Screening for Fetal Alcohol Spectrum Disorder (FASD) in Western Australia: Policy and Practice Recommendations

Supplementary material: GRADE evidence report

JANUARY 2021

Title: Screening for Fetal Alcohol Spectrum Disorder (FASD) in Western Australia: Policy and Practice Recommendations

Using the term Aboriginal

Within Western Australia, the term Aboriginal is used in preference to Aboriginal and Torres Strait Islander, in recognition that Aboriginal people are the original inhabitants of Western Australia. Aboriginal and Torres Strait Islander may be referred to in the national context and Indigenous may be referred to in the international context. No disrespect is intended to our Torres Strait Islander colleagues and community.

Citation

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Introduction

This document includes the evidence and judgement for each recommendation used to make recommendations for the report on *Screening for FASD in Western Australia: Policy and Practice Recommendations*.

Each section, and for each recommendation, contains:

- Recommendation and remarks, which relate to the strength of the recommendation and the quality of the evidence
- An evidence-to-recommendation form, describing the judgement made by the Advisory Group and the Project Group
- An evidence profile table
- References

Commonly used abbreviations

Abbreviation	Full description
ARND	Alcohol related neurodevelopmental disorder
FAE	Fetal alcohol effects
FAS	Fetal alcohol syndrome
FASD	Fetal alcohol spectrum disorder
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ND-PAE	Neurobehavioral disorder associated with prenatal alcohol exposure
NST	Neurobehavioral Screening Test
PAE	Prenatal alcohol exposure
PFAS	Partial fetal alcohol syndrome
PICO	Patient, intervention, comparison, outcome
QUADAS-2	Quality Assessment of Diagnostic Studies-2
TREIN	Tallying Reference Errors in Narrative

Recommendation 1

Conditional recommendation against the use of the Neurobehavioral Screening Test (NST) to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The diagnostic test accuracy of the NST to identify FASD (with and without sentinel facial features) is varied.

Decision domain	Judgement	Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐ No ☒	There is low quality evidence of the diagnostic test accuracy, management effects and effects of the NST in the screening of FASD. The quality of evidence is overall low
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☒ No ☐	The potential benefits of using the NST for FASD screening include early detection of FASD and early access to management strategies. The potential harms due to false positives with the NST include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits of the NST may outweigh the potential harms.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒ No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD related mental health issues, FASD related early death, and stigma and fear.
Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐ No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 1

Question: Should the Neurobehavioral Screening Test (NST) be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The NST and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD,*[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

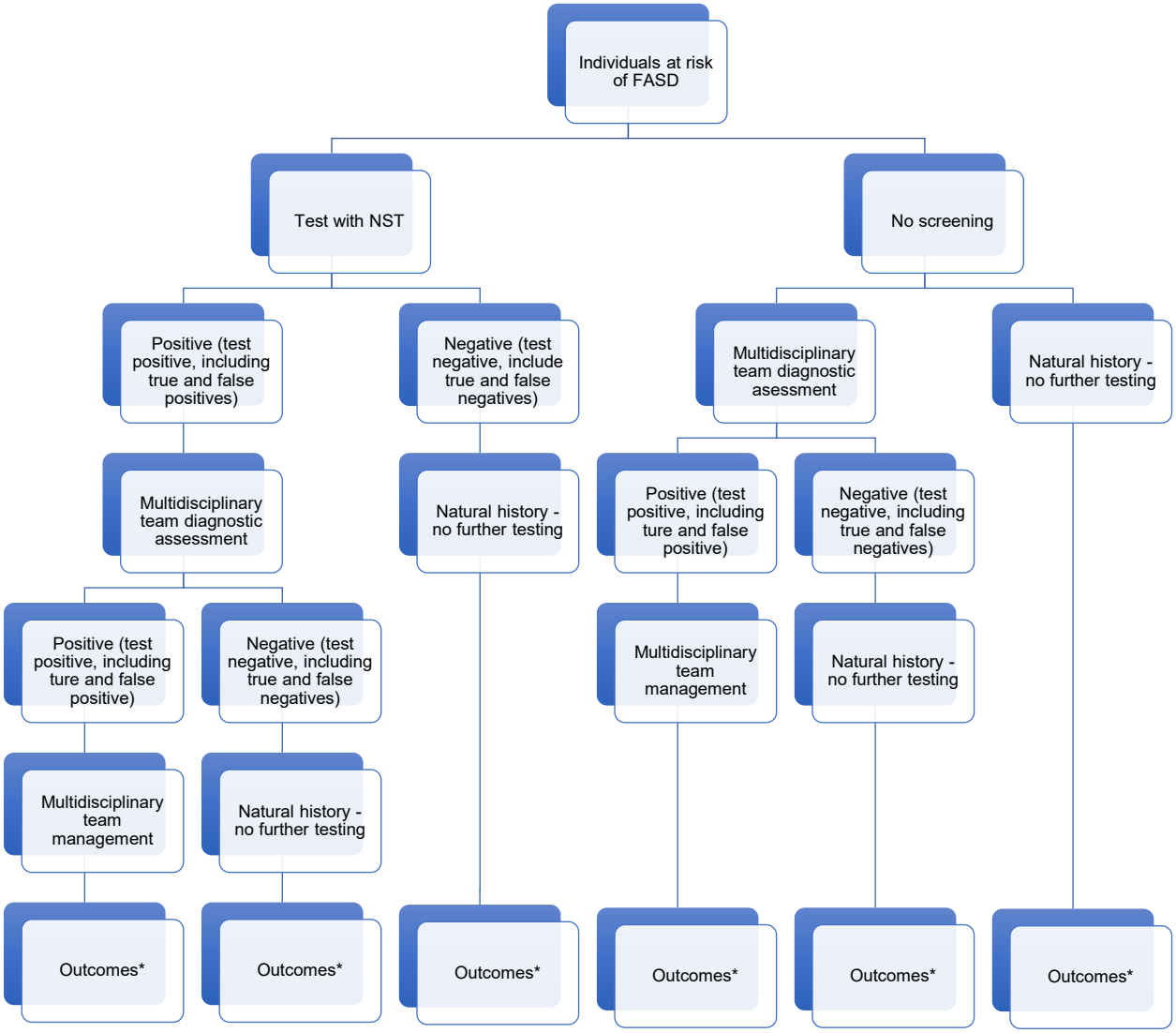
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the NST,[8-11] are available. The NST is a questionnaire, enquiring on the child's behaviour over the past 6 months. Individuals at risk of FASD can be identified from typically developing individuals by using the cut-off scores of the NST.

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[12] Individuals who are falsely identified as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive

appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[13]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[14] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[15] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[13]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☒ Varies	☐ Very inaccurate	☐ Inaccurate	☐ Accurate	☐ Very accurate

Research evidence

Sensitivities and specificities of the NST differ widely across studies. Refer to the GRADE Summary of Findings Table (for full evidence profile see below) for the diagnostic accuracy of NST.

Sensitivity range: 0.63 to 0.98 | Specificity range: 0.42 to 1.00.

Outcomes based on 4 case-control studies (288 individuals)	Effect per 1000 individuals tested for pre-test probability of 0.77%	Quality of the Evidence (GRADE)
True positives (individuals with FASD)	5 to 8	⊕⊕◯◯ LOW due to indirectness[1] and inconsistency[2]
False negatives (individuals incorrectly classified as not having FASD)	0 to 3	
True negatives (individuals without FASD)	417 to 992	⊕⊕◯◯ LOW due to indirectness[1] and inconsistency[2]
False positives (individuals incorrectly classified as having FASD)	0 to 575	

[1]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in individual selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

[2]Estimates of the Neurobehavioral Screening Test sensitivity and specificity were variable despite similar cut-off values and could not be explained by the quality of studies.

Additional considerations

For the diagnostic strategy considered in this scenario, the reference standards used include the Canadian Guidelines and FASD 4-Digit Diagnostic Code.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 417 to 992 out of 1000 individuals would not be referred for further testing (test negatives). Only between 0 to 3 out of those screened negatives would be false negatives. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

There would be 0-3 per 1000 false negative tests with the NST and those individuals would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The undesirable anticipated effects of false positives with the NST are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the NST is low (see GRADE Summary of Findings Table above) owing to indirectness of the population and inconsistency of the test results.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of NST and multidisciplinary team management of FASD is low owing to varied certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐	☒	☐	☐
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[16-18]

Outcome	**Relative importance**
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	**Relative importance**
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☒ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

The strategy involving the NST was overall favoured.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

There are no estimates for the cost of FASD in Australia. In Canada, the NST testing is approximately CAD$20 or AUD$21 per individual.[12] Subsequent cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[12]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with the NST compared with no screening strategy.[12]

Additional considerations

No additional considerations.

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the NST is introduced as a screening strategy due to the nature of the test procedure (easiness to administer). However, it is important to consider that the NST is derived from the Child Behaviour Checklist, which may not be accessible to parents who have lower levels of education, lack of language proficiency, and/or low literacy, as well as culturally and linguistically diverse groups.[19]

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the NST has limited cross cultural validity which could see higher positive screen numbers for culturally and linguistically diverse groups and Aboriginal and Torres Strait Islander people in Western Australia; hence, the NST is likely to have low acceptability in Western Australia.

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

Due to the likelihood of a low acceptability for use in culturally and linguistically diverse populations, the Advisory Group suggested that the NST is not feasible for implementation in Western Australia.

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	Accurate	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☐ We recommend against the intervention or for the comparison	☒ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We suggest against the use of the NST to screen for individuals at risk of FASD in Western Australia (conditional recommendation based on low certainty in the evidence).

Justification

The recommendation was based on low quality of evidence of the diagnostic test accuracy, management effects and effects of the NST in the screening of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement NST in Australia is limited in the current literature. Furthermore, the NST was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the NST has limited cross cultural validity, especially for culturally and linguistically diverse groups and Aboriginal and Torres Strait Islander people in Western Australia. Furthermore, the Advisory Group noted that the Ages and Stages Questionnaire, Third Edition (ASQ-3™), the Ages and Stages Questionnaire: Social-Emotional, Second Edition (ASQ:SE-2™), and the ASQ-TRAK (for use with Aboriginal clients),[20] endorsed for use by the Community Health services in Western Australia, could be considered as a potential screening tool for FASD as it measures components of attention, executive function,

adaptive behaviour, social skills, and social communication that are found in the NST. Also, the ASQ-3™ measures an additional component of motor skills while the ASQ:SE-2™ measures an additional component of affect regulation.

Research priorities

Further studies investigating the diagnostic accuracy of the ASQ in the screening of FASD (with and without sentinel facial features) is warranted.

GRADE evidence profile for Recommendation 1

Sensitivity range: 0.63 to 0.98 | Specificity range: 0.42 to 1.00.

Outcome	№ of studies (№ of individuals)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 individuals tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (individuals with FASD)	4 studies 288 individuals	case-control type accuracy study	serious[a]	not serious	serious[b]	not serious	none	5 to 8	⊕⊕◯◯ LOW
False negatives (individuals incorrectly classified as not having FASD)								0 to 3	
True negatives (individuals without FASD)	4 studies 288 individuals	case-control type accuracy study	serious[a]	not serious	serious[b]	not serious	none	417 to 992	⊕⊕◯◯ LOW
False positives (individuals incorrectly classified as having FASD)								0 to 575	

Explanations

[a]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in individual selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

[b]Estimates of the Neurobehavioral Screening Test sensitivity and specificity were variable despite similar cut-off values and could not be explained by the quality of studies.

