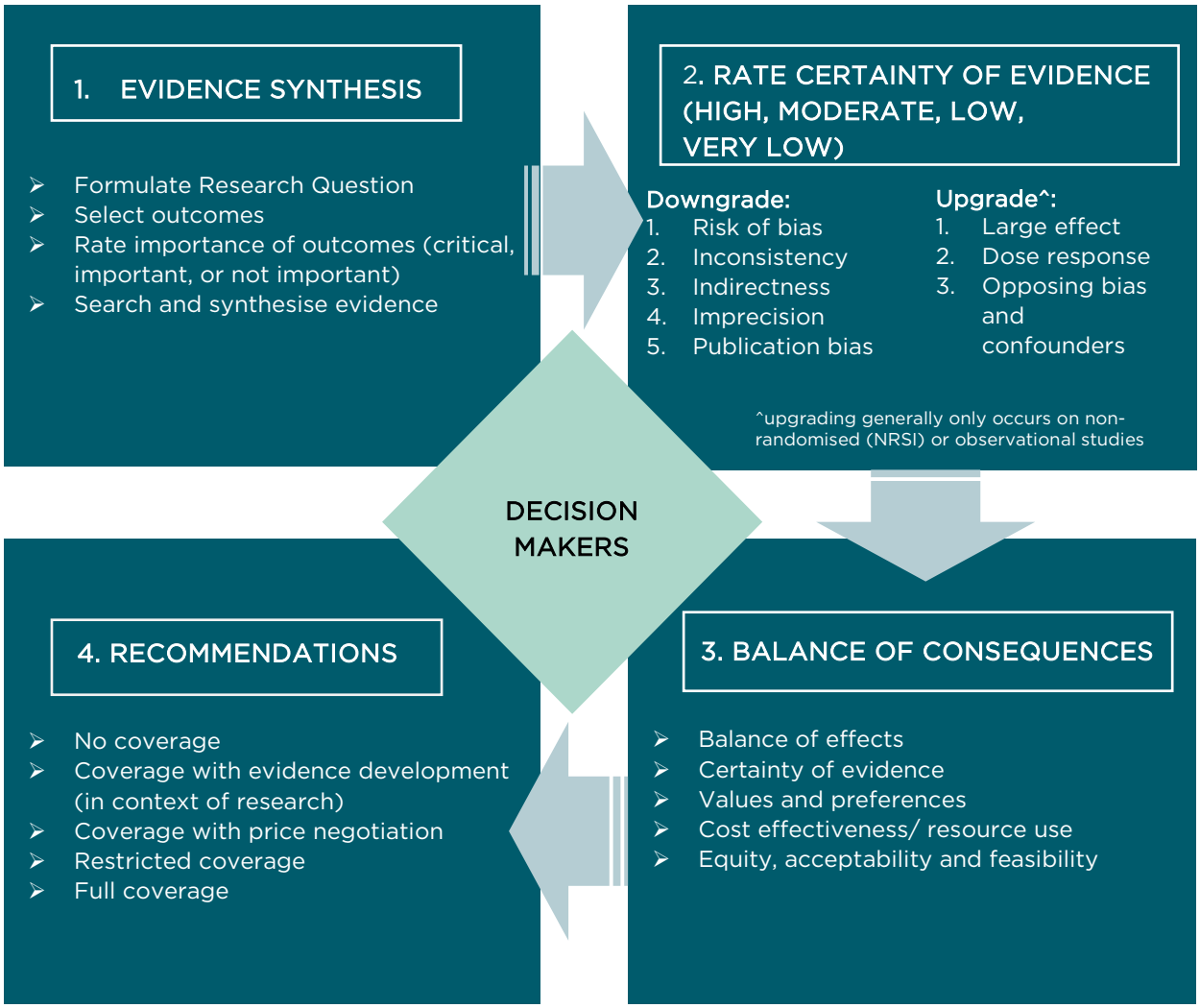
Considering factors outside of the evidence evaluation reports - GRADE Evidence to Decision framework

Decisions about health policy, or public health/clinical recommendations should be informed by evidence. However, translating evidence reports (such as systematic reviews) into decisions can be a complex task, requiring careful consideration of the impact decisions have on the people they affect (for example health professionals, the public and policy makers). The best available evidence for making decisions or recommendations may be low or even very low certainty/quality/strength. Irrespective of the level of certainty of the evidence, decisions and/or recommendations need to be made. Evidence to decision frameworks can help facilitate the decision-making process and are widely used to help structure discussion, ensure that important aspects of decisions or recommendations are not missed and to record outcomes of discussions in a transparent way.

The GRADE Evidence to Decision ***Coverage*** framework is designed to be applied to decisions about how much to pay for health services or technologies (e.g. private health insurance rebates).

Table 1 outlines the evidence to decision framework questions for deciding whether (or not) to recommend coverage of an option.

Figure 1. Overview of the GRADE Evidence to Decision approach[4]



[4] Image adapted from: Muhammad, Rafiq & Boccia, Stefania (2018) at https://pubmed.ncbi.nlm.nih.gov/29410601/

Applying the GRADE Evidence to Decision Coverage framework

The overall 'problem' to be addressed by an evidence to decision framework for the Natural Therapies Review is whether any, some or all the 16 natural therapies excluded from Private Health Insurance rebates on 1 April 2019, should be reincluded as eligible for Private Health Insurance rebates.

If an evidence to decision framework is employed, the decision makers would first need to consider whether:

(1) each individual natural therapy would require an individual decision-making process (i.e. an evidence to decision framework applied to each unique review)
(2) decisions would be made on therapies grouped according to mechanism of action (i.e. manual therapies grouped, physical/exercise therapies grouped)
(3) the evidence evaluations for the 16 therapies are to be considered together, making one recommendation about all 16 therapies at once
(4) coverage eligibility is restricted to certain groups or conditions (e.g. Pilates restricted to private health insurance for low back pain).

Table 1 outlines the series of questions related to the GRADE Evidence to Decision for coverage decisions. The Department commissioned NHMRC to review 16 Natural Therapies. The evidence evaluations will help address questions about *desirable effects*, *undesirable effects* and *certainty of evidence*. Additional factors, not addressed by the commissioned evidence evaluations, may also be included in the balance of effects. For example, assessing the harms or adverse effects, cost-effectiveness or benefits of therapies, all of which were out of scope for the evidence evaluations commissioned to NHMRC.

Questions not addressed by the commissioned evidence evaluation reports can be considered in various ways by decision makers, as part of the GRADE Evidence to Decision framework. An outline of information assessed at each question is summarised in **Table** 1.

In GRADE the terms "intervention" and "option" are used interchangeably, but "intervention" usually refers to something specific (e.g. therapy) being assessed, whereas "option" is often used to describe recommendations. Thus, each systematic review commissioned by NHMRC assesses the intervention. The questions in **Table 1** relate to coverage decisions, so use the term "options."

Useful resource:

A worked example of an Evidence to Decision Framework for a coverage decision on *Opportunistic Prostate Cancer Screening* is provided at **Attachment A**. Examples using an online tool for evidence to decision are available at: https://ietd.epistemonikos.org/#/login 'Explore an Example'.

Table 1. CRITERIA FOR GRADE EVIDENCE TO DECISION FRAMEWORK - COVERAGE DECISIONS

	BALANCE OF EFFECTS * Desirable effects * Undesirable effects	CERTAINTY OF EVIDENCE	VALUES	COST EFFECTIVNESS * Resources * Certainty of resources	EQUITY	ACCEPTABILITY	FEASIBILITY
EVIDENCE TO DECISION FRAMEWORK QUESTION	*Does the balance between desirable and undesirable effects favour the option or the comparison?*	*What is the overall certainty of the evidence of effects?*	*Is there important uncertainty about or variability in how much people value the main outcomes?*	*Does the cost effectiveness of the option favour the option or the comparison?*	*What would be the impact on health equity?*	*Is the option acceptable to key stakeholders?*	*Is the option feasible to implement?*
CONSIDERATIONS	Desirable and undesirable effects can be considered separately. The evidence evaluations commissioned from NHMRC for the Natural Therapies Review did not evaluate harms or adverse events.	Measure of how certain we can be that the evidence is correct.	Assess whether consumers, carers and other stakeholders vary in thinking the option would be good (or bad).	Assess whether the net benefit is worth the cost. Includes assessing cost and uncertainty around costs. The evidence evaluations commissioned from NHMRC for the Natural Therapies Review did not evaluate economic impacts or cost effectiveness.	Assess whether the option would increase or decrease inequality.	Acceptability to consumers, carers, healthcare providers and policy makers. Consider who benefits/is harmed and who pays/saves.	Is the option sustainable? Is there sufficient capacity to meet increased demand or should there be restrictions on cover? Can restricted cover be implemented? Are there legal, bureaucratic or ethical constraints that make it difficult (or impossible) to cover the option?
SOURCES OF EVIDENCE TO INFORM JUDGEMENTS	Systematic review of studies examining the effects of the intervention (NHMRC provided evidence, plus additional sources covering harms and adverse effects)	The overall judgement of certainty from GRADE assessment of certainty as presented in evidence evaluations.	Studies reporting direct measures, indirect measures (e.g. health related quality of life), or other ratings of importance of outcomes (surveys) and qualitative data (e.g. representative focus groups)	Economic evaluations. May require judgement of trade-offs. If there is uncertainty about cost-effectiveness compared with standard care, decision makers may delay a recommendation until evidence of cost-effectiveness is available OR cover the option with monitoring of effects and expenditures.	Evidence relating to PROGRESS -Plus* elements.	Program completion, continued use of therapies, qualitative evidence.	Policy makers or key decision makers.