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Recommendation 2

Conditional recommendation against the use of the eye movement behaviour assessment via machine learning to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The diagnostic test accuracy of the eye movement behaviour assessment via machine learning to identify FASD (with and without sentinel facial features) is inaccurate.

Decision domain	Judgement	Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐ No ☒	There is moderate quality evidence of the diagnostic test accuracy as well as low quality evidence of the management effects and effects of the eye movement behaviours and machine learning approach in the screening of FASD. The quality of evidence is overall low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐ No ☒	The potential benefits of using the eye movement behaviour assessment via machine learning for FASD screening include early detection of FASD and early access to management strategies. The potential harms due to false positives and negatives with the eye movement behaviour assessment via machine learning include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the eye movement behaviour assessment via machine learning.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒ No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD

		related mental health issues, FASD related early death, and stigma and fear.
Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐ No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 2

Question: Should the eye movement behaviour assessment via machine learning be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: Eye movement behaviour assessment via machine learning and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

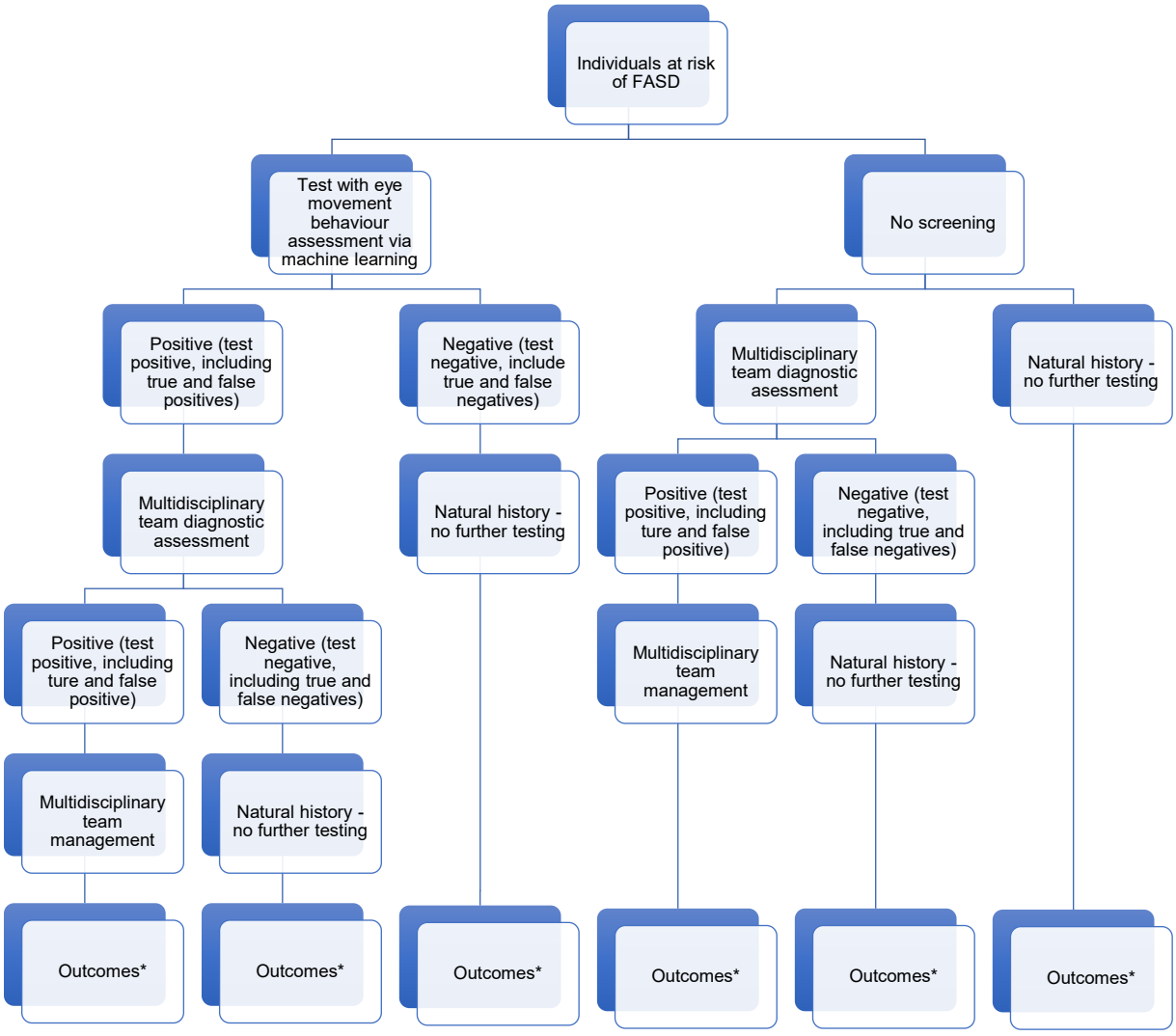
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the eye movement behaviour assessment via machine learning,[8,9] are available. The eye movement behaviour assessment via machine learning uses machine learning to classify eye movement behaviours of typically developing individuals and individuals for FASD to identify those with FASD from typically developing individuals.

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[10] Individuals who are falsely identified as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive

appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[11]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[12] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[13] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[11]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☒ Inaccurate	☐ Accurate	☐ Very accurate

Research evidence

The eye movement behaviour assessment via machine learning has a sensitivity range of 73 to 77% and a specificity range of 79 to 91%. Refer to the GRADE Summary of Findings Table (for full evidence profile see

below) for the diagnostic accuracy of the eye movement behaviour assessment via machine learning.

Sensitivity range: 0.73 to 0.77 | Specificity range: 0.79 to 0.91

Outcomes based on 2 case-control studies (259 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FASD)	6 to 6	⊕⊕⊕◯ MODERATE due to risk of bias[1]
False negatives (individuals incorrectly classified as not having FASD)	2 to 2	
True negatives (individuals without FASD)	784 to 903	⊕⊕⊕◯ MODERATE due to risk of bias[1]
False positives (individuals incorrectly classified as having FASD)	89 to 208	

[1]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the Canadian Guidelines.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

It is beneficial that 786 to 905 out of 1000 individuals with a low suspicion for FASD does not require further testing (test negatives). Only 2 out of those screen negative would be false negatives. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

There would be 2 per 1000 false negative tests with the eye movement behaviour assessment via machine learning and those individuals would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The undesirable anticipated effects of false positives and negatives with the eye movement behaviour assessment via machine learning are judged large due to inaccurate test accuracy, unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the eye movement behaviour assessment via machine learning is moderate (see GRADE Summary of Findings Table above) owing to the risk of bias in the study methodologies used to examine this approach.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of eye movement behaviour assessment via machine learning and multidisciplinary team management of FASD is low owing to moderate certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐	☒	☐	☐
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[14-16]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

The large desirable anticipated effects of the eye movement behaviour assessment via machine learning are balanced out by the equally large undesirable anticipated effect of the eye movement behaviour assessment via machine learning.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

There are no estimates for the cost of FASD in Australia. In Canada, the eye movement behaviour assessment via machine learning testing is approximately CAD$50 or AUD$53 per individual.[9] Subsequent cost of

diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[10]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[10]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the Eye movement behaviour assessment via machine learning is introduced as a screening strategy due to the nature of the test procedure (easiness to administer).

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the Eye movement behaviour assessment via machine learning may not be suitable for children under the age of 5 years and may not be accepted in the various settings:

- In Aboriginal populations and cross-cultural contexts
- In youth detention facilities
- Screening venues with time and space constraints

In addition, the Advisory Group raised concerns about the screening tool design that is based on only one domain of the FASD diagnostic criteria – motor skills, and the cost in the acquisition of the software program and electronic devices needed to operate the eye movement behaviour assessment via machine learning.

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of the eye movement behaviour assessment via machine learning in the screening of FASD in Western Australia is not feasible due to concerns with the cost of the devices required to run this test, the transportability of the devices to rural/remote locations, and the cost of training an administrator or several administrators.

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know	
TEST ACCURACY	Very inaccurate	**Inaccurate**	Accurate	Very accurate	Varies	Don't know	
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**	Varies	Don't know	
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial	Varies	Don't know	
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	Low	**Moderate**	High	No included studies		
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High	No included studies		
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High	No included studies		
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High	No included studies		
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High	No included studies		
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies		
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know	
FEASIBILITY	**No**	Probably no	Probably yes	Yes	Varies	Don't know	

Type of recommendation

Judgement

☐ We recommend against the intervention or for the comparison	☒ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We suggest against the use of the eye movement behaviour assessment via machine learning to screen for individuals at risk of FASD in Western Australia (conditional recommendation based on low certainty in the evidence).

Justification

The recommendation was based on the overall low quality of evidence concerning the effects of the eye movement behaviour assessment via machine learning in the screening and management of FASD as well as the inaccurate diagnostic test accuracy of the eye movement behaviour assessment via machine learning in the screening of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement eye movement behaviour assessment via machine learning in is limited in the current literature. Furthermore, the eye movement behaviour assessment via machine learning was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of the eye movement behaviour assessment via machine learning may be restricted by age (not suitable for children below 5 years of age) and screening settings (e.g., cross-cultural contexts, youth detention facilities, screening venues with time and space

constraints). Furthermore, the Advisory Group noted additional considerations with the use of the eye movement behaviour assessment via machine learning, including the cost of the devices required to run this test, the transportability of the devices to rural/remote locations, and the cost of training an administrator or several administrators.

Research priorities

No further research directions suggested regarding the use of the eye movement behaviour assessment via machine learning as a screening tool for FASD.

GRADE evidence profile for Recommendation 2

Sensitivity range: 0.73 to 0.77 | Specificity range: 0.79 to 0.91

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FASD)	2 studies 259 patients	case-control type accuracy study	serious[a]	not serious	not serious	not serious	none	6 to 6	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having FASD)								2 to 2	
True negatives (patients without FASD)	2 studies 259 patients	case-control type accuracy study	serious[a]	not serious	not serious	not serious	none	784 to 903	⊕⊕⊕◯ MODERATE
False positives (patients incorrectly classified as having FASD)								89 to 208	

Explanations

[a]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

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Recommendation 3

Strong recommendation against the use of the Tallying Reference Errors in Narrative (TREIN) task to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The diagnostic test accuracy of the TREIN task to identify FASD (with and without sentinel facial features) is very inaccurate.

Decision domain	Judgement		Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐	No ☒	There is moderate quality evidence of the diagnostic test accuracy as well as low quality evidence of the management effects and effects of the TREIN task in the screening of FASD. The quality of evidence is overall low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐	No ☒	The potential benefits of using the TREIN task for FASD screening include early detection of FASD and early access to management strategies. The potential harms due to false positives and negatives with the TRIEN task include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the TRIEN task.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒	No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD related mental health issues, FASD related early death, and stigma and fear.
Resource implications *Is the cost small relative to the net benefits for the*	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

recommended strategy?		