* PROGRESS-plus stands for Place or residence, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Education, Socioeconomic status, Social capital, and personal, relationship or time dependent factors which may be associated with equity

Drawing conclusions and recording decisions – using the GRADE Evidence to Decision framework for coverage decisions

After making a judgement on each of the criteria described above, decision makers go on to make an overall recommendation, decision or judgement.

At each criterion there should be a rationale provided by decision makers about the judgement reached - this judgement then informs how strong a recommendation is and determines how confident decision makers are that after considering all relevant criteria, the desirable outcomes of the option outweigh the undesirable outcomes/ consequences.

For coverage decisions, the GRADE Evidence to Decision includes five options to conclude the decision-making process: (1) no coverage, (2) coverage with evidence development (in context of research), (3) coverage with price negotiation, (4) restricted coverage and (5) full coverage.

Conclusion

This document provides an overview of the GRADE Evidence to Decision framework for coverage decisions and is intended as an exemplar for decision making about the Natural Therapies Review or similar issues.

This document is also intended to provide context to the 16 natural therapies' evidence evaluation reports commissioned by NHMRC, noting that under GRADE, systematic reviews are not the only source of information used to consider and provide judgement on evidence-based decisions and recommendations.

References and Resources list

Moberg, J., Oxman, A.D., Rosenbaum, S. et al. The GRADE Evidence to Decision (EtD) framework for health system and public health decisions. Health Res Policy Sys; 2018 [cited June 2022]; 16(45). Available from: https://doi.org/10.1186/s12961-018-0320-2

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ATTACHMENT A
Worked example of Evidence to Decision for a Coverage decision

Opportunistic Prostate Cancer Screening – from Parmelli et al (2015)

Supplementary File 2: GRADE Evidence to Decision framework for a coverage decision

An interactive version of this framework that includes more subgroup information is available at: http://ietd.epistemonikos.org/#/frameworks/54cb63812b3867639eed4bff/question

GRADE DECIDE **Authors:** *E. Parmelli, L.Amato, M.Brunetti, C. Saitto*

Interactive Evidence to Decision Framework **Date:** *Jan 2015*

ASSESSMENTS

Problem

Is the problem a priority?

Judgment

☐ Don't know	☐ Varies	☐ No	☐ Probably No	x Probably Yes	☐ Yes

Research evidence

Prostate cancer is the most commonly diagnosed cancer and the third leading cause of death in men in high-income countries. Advanced age is the primary risk factor: more than 75% of all prostate cancers are diagnosed in men aged 65 years and over.

The vast majority of men with prostate cancer have no symptoms and their tumours are detected by routine testing. Lower urinary tract symptoms due to benign prostatic obstruction are common in elderly men and may result in increased concentrations of prostate specific antigen (PSA) but are not associated with an increased prostate cancer incidence. For most men prostate cancer is slow growing and does not result in clinical signs or symptoms during their lifetime.

Desirable effects

How substantial are the desirable anticipated effects?