GRADE evidence-to-recommendation form for Recommendation 3

Question: Should the Tally Reference Errors in Narrative task (TREIN) be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The TREIN task and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

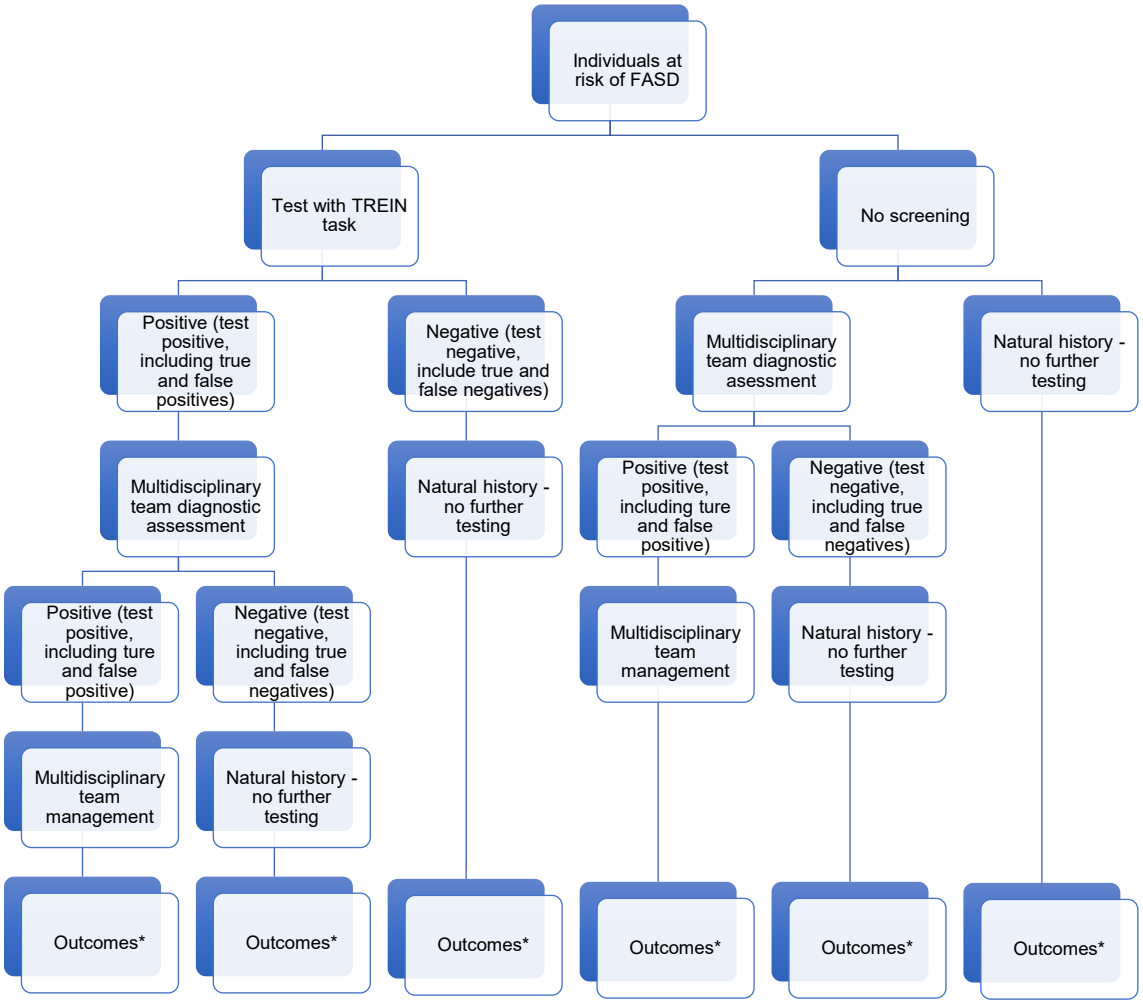
According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the TREIN task,[8] are available. The TREIN task uses the analysis of communication skills through a narrative assessment task to identify individuals with FASD from typically developing individuals.

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[9] Individuals who are falsely identified as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[10]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[11] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[12] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[10]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☒ Very inaccurate	☐ Inaccurate	☐ Accurate	☐ Very accurate

Research evidence

The TREIN task has a sensitivity of 54% and a specificity of 96%. Refer to the GRADE Summary of Findings Table (for full evidence profile see below) for the diagnostic accuracy of the TREIN task.

Sensitivity: 0.54 | Specificity: 0.96

Outcomes based on 1 case-control study (138 individuals)	Effect per 1000 individuals tested for pre-test probability of 0.77%	Quality of the Evidence (GRADE)
True positives (individuals with FASD)	4	⊕⊕⊕◯ MODERATE due to risk of bias[1]
False negatives (individuals incorrectly classified as not having FASD)	4	
True negatives (individuals without FASD)	953	⊕⊕⊕◯ MODERATE due to risk of bias[1]
False positives (individuals incorrectly classified as having FASD)	39	

[1]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the FASD 4-Digit Diagnostic Code.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 957 out of 1000 individuals would not be referred for further testing (test negatives). Only 4 out of those screened negatives would be false negatives. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with

FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

There would be 4 per 1000 false negative tests (e.g., half of the true cases are missed) with the TREIN task and those individuals would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The undesirable anticipated effects of false positives and negatives with the TREIN task are judged large due to inaccurate test accuracy, unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team.

Additional considerations

No additional considerations

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the TREIN task is moderate (see GRADE Summary of Findings Table above) owing to the risk of bias in the study methodologies used to examine this approach.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the TREIN task and multidisciplinary team management of FASD is low owing to moderate certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐	☒	☐	☐
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[13-15]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

The large desirable anticipated effects of the TREIN task are balanced out by the equally large undesirable anticipated effect of the TRIEN task.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

The cost of the TREIN task testing is not reported. In addition, there are no estimates for the cost of FASD in Australia. In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no

screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[9]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[9]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the TREIN task is introduced as a screening strategy. However, it is important to consider that the TREIN task[8] depends largely on an individual's communication abilities and thus the impact of health equity on individuals with poor communication abilities would be reduced.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the TREIN task may not be suitable for young children who have not acquired language abilities. In addition, the Advisory Group raised concerns about the screening tool design that is based on only one domain of the FASD diagnostic criteria – communication skills.

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of TREIN task in the screening of FASD in Western Australia is not feasible due to concerns with the time taken to administer this test and the cost of training the administrator or several administrators.

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**	Varies	Don't know	
TEST ACCURACY	**Very inaccurate**	Inaccurate	Accurate	Very accurate	Varies	Don't know	
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**	Varies	Don't know	
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial	Varies	Don't know	
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	Low	**Moderate**	High	No included studies		
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High	No included studies		
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High	No included studies		
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High	No included studies		
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High	No included studies		
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High	No included studies		
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	**No**	Probably no	Probably yes	Yes	Varies	Don't know	
FEASIBILITY	**No**	Probably no	Probably yes	Yes	Varies	Don't know	

Type of recommendation

Judgement

☒ We recommend against the intervention or for the comparison	☐ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We recommend against the use of the TREIN task to screen for individuals at risk of FASD in Western Australia (strong recommendation based on low certainty in the evidence).

Justification

The recommendation was based on the overall low quality of evidence concerning the effects of the TREIN task in the screening and management of FASD as well as very inaccurate diagnostic test accuracy of the TREIN task in the screening of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement TREIN task is limited in the current literature. Furthermore, the TREIN task was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of the TREIN may be restricted by age, such as young children who have not acquired language abilities. Furthermore, the Advisory Group noted additional considerations with the TREIN task, including the time taken to administer this test and the cost of training the administrator or several administrators.

Research priorities

No further research directions suggested regarding the use of the TREIN task as a screening tool for FASD.

GRADE evidence profile for Recommendation 3

Sensitivity: 0.54 | Specificity: 0.96

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FASD)	1 study 138 patients	case-control type accuracy study	serious[a]	not serious	not serious	not serious	none	4	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having FASD)								4	
True negatives (patients without FASD)	1 study 138 patients	case-control type accuracy study	serious[a]	not serious	not serious	not serious	none	953	⊕⊕⊕◯ MODERATE
False positives (patients incorrectly classified as having FASD)								39	

Explanations

[a]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

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Recommendation 4

Strong recommendation against the use of the dysmorphic examination via photographs to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on very low certainty in the evidence).

Remarks: The evidence for the use of the dysmorphic examination via photographs in the screening for FASD (with and without sentinel facial features) is very low as the test is designed for use to identify individuals at risk of FAS, which is a term to classify FASD with sentinel facial features.

Decision domain	Judgement		Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐	No ☒	There is very low quality evidence of the diagnostic test accuracy and effects of the dysmorphic examination via photographs in the screening of FASD as well as low quality evidence of the management effects. The quality of evidence is overall very low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐	No ☒	The potential benefits of using the dysmorphic examination via photographs for FASD screening include early detection of FASD and early access to management strategies. The potential harms include not able to detect FASD without sentinel facial features and false positives with the dysmorphic examination include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the dysmorphic examination.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒	No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD

			related mental health issues, FASD related early death, and stigma and fear.
Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 4

Question: Should the dysmorphic examination via photographs be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The dysmorphic examination via photographs and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

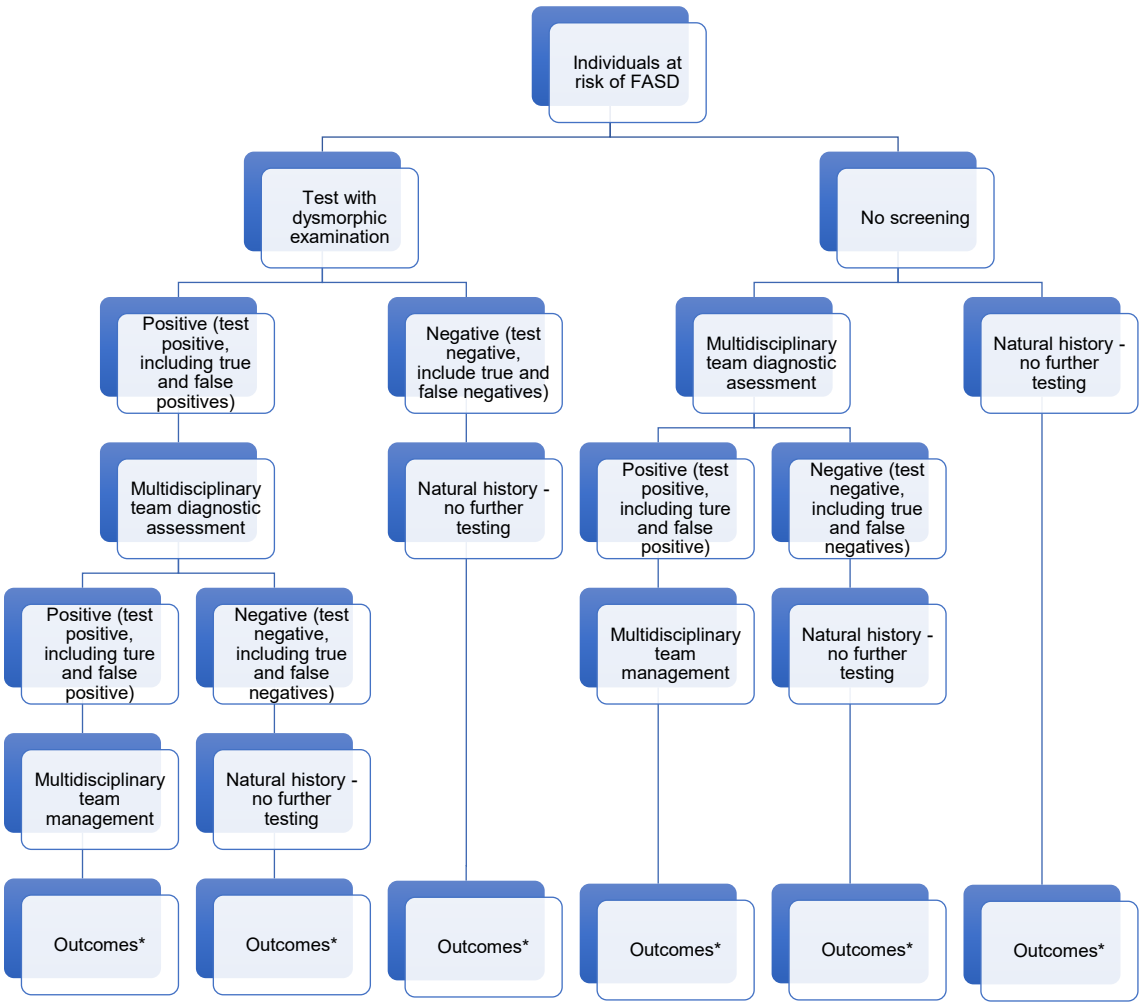
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the dysmorphic examination,[8,9] are available. The dysmorphic examination uses an image analysis technology to examine the facial features of individuals through headshot photographs to identify individuals with fetal alcohol syndrome (FAS) from typically developing individuals. FAS is not used as a diagnostic term in Australia.[1] It is a diagnostic term used by the FASD diagnostic guideline in the United States to describe FASD with sentinel facial features and is commonly categorised under the umbrella term of FASD.[10]

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[11] Individuals who are falsely identified

as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[12]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[13] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[14] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[12]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☐ Inaccurate	☐ Accurate	☒ Very accurate

Research evidence

The dysmorphic examination has a sensitivity of 100% and a specificity range of 99 to 100% for FAS. Refer to the GRADE Summary of Findings

Table (for full evidence profile see below) for the diagnostic accuracy of the dysmorphic examination.

Sensitivity range: 1.00 to 1.00 | Specificity range: 0.99 to 1.00

Outcomes based on 1 cohort study and 1 case-control study (726 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FAS)	8 to 8	⊕◯◯◯ VERY LOW due to risk of bias[1] and indirectness[2]
False negatives (individuals incorrectly classified as not having FAS)	0 to 0	
True negatives (individuals without FAS)	982 to 992	⊕◯◯◯ VERY LOW due to risk of bias[1] and indirectness[2]
False positives (individuals incorrectly classified as having FAS)	0 to 10	

[1]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

[2]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection, index test and reference standard due to the target group, index test, and reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the expert opinion of medical professionals who specialise in the diagnosis of individuals with FAS and 4-Digit Diagnostic Code.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 982 to 992 out of 1000 individuals would not be referred for further testing (test negatives for FAS). None of that screened negative would be false negative for FAS; however, the rate of false negatives for FASD is unclear. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

While there are no false negative tests with the dysmorphic examination, the dysmorphic examination can only detect those with FAS. Individuals

with FASD, other than FAS, would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The global prevalence of FAS is five times less than that of FASD, which is 1.5 per 1000 population and 7.7 per 1000 population,[3,15] respectively. Additionally, "FAS" is not used as a diagnostic term in Australia.[1] Therefore, the undesirable anticipated effects of not detecting individuals with FASD other than FAS via the dysmorphic examination is large. In addition, the undesirable anticipated effects of false positives with the dysmorphic examination are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team. Overall, the undesirable anticipated effects are considered to be large.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the dysmorphic examination is very low (see GRADE Summary of Findings Table above) owing to the risk of bias in the study methodologies and indirectness of the population studied.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the dysmorphic examination and multidisciplinary team management of FASD is very low owing to very low certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐ Important uncertainty or variability	☒ Possibly important uncertainty or variability	☐ Probably no important uncertainty or variability	☐ No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[16-18]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

The large desirable anticipated effects of the dysmorphic examination are balanced out by the equally large undesirable anticipated effect of the dysmorphic examination.

Additional considerations

No additional considerations.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

The cost of the dysmorphic examination testing is not reported. In addition, there are no estimates for the cost of FASD in Australia. In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[11]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[11]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the dysmorphic examination is introduced as a screening strategy. However, it is important to consider that the dysmorphic examination[8,9] is designed to identify individuals with FAS and not individuals with FASD, and thus only the health equity of those with FAS will be increased.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the dysmorphic examination may not be suitable for use in the Aboriginal populations and in cross-cultural contexts due to cultural sensitivity around the storing of images of people, privacy issues and the identification of normative data in relation to facial features for different groups of people in Western Australia. In addition, the Advisory Group raised concerns about the cost in the acquisition of the software program and electronic devices needed to operate the dysmorphic examination. The Advisory Group also noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of dysmorphic examination in the screening of FASD in Western Australia is not feasible due to several reasons:

- Many individuals with FASD do not have sentinel facial features, and thus this test will not be able to detect individuals at risk of FASD and without sentinel facial features
- Concerns with the secure storage of images for health records
- Difficult to obtain consent of the school and parents for this test
- High cost related to the acquisition of software program and electronic devices, transportation of the devices to rural/remote locations, and the training of an administrator or several administrators.

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	Accurate	**Very accurate**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	**Very low**	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	**Very low**	Low	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☒ We recommend against the intervention or for the comparison	☐ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We recommend against the use of the dysmorphic examination via photographs to screen for individuals at risk of FASD in Western Australia (strong recommendation based on very low certainty in the evidence).

Justification

The recommendation was based on the overall very low quality of evidence concerning the effects of dysmorphic examination in the screening and management of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement dysmorphic examination in Australia is limited in the current literature. Furthermore, the dysmorphic examination was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of the dysmorphic examination may be restricted by cultural contexts (e.g., cultural sensitivity around the storing of images of people, privacy issues and the identification of normative data in relation to facial features for different groups of people in Western Australia). Furthermore, the Advisory Group noted additional considerations with the use of the dysmorphic examination, including the difficulty in detecting individuals at risk of FASD without sentinel facial features, concerns with secure storage of images for health records,

difficulty in obtaining consent of the school and parents for this test, the cost of the devices required to run this test, the transportability of the devices to rural/remote locations, and the cost of training an administrator or several administrators.

Research priorities

No further research directions suggested regarding the use of the dysmorphic examination as a screening tool for FASD.

GRADE evidence profile for Recommendation 4

Sensitivity range: 1.00 to 1.00 | Specificity range: 0.99 to 1.00

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FAS)	2 studies 726 patients	cohort & case-control type studies	serious[a]	very serious[b]	not serious	not serious	none	8 to 8	⊕◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having FAS)								0 to 0	
True negatives (patients without FAS)	2 studies 726 patients	cohort & case-control type studies	serious[a]	very serious[b]	not serious	not serious	none	982 to 992	⊕◯◯◯ VERY LOW
False positives (patients incorrectly classified as having FAS)								0 to 10	

Explanations

[a]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design and high risk of bias in study flow due to only some participants received both index and reference tests.

[b]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection, index test and reference standard due to the target group, index test, and reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

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Recommendation 5

Conditional recommendation against the use of the physical and dysmorphic examination to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The evidence for the use of the physical and dysmorphic examination in the screening for FASD (with and without sentinel facial features) is low as the test is designed for use to identify individuals at risk of FAS, which is a term to classify FASD with sentinel facial features.

Decision domain	Judgement	Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐ No ☒	There is low quality evidence of the diagnostic test accuracy, management effects and the effects of the physical and dysmorphic examination in the screening of FASD. The quality of evidence is overall low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐ No ☒	The potential benefits of using the physical and dysmorphic examination for FASD screening include early detection of FASD and early access to management strategies. The potential harms include not able to detect FASD without sentinel facial features and false positives with the physical and dysmorphic examination include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the physical and dysmorphic examination.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒ No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD related mental health issues, FASD related early death, and stigma and fear.

Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 5

Question: Should the physical and dysmorphic examination be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The physical and dysmorphic examination and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

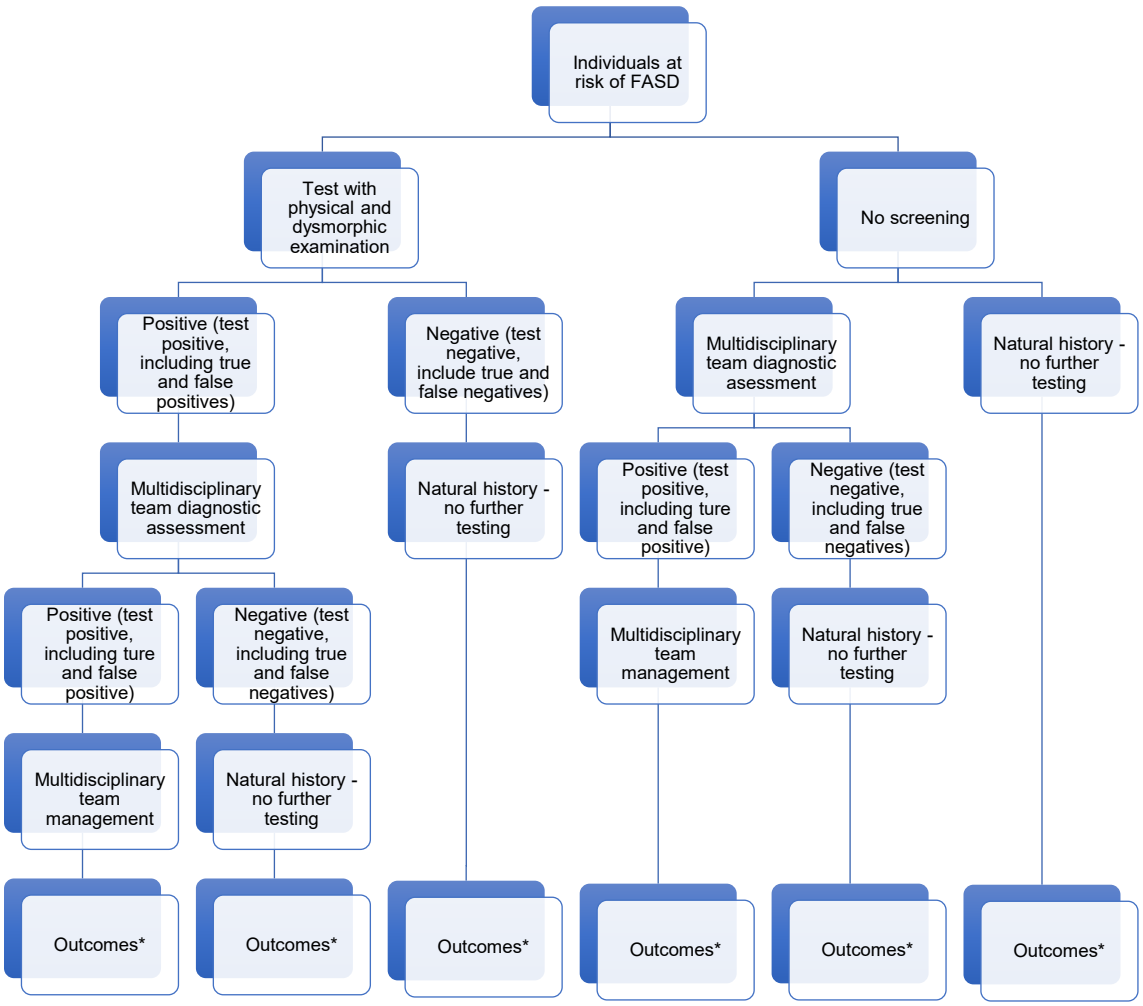
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the physical and dysmorphic examination,[8] are available. The physical and dysmorphic examination entails the evaluation of various physical and facial features of the individual to differentiate individuals with fetal alcohol syndrome (FAS) from typically developing individuals. FAS is not used as a diagnostic term in Australia.[1] It is a diagnostic term used by the FASD diagnostic guideline in the United States to describe FASD with sentinel facial features and is commonly categorised under the umbrella term of FASD.[9]

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[10] Individuals who are falsely identified

as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[11]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[12] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[13] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[11]

Additional considerations

No additional considerations

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☐ Inaccurate	☒ Accurate	☐ Very accurate

Research evidence

The physical and dysmorphic examination has a sensitivity of 100% and a specificity of 89% for FAS. Refer to the GRADE Summary of Findings Table

(for full evidence profile see below) for the diagnostic accuracy of the physical and dysmorphic examination.