Judgment

☐ Don't know	☐ Varies	☐ Trivial	x Small	☐ Moderate	☐ Large

Research evidence

Summary of findings: PSA screening for prostate cancer in asymptomatic men aged 50 or older

(See an interactive version here)

Outcome	Plain language summary	Absolute Effect: Without PSA	Absolute Effect: With psa	Relative effect (95% CI) N° of participants & studies	Certainty of the evidence (GRADE)
All-cause mortality	*No statistically significant difference between men randomised to screening and control groups.*	210 per 1000	210 per 1000	RR 1 (0.96 to 1.03) Based on data from 294856 Men in 4 studies	⊕⊕⊕◯ Moderate
		Difference 0 more per 1000 Men (95% CI: 1 less to 1 more per 1000 Men)			
Prostate cancer mortality	*No statistically significant difference between men randomised to screening and control groups.*	7 per 1000	7 per 1000	RR 1 (0.86 to 1.17) Based on data from 341342 Men in 5 studies	⊕⊕⊕◯ Moderate
		Difference 0 more per 1000 Men (95% CI: 1 less to 1 more per 1000 Men)			
Prostate cancer diagnosis	*Diagnosis of prostate cancer is significantly greater in men randomised to screening compared to those randomised to control.*	68 per 1000	88 per 1000	RR 1.3 (1.02 to 1.65) Based on data from 294856 Men in 4 studies	⊕⊕◯◯ Low
		Difference 20 more per 1000 Men (95% CI: 1 to 42 more per 1000 Men)			

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgment

☐ Don't know	☐ Varies	x Large	☐ Moderate	☐ Small	☐ Trivial

Research evidence

See summary of findings table above.

Certainty of the evidence

What is the overall certainty of the evidence of effects?

Judgment

☐ No included studies	☐ Very low	☐ Low	x Moderate	☐ High

Research evidence

See summary of findings table above.

Values

Is there important uncertainty about how much people value the main outcomes?

Judgment

☐ Important uncertainty	☐ Possibly important uncertainty	x Probably no important	☐ No important uncertainty

Research evidence

A 2012 study (de Bekker-Grob 2012) aimed at determining men's preferences for prostate cancer screening found that men were willing to trade-off some risk reduction of prostate cancer related death to be relieved of the burden of biopsies or unnecessary treatments. Increasing knowledge on overdiagnosis and overtreatment, especially for men with lower educational level, is warranted to prevent unrealistic expectations from screening. The study results are based on a discrete choice experiment conducted among a representative sample of 1000 men (55-75 years old).

A 2008 study (Sanda 2008) aimed at identifying determinants of health-related quality of life after primary treatment of prostate cancer and measuring the effects of such determinants on satisfaction with the outcome of treatment. They prospectively collected outcomes reported by 1201 patients and 625 spouses or partners at multiple centers before and after radical prostatectomy, brachytherapy, or external-beam radiotherapy and evaluated factors associated with changes in quality of life within study groups and determined the effects on satisfaction with the treatment outcome. Each prostate-cancer treatment was associated with a distinct pattern of change in quality-of-life domains related to urinary, sexual, bowel, and hormonal function. These changes influenced satisfaction with treatment outcomes among patients and their spouses or partners.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

Judgment

☐ Don't know	☐ Varies	x Favors the comparison	☐ Probably favors the comparison	☐ Does not favor either the intervention or the comparison	☐ Probably favors the intervention	☐ Favors the intervention

Research evidence

See table values of the main outcomes of interest, and summary of findings table above.

Resources required

How large are the resource requirements (costs)?

Judgment

☐ Don't know	☐ Varies	☐ Large costs	x Moderate costs	☐ Negligible costs or savings	☐ Moderate savings	☐ Large savings

Research evidence

Age	Total population (age range)	N° of patients	N° of PSA performed	% patients	Single cost €	Total costs €
50-59	36 781	6 302	8 754	17.1	7.41	64 867
60-69	26 975	9 058	14 631	33.6	7.41	108 416
70-79	22 461	11 133	20 275	49.6	7.41	150 238
>79	13 038	5 929	10 716	45.5	7.41	79 406
≥ 50	**99 255**	**32 422**	**54 376**	**32.7**	7.41	**434 781**

In this table both symptomatic and asymptomatic men are included.
Other possible costs related to PSA screening are: biopsies (50 € each), specialists' visits (30 € each), treatment (3000 € each), complications' treatments (200 € each).
Data are for 2013 from Roma E Italian Local Health Authorithies (population of 537,002 inhabitants).

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

Judgment

☐ No included studies	☐ Very low	☐ Low	x Moderate	☐ High

Research evidence

The data about costs derives from Local Health Authorithies database with the analysis of actual patient information.

Cost-effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

Judgment

☐ Don't know	☐ Varies	x Favors the comparison	☐ Probably favors the comparison	☐ Does not favor either the intervention or the comparison	☐ Probably favors the intervention	☐ Favors the intervention

Research evidence

Shteynshlyuger (2011) evaluated the cost-effectiveness of prostate specific antigen screening using data from the European Randomized Study of Screening for Prostate Cancer protocol extrapolated to the United States. They used Surveillance, Epidemiology and End Results (SEER) Medicare data and a nationwide sample of employer provided estimates of costs of care for patients with prostate cancer. The lifetime cost of screening with prostate specific antigen, evaluating abnormal prostate

specific antigen and treating identified prostate cancer to prevent 1 death from prostate cancer was $5,227,306 based on the European findings and extrapolated to the United States. If screening achieved a similar decrease in overall mortality as the decrease in prostate cancer specific mortality in the European study, screening would cost $262,758 per life-year saved. The study authors used a cost-effectiveness threshold of $100,000/LYS (that can be considered high), suggesting that opportunistic PSA screening for prostate cancer is not good value for money.

Shin S (2014) performed a cost-utility analysis on the adoption of PSA screening program among men aged 50-74-years in Korea from the healthcare system perspective. PSA screening was not cost-effective. Several data sources were used for the cost-utility analysis, including general health screening data, the Korean Central Cancer Registry, national insurance claims data, and cause of

mortality data from the National Statistical Office. The net benefits of PSA screening were estimated to be very low. The incremental cost effectiveness ratio (ICER) was about 94 million KRW (approximately $76,140) per QALY.

Pataky R (2014) evaluate the cost-effectiveness of PSA screening, with and without adjustment for quality of life, for the British Columbia (BC) population. They adapted an existing natural history model using BC incidence, treatment, cost and mortality patterns. The modeled mortality benefit of screening derives from a stage-shift mechanism, assuming mortality reduction consistent with the European Study of Randomized Screening for Prostate Cancer. After utility adjustment, all screening strategies resulted in a loss of quality-adjusted life years (QALYs); however, this result was very sensitive to utility estimates.

Equity

What would be the impact on health equity?

Judgment

☐ Don't know	☐ Varies	☐ Reduced	☐ Probably reduced	x Probably no impact	☐ Probably increased	☐ Increased

Research evidence

No evidence found.

Acceptability

Is the intervention acceptable to key stakeholders?

Judgment

☐ Don't know	☐ Varies	☐ No	☐ Probably No	x Probably Yes	☐ Yes

Research evidence

No evidence found.

Additional considerations

PSA screening for men over 50 is used widely in Italy. Stopping coverage might not be acceptable

- men who already had screening

- men who ask for screening because they know that it was a routine examination in the past
- men with a family history of prostate cancer

Feasibility

Is the intervention feasible to implement?

Judgment

☐ Don't know	☐ Varies	☐ No	☐ Probably No	x Probably Yes	☐ Yes

Research evidence

No evidence found.

Additional considerations

Clinicians might potentially continue to order PSA tests for asymptomatic men and provide an incorrect reason for testing or suggest that patients pay out-of-pocket.

CONCLUSIONS

Type of decision

x Do not cover	☐ Cover with evidence development	☐ Cover with price negotiation	☐ Restricted coverage	☐ Cover

Research evidence

None

Decision

Stop covering opportunistic PSA screening for asymptomatic men.

Justification

Opportunistic PSA screening in asymptomatic men aged 50 or older probably has no benefits in terms of mortality or quality of life and has a number of undesirable effects, including bleeding, bruising, short-term anxiety, and overdiagnosis and overtreatment, which can lead to erectile dysfunction and incontinence, infections, and blood loss requiring transfusion.

Detailed justification

Desirable effects: No evidence of efficacy on mortality.

Undesirable effects: Undesirable effects of PSA screening include minor and major adverse events such as bleeding, bruising, short-term anxiety, overdiagnosis and overtreatment, erectile dysfunction and incontinence, infections, blood loss requiring transfusion, pneumonia.

Restrictions

No restrictions.

Implementation considerations

Patient information should be provided and reasons for not screening should be communicated clearly to eligible men.

Monitoring and evaluation

The use of PSA screening in asymptomatic men should be monitored.