Sensitivity: 1.00 (95% CI: 0.91 to 1.00) | Specificity: 0.89 (95% CI: 0.83 to 0.94)

Outcomes based on 1 cross-sectional cohort study (194 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FAS)	8 (7 to 8)	⊕⊕◯◯ LOW due to indirectness[1]
False negatives (individuals incorrectly classified as not having FAS)	0 (0 to 1)	
True negatives (individuals without FAS)	883 (824 to 933)	⊕⊕◯◯ LOW due to indirectness[1]
False positives (individuals incorrectly classified as having FAS)	109 (59 to 168)	

[1]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection and reference standard due to the target group and reference testing concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the gestalt method in the diagnosis of FAS.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 883 out of 1000 individuals would not be referred for further testing (test negatives). Only between 0 to 1 out of those screened negatives would be false negatives for FAS; however, the rate of false negatives for FASD is unclear. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

While there would be 0-1 per 1000 false negative tests with the physical and dysmorphic examination, the physical and dysmorphic examination can only detect those with FAS. Individuals with FASD, other than FAS, would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The global prevalence of FAS is five times less than that of FASD, which is 1.5 per 1000 population and 7.7 per 1000 population,[3,14] respectively. Additionally, "FAS" is not used as a diagnostic term in Australia.[1] Therefore, the undesirable anticipated effects of not detecting individuals with FASD other than FAS via the

dysmorphic examination is large. In addition, the undesirable anticipated effects of false positives with the dysmorphic examination are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team. Overall, the undesirable anticipated effects are considered to be large.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the physical and dysmorphic examination is low (see GRADE Summary of Findings Table above) owing to the indirectness of the population studied.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the physical and dysmorphic examination and multidisciplinary team management of FASD is low owing to low certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐ Important uncertainty or variability	☒ Possibly important uncertainty or variability	☐ Probably no important uncertainty or variability	☐ No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[15-17]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

The large desirable anticipated effects of the physical and dysmorphic examination are balanced out by the equally large undesirable anticipated effect of the physical and dysmorphic examination.

Additional considerations

No additional considerations.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

The cost of the physical and dysmorphic examination testing is not reported. In addition, there are no estimates for the cost of FASD in Australia. In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In

comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[10]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[10]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the physical and dysmorphic examination is introduced as a screening strategy. However, it is important to consider that the physical and dysmorphic examination[8] is designed to identify individuals with FAS and not individuals with FASD, and thus only the health equity of those with FAS will be increased.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the physical and dysmorphic examination may not be suitable for use in Western Australia due to measurements of facial features may not be acceptable in some cultures and the high cost related to the training of health professionals to administer this test and the administration of this test. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of the physical and dysmorphic examination in the screening of FASD in Western Australia is not feasible due to several reasons:

- Many individuals with FASD do not have sentinel facial features, and thus this test will not be able to detect individuals at risk of FASD and without sentinel facial features
- High cost in training health professionals to administer this test and high cost in the administration of this test (in relation to the time taken to measure facial features).

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☐ We recommend against the intervention or for the comparison	☒ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We suggest against the use of the physical and dysmorphic examination to screen for individuals at risk of FASD in Western Australia (conditional recommendation based on low certainty in the evidence).

Justification

The recommendation was based on low quality of evidence of the diagnostic test accuracy, management effects and effects of the physical and dysmorphic examination in the screening of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement physical and dysmorphic examination in Australia is limited in the current literature. Furthermore, the physical and dysmorphic examination was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of the physical and dysmorphic examination may not be suitable in Western Australia due to measurements of facial features may not be acceptable in some cultures, high cost in relation to training and administration of this test, and the difficulty in detecting individuals at risk of FASD without sentinel facial features.

Research priorities

No further research directions suggested regarding the use of the physical and dysmorphic examination as a screening tool for FASD.

GRADE evidence profile for Recommendation 5

Sensitivity: 1.00 (95% CI: 0.91 to 1.00) | Specificity: 0.89 (95% CI: 0.83 to 0.94)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FAS)	1 study 194 patients	cross-sectional (cohort type accuracy study)	not serious	very serious[a]	not serious	not serious	none	8 (7 to 8)	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having FAS)								0 (0 to 1)	
True negatives (patients without FAS)	1 study 194 patients	cross-sectional (cohort type accuracy study)	not serious	very serious[a]	not serious	not serious	none	883 (824 to 933)	⊕⊕◯◯ LOW
False positives (patients incorrectly classified as having FAS)								109 (59 to 168)	

Explanations

[a]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection and reference standard due to the target group and reference testing concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

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Recommendation 6

Strong recommendation against the use of the craniofacial measurement approach to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on very low certainty in the evidence).

Remarks: The evidence for the use of the craniofacial measurements approach in the screening for FASD (with and without sentinel facial features) is very low as the test is designed for use to identify individuals at risk of FAS and PFAS, which are terms to classify FASD with sentinel facial features.

Decision domain	Judgement		Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐	No ☒	There is very low quality evidence of the diagnostic test accuracy and effects of the craniofacial measurement approach in the screening of FASD as well as low quality evidence of the management effects. The quality of evidence is overall very low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐	No ☒	The potential benefits of using the craniofacial measurement approach for FASD screening include early detection of FASD and early access to management strategies. The potential harms include not able to detect FASD without sentinel facial features and false positives with the craniofacial measurement approach include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the craniofacial measurement approach.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒	No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD

			related mental health issues, FASD related early death, and stigma and fear.
Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 6

Question: Should the craniofacial measurement approach be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The craniofacial measurement approach and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

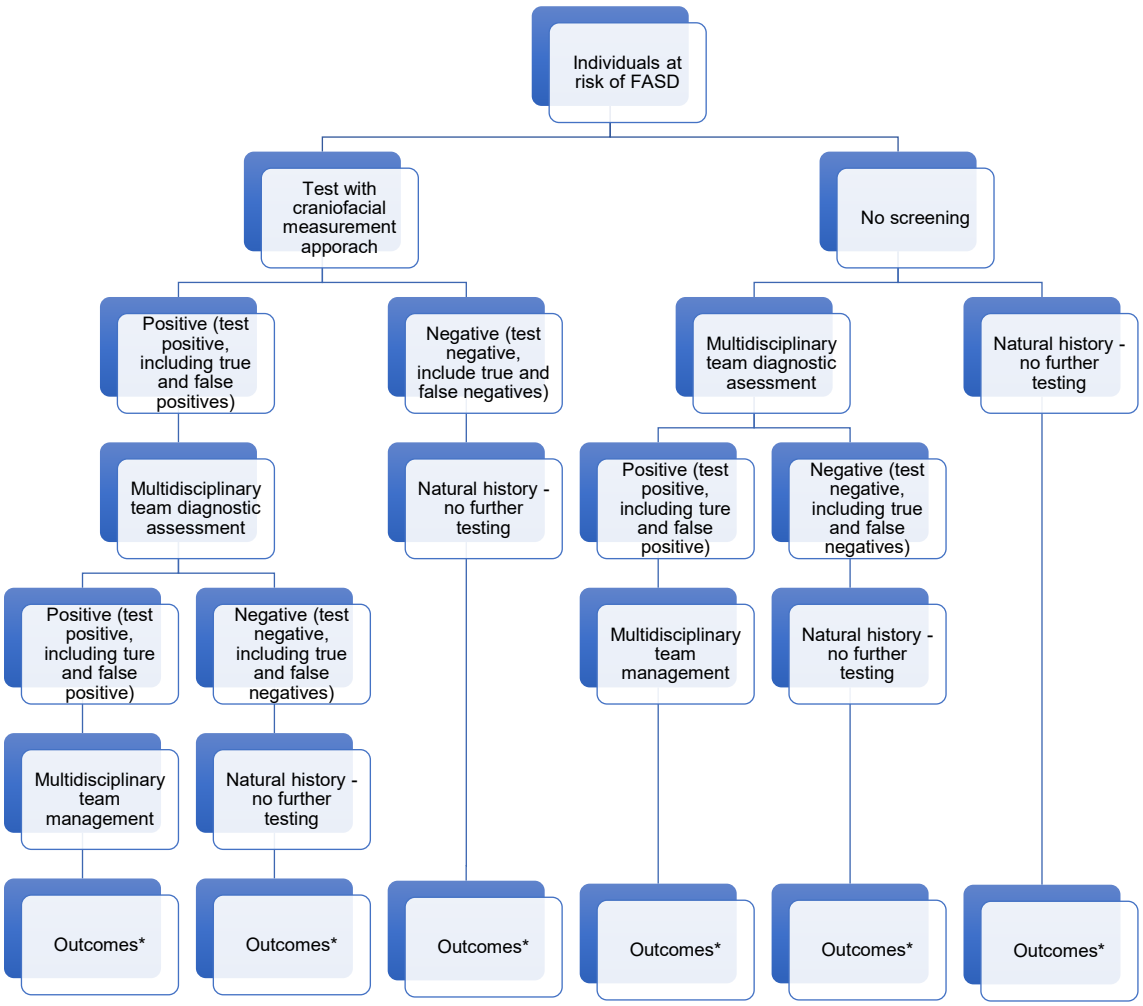
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the craniofacial measurement approach,[8] are available. The craniofacial measurement approach uses an anthropometric analysis of head and facial measures of the individual to differentiate individuals with fetal alcohol syndrome (FAS) and partial FAS (PFAS) from typically developing individuals. FAS and PFAS are not used as diagnostic terms in Australia.[1] They are diagnostic terms used by the FASD diagnostic guideline in the United States to describe FASD with sentinel facial features and are commonly categorised under the umbrella term of FASD.[9]

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[10] Individuals who are falsely identified

as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[11]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[12] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[13] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[11]

Additional considerations

No additional considerations

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☐ Inaccurate	☒ Accurate	☐ Very accurate

Research evidence

The craniofacial measurement approach has a sensitivity of 98% and a specificity of 90% for FAS/PFAS. Refer to the GRADE Summary of Findings

Table (for full evidence profile see below) for the diagnostic accuracy of the craniofacial measurement approach.

Sensitivity: 0.98 (95% CI: 0.93 to 1.00) | Specificity: 0.90 (95% CI: 0.74 to 0.98)

Outcomes based on 1 cross-sectional cohort study (129 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FAS/PFAS)	8 (7 to 8)	⊕◯◯◯ VERY LOW due to risk of bias[1] and indirectness[2]
False negatives (individuals incorrectly classified as not having FAS/PFAS)	0 (0 to 1)	
True negatives (individuals without FAS/PFAS)	893 (737 to 972)	⊕◯◯◯ VERY LOW due to risk of bias[1] and indirectness[2]
False positives (individuals incorrectly classified as having FAS/PFAS)	99 (20 to 255)	

[1]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design, high risk of bias in index test due to lack of assessor blinding, and high risk of bias in study flow due to only some participants received both index and reference tests.

[2]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection due to the target group concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the 1996 Institute of Medicine criteria for diagnosis of FASD.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 893 out of 1000 individuals would not be referred for further testing (test negatives). Only between 0 to 1 out of those screen negative would be false negatives for FAS/PFAS; however, the rate of false negatives for FASD is unclear. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

While there would be 0-1 per 1000 false negative tests with the craniofacial measurement approach, the craniofacial measurement approach can only

detect those with FAS/PFAS. Individuals with FASD, other than FAS, would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The global prevalence of FAS is five times less than that of FASD, which is 1.5 per 1000 population and 7.7 per 1000 population,[3,14] respectively. Additionally, "FAS" and "PFAS" are not used as diagnostic terms in Australia.[1] Therefore, the undesirable anticipated effects of not detecting individuals with FASD other than FAS via the physical and dysmorphic examination is large. In addition, the undesirable anticipated effects of false positives with the physical and dysmorphic examination are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team. Overall, the undesirable anticipated effects are considered to be large.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the craniofacial measurement approach is very low (see GRADE Summary of Findings Table above) owing to the risk of bias in the study methodologies and indirectness of the population studied.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the craniofacial measurement approach and multidisciplinary team management is very low owing to very low certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐ Important uncertainty or variability	☒ Possibly important uncertainty or variability	☐ Probably no important uncertainty or variability	☐ No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[15-17]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

The large desirable anticipated effects of the craniofacial measurement approach are balanced out by the equally large undesirable anticipated effect of the craniofacial measurement approach.

Additional considerations

No additional considerations.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

The cost of the craniofacial measurement approach testing is not reported. In addition, there are no estimates for the cost of FASD in Australia. In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[10]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☒ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[10]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the craniofacial measurement approach is introduced as a screening strategy. However, it is important to consider that the craniofacial measurement approach[8] is designed to identify individuals with FAS/PFAS and not individuals with FASD, and thus only the health equity of those with FAS/PFAS will be increased.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the craniofacial measurement approach may not be suitable for use in Western Australia due to measurements of facial features may not be acceptable in some cultures and the high cost related to the training of health professionals to administer this test and the administration of this test. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of the craniofacial measurement approach in the screening of FASD in Western Australia is not feasible due to several reasons:

- Many individuals with FASD do not have sentinel facial features, and thus this test will not be able to detect individuals at risk of FASD and without sentinel facial features
- High cost in training health professionals to administer this test and high cost in the administration of this test (in relation to the time taken to measure facial features).

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	**Very low**	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	**Very low**	Low	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☒ We recommend against the intervention or for the comparison	☐ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We recommend against the use of the craniofacial measurement approach to screen for individuals at risk of FASD in Western Australia (strong recommendation based on very low certainty in the evidence).

Justification

The recommendation was based on the overall very low quality of evidence concerning the effects of the craniofacial measurement approach in the screening and management of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement physical and dysmorphic examination in Australia is limited in the current literature. Furthermore, the craniofacial measurement approach was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of the craniofacial measurement approach may not be suitable in Western Australia due to measurements of facial features may not be acceptable in some cultures, high cost in relation to training and administration of this test, and the difficulty in detecting individuals at risk of FASD without sentinel facial features.

Research priorities

No further research directions suggested regarding the use of the craniofacial measurement approach as a screening tool for FASD.

GRADE evidence profile for Recommendation 6

Sensitivity: 0.98 (95% CI: 0.93 to 1.00) | Specificity: 0.90 (95% CI: 0.74 to 0.98)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FAS/ PFAS)	1 study 129 patients	cross-sectional (cohort type accuracy study)	very serious[a]	serious[b]	not serious	not serious	none	8 (7 to 8)	⊕◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having FAS/PFAS)								0 (0 to 1)	
True negatives (patients without FAS/PFAS)	1 study 129 patients	cross-sectional (cohort type accuracy study)	very serious[a]	serious[b]	not serious	not serious	none	893 (737 to 972)	⊕◯◯◯ VERY LOW
False positives (patients incorrectly classified as having FAS/PFAS)								99 (20 to 255)	

Explanations

[a]Risk of bias was assessed using QUADAS-2. Studies demonstrated high risk of bias in patient selection due to the study design, high risk of bias in index test due to lack of assessor blinding, and high risk of bias in study flow due to only some participants received both index and reference tests.

[b]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in patient selection due to the target group concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

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1. Bower C, Elliott EJ, and on behalf of the Steering Group. Report to the Australian Government Department of Health: "Australian Guide to the diagnosis of Fetal Alcohol Spectrum Disorder (FASD)". Australian Government Department of Health; 2016. ISBN: 978-0-6481297-4-5.
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Recommendation 7

Strong recommendation against the use of the FAS Screen to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The evidence for the use of the FAS Screen in the screening for FASD (with and without sentinel facial features) is low as the test is designed for use to identify individuals at risk of FAS and PFAS, which are terms to classify FASD with sentinel facial features.

Decision domain	Judgement		Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐	No ☒	There is low quality evidence of the diagnostic test accuracy, management effects and the effects of FAS Screen in the screening of FASD. The quality of evidence is overall low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐	No ☒	The potential benefits of using the FAS Screen for FASD screening include early detection of FASD and early access to management strategies. The potential harms include not able to detect FASD without sentinel facial features and false positives with the FAS Screen include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the FAS Screen.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒	No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD related mental health issues, FASD related early death, and stigma and fear.
Resource implications	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

Is the cost small relative to the net benefits for the recommended strategy?		

GRADE evidence-to-recommendation form for Recommendation 7

Question: Should the fetal alcohol syndrome screen (FAS Screen) be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The fetal alcohol syndrome screen (FAS Screen) and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD,*[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

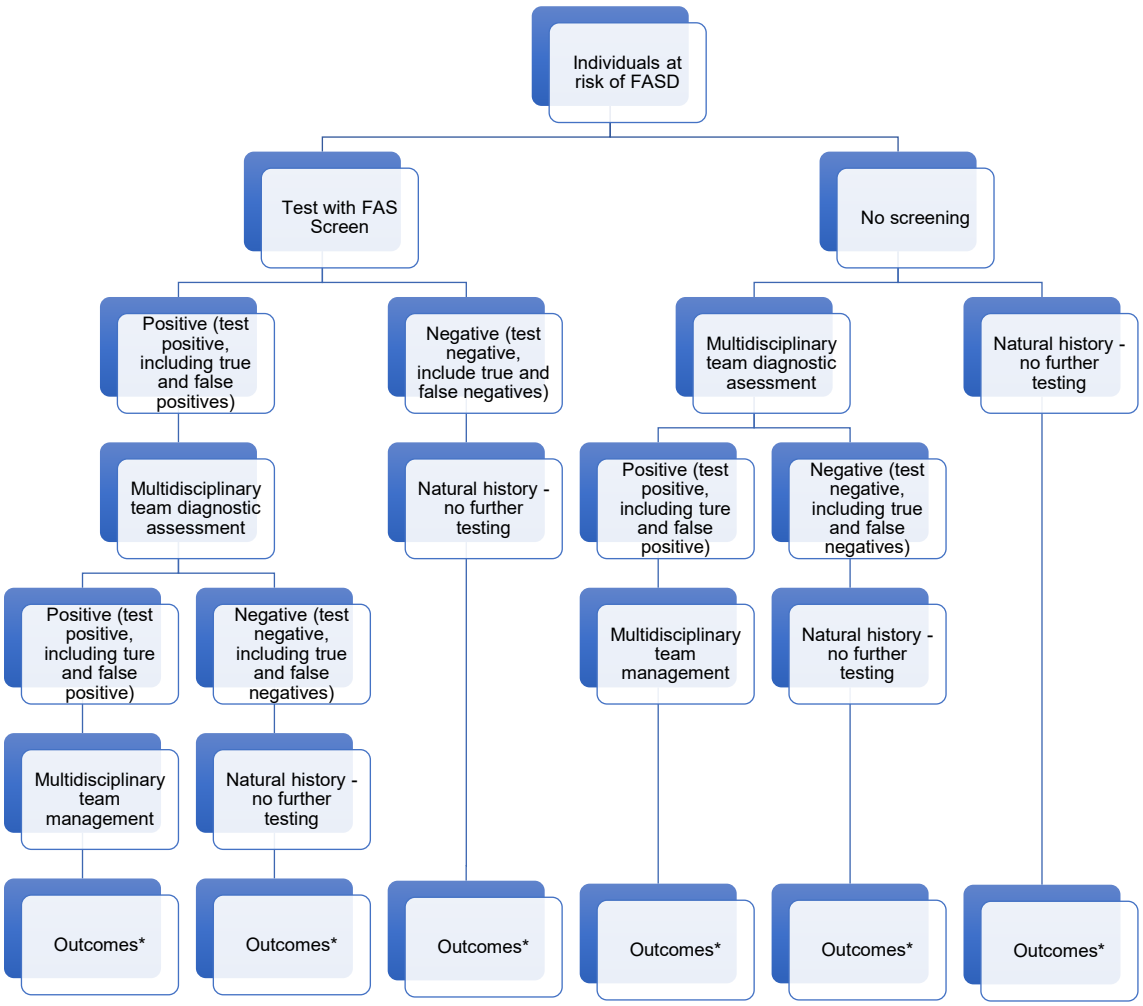
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the FAS Screen,[8,9] are available. The FAS Screen is a checklist, containing items regarding the child's anthropometric and development features. Individuals at risk of fetal alcohol syndrome (FAS) or partial FAS (PFAS) can be identified from typically developing individuals by using the cut-off scores of the FAS Screen. FAS and PFAS are not used as diagnostic terms in Australia.[1] They are diagnostic terms used by the FASD diagnostic guideline in the United States to describe FASD with sentinel facial features and are commonly categorised under the umbrella term of FASD.[10]

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD comes at high resource use and cost.[11] Individuals who are falsely identified

as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[12]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[13] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[14] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[12]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☐ Inaccurate	☒ Accurate	☐ Very accurate

Research evidence

The FAS Screen has a sensitivity of 100% and a specificity range of 94 to 95% for FAS/PFAS. Refer to the GRADE Summary of Findings Table (for full evidence profile see below) for the diagnostic accuracy of the FAS Screen.

Sensitivity range: 1.00 to 1.00 | Specificity range: 0.94 to 0.95

Outcomes based on 2 cross-sectional cohort studies (2397 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FAS/PFAS)	8 to 8	⊕⊕◯◯ LOW due to indirectness[1]
False negatives (individuals incorrectly classified as not having FAS/PFAS)	0 to 0	
True negatives (individuals without FAS/PFAS)	934 to 947	⊕⊕◯◯ LOW due to indirectness[1]
False positives (individuals incorrectly classified as having FAS/PFAS)	45 to 58	

[1]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in index test and reference standard due to the index test and reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the gestalt method and Institute of Medicine criteria for the diagnosis of FAS/PFAS.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 934 to 947 out of 1000 individuals would not be referred for further testing (test negatives). None of those screened negatives would be false negatives for FAS/PFAS; however, the rate of false negatives for FASD is unclear. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

While none are tested false negative with the FAS Screen, the FAS Screen can only detect those with FAS/PFAS. Individuals with FASD, other than FAS, would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The global prevalence of FAS is five times less than that of FASD, which is 1.5 per 1000 population and 7.7 per 1000 population,[3,15] respectively. Additionally, "FAS" and "PFAS" are not used as diagnostic terms in Australia.[1] Therefore, the undesirable anticipated effects of not detecting individuals with FASD other than FAS via the physical and dysmorphic examination is large. In addition,

the undesirable anticipated effects of false positives with the physical and dysmorphic examination are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team. Overall, the undesirable anticipated effects are considered to be large.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the FAS Screen is low (see GRADE Summary of Findings Table above) owing to the indirectness of the population studied.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the FAS Screen and multidisciplinary team management is low owing to low certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐	☒	☐	☐
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[16-18]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

The large desirable anticipated effects of the FAS Screen are balanced out by the equally large undesirable anticipated effect of the FAS Screen.

Additional considerations

No additional considerations.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

There are no estimates for the cost of FASD in Australia. In Canada, the eye movement behaviour assessment via machine learning testing is approximately USD$8-13 or AUD$11-18 per individual.[8,9] In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no

screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[11]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[11]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the FAS Screen is introduced as a screening strategy. However, it is important to consider that the FAS Screen[8,9] is designed to identify individuals with FAS and not individuals with FASD, and thus only the health equity of those with FAS/PFAS will be increased.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the FAS Screen may not be suitable for use in Western Australia due to measurements of facial features may not be acceptable in some cultures, the large number of items to assess in the test, and the high cost related to the training of health professionals to administer this test and the administration of this test. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of the FAS Screen in the screening of FASD in Western Australia is not feasible due to several reasons:

- Many individuals with FASD do not have sentinel facial features, and thus this test will not be able to detect individuals at risk of FASD and without sentinel facial features
- Time taken to complete the test per individual is expected to be long
- High cost in training health professionals to administer this test and high cost in the administration of this test (in relation to the time taken to measure facial features).

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☒ We recommend against the intervention or for the comparison	☐ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We recommend against the use of the FAS Screen to screen for individuals at risk of FASD in Western Australia (strong recommendation based on low certainty in the evidence).

Justification

The recommendation was based on low quality of evidence of the diagnostic test accuracy, management effects and effects of the FAS Screen in the screening of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement the FAS Screen in Australia is limited in the current literature. Furthermore, the FAS Screen was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of FAS Screen may not be suitable in Western Australia due to measurements of facial features may not be acceptable in some cultures, time taken to complete the test is expected to be long, high cost in relation to training and administration of this test, and the difficulty in detecting individuals at risk of FASD without sentinel facial features. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

Furthermore, the Advisory Group noted that the Ages and Stages Questionnaire, Third Edition (ASQ-3™), the Ages and Stages Questionnaire: Social-Emotional, Second Edition (ASQ:SE-2™), and the ASQ-TRAK (for use with Aboriginal clients),[19] endorsed for use by the Community Health services in Western Australia, could be considered as a potential screening tool for FASD as it measures components of language, attention and executive function that are found in the FAS Screen. Also, the ASQ-3™ measures an additional component of motor skills while the ASQ:SE-2™ measures an additional component of affect regulation.

Research priorities

Further studies investigating the diagnostic accuracy of the ASQ in the screening of FASD (with and without sentinel facial features) is warranted.

GRADE evidence profile for Recommendation 7

Sensitivity range: 1.00 to 1.00 | Specificity range: 0.94 to 0.95

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FAS/ PFAS)	2 studies 2397 patients	cross-sectional (cohort type accuracy study)	not serious	very serious[a]	not serious	not serious	none	8 to 8	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having FAS/PFAS)								0 to 0	
True negatives (patients without FAS/PFAS)	2 studies 2397 patients	cross-sectional (cohort type accuracy study)	not serious	very serious[a]	not serious	not serious	none	934 to 947	⊕⊕◯◯ LOW
False positives (patients incorrectly classified as having FAS/PFAS)								45 to 58	

Explanations

[a]Indirectness was assessed using QUADAS-2. Studies demonstrated high risk in applicability in index test and reference standard due to the index test and reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

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Recommendation 8

Strong recommendation against the use of the FAS diagnostic checklist to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia (based on low certainty in the evidence).

Remarks: The evidence for the use of the FAS diagnostic checklist in the screening for FASD (with and without sentinel facial features) is low as the test is designed for use to identify individuals at risk of FAS and PFAS, which are terms to classify FASD with sentinel facial features.

Decision domain	Judgement		Summary of reason for judgement
Quality of evidence *Is there high- or moderate quality evidence?*	Yes ☐	No ☒	There is moderate quality evidence of the diagnostic test accuracy as well as low quality evidence of the management effects and effects of the FAS diagnostic checklist in the screening of FASD. The quality of evidence is overall low.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐	No ☒	The potential benefits of using the FAS diagnostic checklist for FASD screening include early detection of FASD and early access to management strategies. The potential harms include not able to detect FASD without sentinel facial features and false positives with the FAS diagnostic checklist include unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD. Overall, the potential benefits may be balanced out by the potential harms of using the FAS diagnostic checklist.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒	No ☐	There is an assumed high value in the use of a screening strategy versus no screening under a proposed model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies. This could result in a reduction of undetected FASD, FASD related mental health issues, FASD related early death, and stigma and fear.

Resource implications *Is the cost small relative to the net benefits for the recommended strategy?*	Yes ☐	No ☒	Unable to judge due to a lack of information pertaining to Australia available in the literature.

GRADE evidence-to-recommendation form for Recommendation 8

Question: Should the fetal alcohol syndrome diagnostic checklist be used to screen for individuals at risk of fetal alcohol spectrum disorder (FASD) in Western Australia?

Population and problem: Individuals at risk of FASD

Intervention: The fetal alcohol syndrome (FAS) diagnostic checklist and management of FASD

Comparison: No screening and management of FASD

Purpose of the test: Screening for FASD (with and without sentinel facial features)

Linked management of FASD: The management of FASD is typically provided to individuals confirmed with FASD through a diagnostic assessment conducted by a multidisciplinary team.[1] Management strategies prescribed are dependent on the strengths and weaknesses of individuals with FASD and are preferably carried out by a multidisciplinary team.[2]

Anticipated outcomes*:

- Ameliorate direct impairments associated with FASD (neurodevelopmental impairments)
- Prevent or reduce indirect impairments associated with FASD (disengagement from education, employment; mental health difficulties; suicide; justice contact)
- Burden of diagnostic assessment and management of FASD

Setting: Various settings

Screening strategy	Proposed setting
Universal	Community child health
Targeted	Clinic
Selective	Child protection/justice settings

Perspective: Societal perspective

Background

FASD is a neurodevelopmental disorder caused by prenatal exposure to alcohol with a global prevalence of 7.7 per 1000 population.[3] Available data suggest a twofold increase in FASD notifications in Western Australia over the last 30 years, in both Aboriginal and non-Aboriginal children, with the prevalence of FASD in Aboriginal children born in 1980 to 1989 increasing from 3 per 1000 births to 6 per 1000 births in 2000 to 2010.[4] Individuals with FASD experience a range of severe neurodevelopmental impairments and may also display facial anomalies and differences in physical development.[1,5] Together, the physiological and neurocognitive difficulties experience by individuals with FASD adversely impact daily function at home, school, and work.[6,7]

Australian FASD Diagnostic Guidelines

According to the *Australian Guide to the diagnosis of FASD*,[1] FASD can be classified into two sub-categories: FASD with three sentinel facial features and FASD with less than three sentinel facial features.

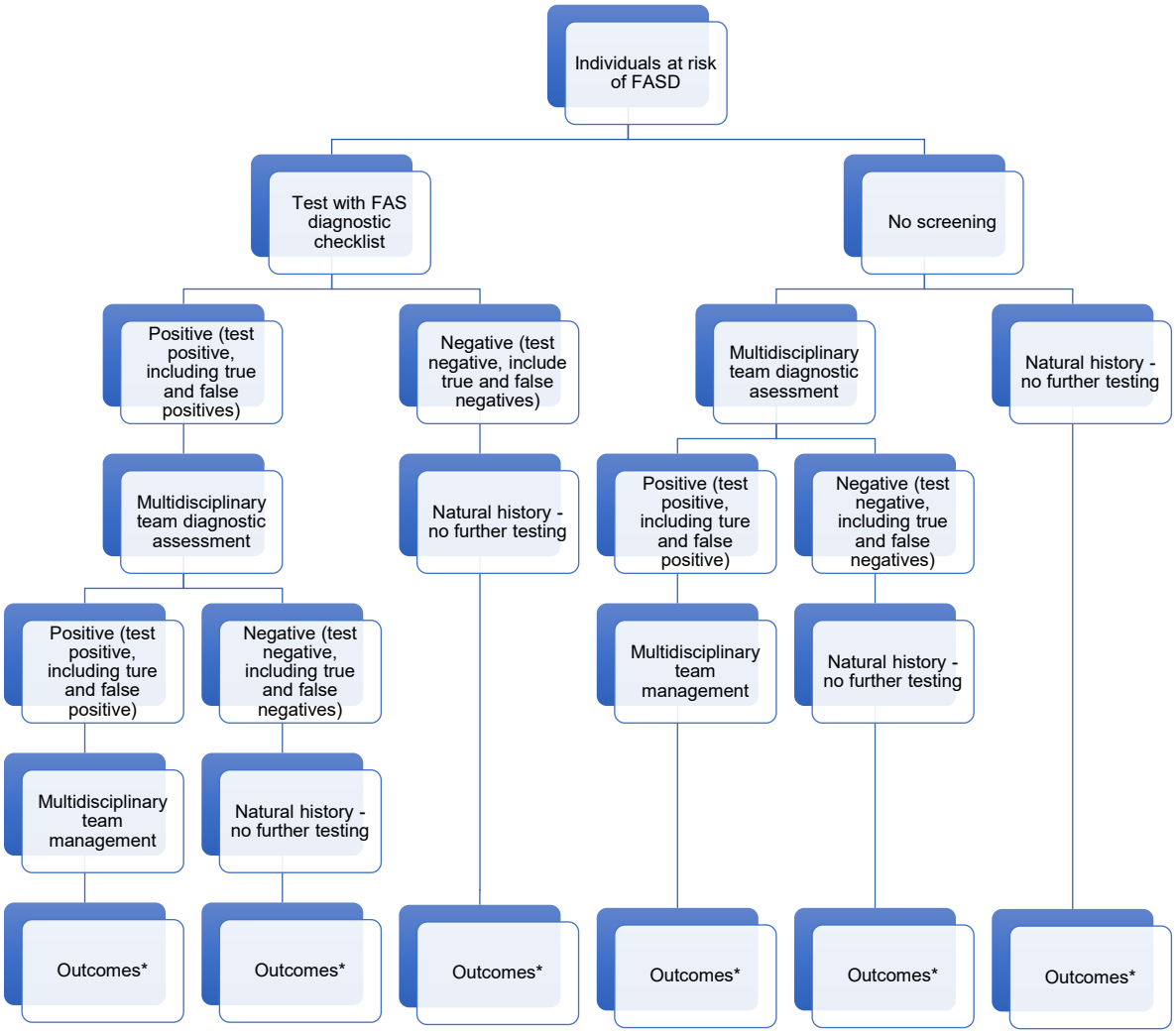
While there is currently no validated standardised screening tool for FASD (with and without sentinel facial features), non-validated screening tools, such as the FAS diagnostic checklist,[8] are available. The FAS diagnostic checklist contains items regarding the child's anthropometric and development features. Individuals at risk of fetal alcohol syndrome (FAS) or partial FAS (PFAS) can be identified from typically developing individuals by using the cut-off scores of the FAS diagnostic checklist. FAS and PFAS are not used as diagnostic terms in Australia.[1] They are diagnostic terms used by the FASD diagnostic guideline in the United States to describe FASD with sentinel facial features and are commonly categorised under the umbrella term of FASD.[9]

Proposed Model of Care

Under the proposed model of care, individuals screened positive for FASD would be referred for diagnostic assessment conducted by a multidisciplinary team.[1] No further test or management of FASD may be administered to those screen negative for FASD. Management of FASD

comes at high resource use and cost.[10] Individuals who are falsely identified as having FASD when they do not (false positives) would undergo unnecessary diagnostic assessment Individuals who are falsely identified as not having a FASD (false negatives) would not be able to receive appropriate practical and psychological support to manage the difficulties of FASD.

Subgroups: Individuals in care, correctional, special education, specialised clinical and Aboriginal populations.[11]



Analytic PICO framework

1. Problem

Is the problem a priority?

Judgement

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

Research evidence

FASD is a neurodevelopmental disorder that affects approximately eight in 1000 persons per year globally.[3] While this overall prevalence is low, the prevalence of women who consume alcohol during pregnancy is approximately 10-15% of the general population in Canada and the United States.[12] The number of women who consume alcohol during pregnancy is even higher in Australia at 50% of the general population.[13] Information on women who consume alcohol during pregnancy in Western Australia is currently not available. It is important to note that alcohol use disproportionately affects disadvantaged groups.[11]

Additional considerations

No additional considerations.

2. Test accuracy

How accurate is the test or strategy?

Judgement

☐ Don't know	☐ Varies	☐ Very inaccurate	☐ Inaccurate	☒ Accurate	☐ Very accurate

Research evidence

The FAS diagnostic checklist has a sensitivity of 89% and a specificity of 72% for FAS/PFAS. Refer to the GRADE Summary of Findings Table (for full

evidence profile see below) for the diagnostic accuracy of the FAS diagnostic checklist.

Sensitivity: 0.89 | Specificity: 0.72

Outcomes based on 2 cross-sectional cohort studies (2397 individuals)	**Effect per 1000 individuals tested for pre-test probability of 0.77%**	**Quality of the Evidence (GRADE)**
True positives (individuals with FAS/PFAS)	7	⊕⊕⊕◯ MODERATE due to indirectness[1]
False negatives (individuals incorrectly classified as not having FAS/PFAS)	1	
True negatives (individuals without FAS/PFAS)	711	⊕⊕⊕◯ MODERATE due to indirectness[1]
False positives (individuals incorrectly classified as having FAS/PFAS)	281	

[1] Indirectness was assessed using QUADAS-2. Studies demonstrated unclear risk in patient selection due to the inclusion of only individuals with fetal alcohol syndrome and partial fetal alcohol syndrome, and high risk in applicability in reference standard due to the reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

Additional considerations

For the diagnostic strategy considered in the scenario, the reference standards used include the 1996 Institute of Medicine criteria for the diagnosis of FAS/PFAS.

3. Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Research evidence

Using this test, 712 out of 1000 individuals would not be referred for further testing (test negatives). Only 1 out of those screened negatives would be false negatives for FAS/PFAS; however, the rate of false negatives for FASD is unclear. Using a model of care in which individuals who screen positive are referred for diagnostic assessment and those diagnosed with FASD are referred to appropriate management strategies, it is anticipated that the desirable effects of downstream management of individuals with true FASD are large. The avoidance of more detailed diagnostic assessment with a multidisciplinary team would reduce health system costs and burden on families.

Additional considerations

No additional considerations.

4. Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Research evidence

While there would be only 1 per 1000 false negative tests with the FAS diagnostic checklist, the FAS diagnostic checklist can only detect those with

FAS/PFAS. Individuals with FASD, other than FAS, would suffer the consequences of not being diagnosed and having access to appropriate management and support (FASD causing difficulty with functioning at home, in school, and at work). The global prevalence of FAS is five times less than that of FASD, which is 1.5 per 1000 population and 7.7 per 1000 population,[3,14] respectively. Additionally, "FAS" and "PFAS" are not used as diagnostic terms in Australia.[1] Therefore, the undesirable anticipated effects of not detecting individuals with FASD other than FAS via the physical and dysmorphic examination is large. In addition, the undesirable anticipated effects of false positives with the physical and dysmorphic examination are judged moderate due to unnecessary resource use, stigma and anxiety, opportunity cost and financial cost related to assessment and management of FASD with a multidisciplinary team. Overall, the undesirable anticipated effects are considered to be large.

Additional considerations

No additional considerations.

5. Certainty of evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

Judgement

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

Research evidence

The certainty of the evidence for test accuracy of the FAS diagnostic checklist is moderate (see GRADE Summary of Findings Table above) owing to the indirectness of the population studied.

Additional considerations

No additional considerations.

6. Certainty of evidence of test's effects

What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

Judgement

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

Research evidence

Nil.

Additional considerations

No additional considerations.

7. Certainty of evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

Judgement

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

Research evidence

There are a variety of management strategies for FASD, depending on the individual's strengths and weaknesses. One systematic review evaluated the clinical outcomes of various management strategies designed for individuals with FASD.[2] The review found that some of the management strategies were beneficial in the improvement of academic, learning, social communication, and behavioural skills of individuals with FASD. The overall certainty of all available evidence is low owing to limitations of the studies that examined the management strategies (e.g., inadequate study design, allocation concealment, assessor blinding, and small sample size).

Additional considerations

It is also important to note that FASD is associated with a highly heterogeneous clinical profile and a "one size fits all" management approach is unlikely to become available.

8. Certainty of evidence of test result / management

How certain is the link between test results and management decisions?

Judgement

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

Research evidence

Nil.

Additional considerations

Observations from clinical practice suggest that the administration of management of FASD to individuals with confirmed FASD varies depending on several considerations, including (1) the state in which the individual live in, (2) the availability of funding, and (3) waitlist to access multidisciplinary team care. It is most likely that any management decisions would be made based on the results of a full diagnostic assessment.

9. Certainty of effects

What is the overall certainty of the evidence of effects of the test?

Judgement

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

Research evidence

The overall certainty of the evidence concerning the effects of the FAS diagnostic checklist and multidisciplinary team management is low owing to moderate certainty for test accuracy and low certainty of the effects of management of FASD.

Additional considerations

No additional considerations.

10. Values

Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?

Judgement

☐ Important uncertainty or variability	☒ Possibly important uncertainty or variability	☐ Probably no important uncertainty or variability	☐ No important uncertainty or variability

Research evidence

Important values for some of the outcomes.[15-17]

Outcome	Relative importance
Undetected FASD	Critical
Mental health issues	Critical
Stigma and fear	Critical
Early death	Critical

Additional considerations

Some of the outcomes suggested by the Advisory Group:

Outcome	Relative importance
Unnecessary management of FASD	Critical
Access to early intervention	Critical

11. Balance of effects

Does the balance between desirable and undesirable health effects favour the test or the comparison?

Judgement

☐ Don't know	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☒ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

The large desirable anticipated effects of the FAS diagnostic checklist are balanced out by the equally large undesirable anticipated effect of the FAS diagnostic checklist.

Additional considerations

No additional considerations.

12. Resources required

How large are the resource requirements (costs)?

Judgement

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

Research evidence

The cost of the FAS diagnostic checklist testing is not reported. In addition, there are no estimates for the cost of FASD in Australia. In Canada, cost of diagnostic assessment and management of FASD are about CAD$4,182,644 or AUD$4,393,240 per 100 individuals. In comparison, the total cost for no screening is approximately CAD$4,366,539 or AUD$4,586,394 per 100 individuals.[10]

Additional considerations

Resource requirements vary with depending on the different locations of Western Australia, for example metropolitan and rural areas of Western Australia.

13. Certainty of evidence of required resources

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

Judgement

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

Research evidence

Nil.

Additional considerations

Resource requirements vary in different countries. The resource requirements can also vary in different locations of Western Australia, for example metropolitan and rural areas of Western Australia. Resources required for individuals to benefit from FASD screening include:

- The cost of the FASD screening test
- The cost of diagnostic assessment
- The cost of resources for supporting diagnosed individuals.

14. Cost-effectiveness

Does the cost-effectiveness of the test favour the test or the comparison?

Judgement

☒ No included studies	☐ Varies	☐ Favours the comparison	☐ Probably favours the comparison	☐ Does not favour either the intervention or the comparison	☐ Probably favours the intervention	☐ Favours the intervention

Research evidence

Nil.

Additional considerations

There are no estimates for the cost of FASD in Australia. In Canada, an approximate cost of CAD$183,895 or AUD$193,154 per 100 individuals is saved when individuals are screened with a tool designed to identify FASD compared with no screening strategy.[10]

15. Equity

What would be the impact on health equity?

Judgement

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

Research evidence

Nil.

Additional considerations

Inequities will overall be reduced if the FAS diagnostic checklist is introduced as a screening strategy. However, it is important to consider that the FAS diagnostic checklist [8] is designed to identify individuals with FAS and not individuals with FASD, and thus only the health equity of those with FAS/PFAS will be increased.

16. Acceptability

Is the test acceptable to key stakeholders?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the FASD diagnostic checklist may not be suitable for use in Western Australia due to measurements of facial features may not be acceptable in some cultures, the large number of items to assess in the test, and the high cost related to the training of health professionals to administer this test and the administration of this test. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups (e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

17. Feasibility

Is the test feasible to implement?

Judgement

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

Research evidence

Nil.

Additional considerations

The Advisory Group suggested that the use of the FAS Screen in the screening of FASD in Western Australia is not feasible due to several reasons:

- Many individuals with FASD do not have sentinel facial features, and thus this test will not be able to detect individuals at risk of FASD and without sentinel facial features
- Parents may have difficulties disclosing truthfully alcohol consumption during pregnancy
- Time taken to complete the test per individual is expected to be long
- High cost in training health professionals to administer this test and high cost in the administration of this test (in relation to the time taken to measure facial features).

CONCLUSIONS

Summary of judgements

CRITERIA	SUMMARY OF JUDGEMENTS						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Large**	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	Low	**Moderate**	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High		No included studies	
CERTAINTY OF THE EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	High		No included studies	
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High		No included studies	
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High		No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	**No**	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Judgement

☒ We recommend against the intervention or for the comparison	☐ We suggest against the intervention or for the comparison	☐ We suggest either the intervention or the comparison	☐ We suggest the intervention	☐ We recommend the intervention

Recommendation

We recommend against the use of the FAS diagnostic checklist to screen for individuals at risk of FASD in Western Australia (strong recommendation based on low certainty in the evidence).

Justification

The recommendation was based on the overall low quality of evidence concerning the effects of the FAS diagnostic checklist in the screening and management of FASD (with and without sentinel facial features). The evidence concerning the resources required to implement the FAS diagnostic checklist in Australia is limited in the current literature. Furthermore, the FAS diagnostic checklist was not considered to be acceptable and feasible for use in Western Australia.

Considerations

The Advisory Group suggested that the use of FAS diagnostic checklist may not be suitable in Western Australia due to measurements of facial features may not be acceptable in some cultures, time taken to complete the test is expected to be long, parents may have difficulties truthfully disclosing alcohol consumption during pregnancy, high cost in relation to training and administration of this test, and the difficulty in detecting individuals at risk of FASD without sentinel facial features. However, the Advisory Group noted that this test may have an application for targeted screening in subgroups

(e.g., individuals in care, correctional, special education, specialised clinical and Aboriginal populations).

Research priorities

No further research directions suggested regarding the use of the FAS diagnostic checklist as a screening tool for FASD.

GRADE evidence profile for Recommendation 8

Sensitivity: 0.89 | Specificity: 0.72

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Quality of evidence
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.77%	
True positives (patients with FAS/ PFAS)	1 study 352 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	7	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having FAS/PFAS)								1	
True negatives (patients without FAS/PFAS)	1 study 352 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	711	⊕⊕⊕◯ MODERATE
False positives (patients incorrectly classified as having FAS/PFAS)								281	

Explanations

[a]Indirectness was assessed using QUADAS-2. Studies demonstrated unclear risk in patient selection due to the inclusion of only individuals with fetal alcohol syndrome and partial fetal alcohol syndrome, and high risk in applicability in reference standard due to the reference test concerning only individuals with fetal alcohol syndrome but not those with fetal alcohol spectrum disorder.

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