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1267

Final Decision  
Analytic Protocol  
(DAP) to guide the  
assessment of HbA1c  
testing for the  
diagnosis of diabetes  
mellitus

1267 - Final DAP

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January 2013

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## Table of Contents

<b>MSAC and PASC</b> .....	<b>3</b>
<b>Purpose of this document</b> .....	<b>3</b>
<b>Purpose of application</b> .....	<b>4</b>
<b>Background</b> .....	<b>4</b>
Current arrangements for public reimbursement .....	4
Regulatory status .....	4
<b>Intervention</b> .....	<b>5</b>
Description .....	5
Delivery of the intervention .....	5
Prerequisites .....	6
Co-administered and associated interventions .....	6
<b>Listing proposed and options for MSAC consideration</b> .....	<b>6</b>
Proposed MBS listing .....	6
Clinical place for proposed intervention .....	9
<b>Comparator</b> .....	<b>12</b>
<b>Outcomes</b> .....	<b>14</b>
<b>Summary of PICO to be used for assessment of evidence (systematic review)</b> .....	<b>16</b>
<b>Clinical claim</b> .....	<b>17</b>
<b>Outcomes and health care resources affected by introduction of proposed intervention</b> .....	<b>19</b>
Outcomes for economic evaluation.....	19
Health care resources .....	19
<b>Proposed structure of economic evaluation (decision-analytic)</b> .....	<b>21</b>
<b>References</b> .....	<b>23</b>

## MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Australian Government Health Minister to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Commonwealth Minister for Health and Ageing on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

## Purpose of this document

This document is intended to provide a decision analytic protocol (DAP) that will be used to guide the assessment of HbA1c testing for the diagnosis of diabetes mellitus. The draft protocol has been finalised after inviting relevant stakeholders to provide input. This protocol will provide the basis for the assessment of the intervention.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

- Patients** – specification of the characteristics of the patients or population in whom the intervention is to be considered for use;
- Intervention** – specification of the proposed intervention;
- Comparator** – specification of the test and/or therapy most likely to be replaced by the proposed intervention; and
- Outcomes** – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention.

## Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of HbA1c testing for diagnosis of diabetes mellitus was received from the Australian Diabetes Society, the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists by the Department of Health and Ageing in May 2012. The proposal relates to four new items on the MBS. HbA1c testing for the *management* of established diabetes is currently reimbursed through the MBS (MBS item 66551, and 66554 in pregnant patients). This proposal relates to using the same test as a *diagnostic* tool for diabetes mellitus, in patients with previously undiagnosed diabetes.

Adelaide Health Technology Assessment (AHTA), University of Adelaide, as part of its contract with the Department of Health and Ageing, drafted this decision analytic protocol to guide the assessment of the safety, effectiveness and cost-effectiveness of HbA1c testing to diagnose diabetes. The assessment will inform MSAC's decision-making regarding public funding of the intervention.

## Background

### Current arrangements for public reimbursement

Currently the HbA1c test is used to monitor the effectiveness of diabetes treatment (long-term blood glucose) in people with established diabetes, and is funded under item 66551 (66554 in pregnant patients). The current methods for diagnosing diabetes include random or fasting plasma glucose tests and, in some patients, an additional oral glucose tolerance test. The plasma glucose tests are reimbursed under item 66500 and the oral glucose tolerance tests are reimbursed under item 66542 (66545 or 66548 for diagnosis of gestational diabetes in pregnant women).

### Regulatory status

An assay designed for HbA1c testing is classified as an in vitro diagnostic medical device (IVD). IVDs are, in general, pathology tests and related instrumentation used to carry out testing on human samples, where the results are intended to assist in clinical diagnosis or in making decisions concerning clinical management (Therapeutic Goods Administration 2011).

The Therapeutic Goods Administration (TGA) regulatory framework for IVDs changed in July 2010. All IVDs now require premarket approval by the TGA (unless they were offered prior to July 1 2010 in Australia where a transition period up to 2014 applies). As the test was available before July 1 2010, it is exempt from registration on the register of therapeutic goods in Australia, however will be required to be registered by 2014. The applicant states that the test is a Class 2 IVD, or could be a Class 3 IVD; this needs confirmation.

## Intervention

### Description

The test of HbA1c is a biochemical test that measures the level of glucose in the blood over a 2-3 month period; that is, it is a measure of long-term blood glucose. Currently the test is used and publicly funded for the management of diabetes, to monitor the effectiveness of treatment for hyperglycaemia. The proposal is to use the test in the diagnosis of diabetes in previously undiagnosed people; predominantly to test for type II diabetes. In type I diabetes, the clinical presentation is usually clear and this form of diabetes is not usually diagnosed in asymptomatic patients. The proposal, whilst it does not explicitly exclude pregnant women, does not apply to this population, as alternative tests are recommended for the detection of gestational diabetes by the Australasian Diabetes in Pregnancy Society in their guidelines (Hoffman 2002). Thus pregnant women are not considered further in this protocol.

Patients with HbA1c results of 6.5% or above would be considered to have diabetes, which is consistent with the diagnostic cut-offs recommended by the World Health Organisation (World Health Organisation. 2011). This cut-off was determined based on cross-sectional data examining the rates of diabetic retinopathy at different levels of HbA1c (Colagiuri et al 2011).

### Delivery of the intervention

The test would be used as part of the case detection pathway for diabetes mellitus. The test would be performed in NATA accredited laboratories, consistent with item 66551, or alternatively performed at the point-of-care (PoC), as has been funded under the Quality Assurance for the Aboriginal and Torres Strait Islander Medical Services (QAAMS). Medical practitioners would order the test under the same circumstances they would order the existing diabetes diagnostic tests: fasting blood glucose and (in some patients) the oral glucose tolerance test. There are NHMRC guidelines (Colagiuri et al 2009a) to follow for case detection of Type II diabetes, and the HbA1c test would be used in place of the random blood glucose or fasting blood glucose test and the oral glucose tolerance test (where required) in the case detection pathway. Re-testing in subjects without diabetes would occur at relevant time points according to the guidelines. PASC suggests that HbA1c be examined for diagnosis with a minimum frequency of once per year but only allowing for a confirmatory test within 12 months if the initial result is > 6.5% or the patient has diabetic symptoms.

Should diabetes be diagnosed, subsequent HbA1c tests would then be conducted as part of the management of the disease and billed under item 66551 (Colagiuri et al 2009b).

## Prerequisites

To ensure high quality results, the applicant has recommended that the test be undertaken within an accreditation framework, including NATA accredited laboratories and accredited point-of-care facilities.<sup>1</sup> The geographical spread of such facilities would need to be considered when implementing the test for diagnosis. The test is already commonly performed for the management of diabetes; however it is not known whether the test as performed in the laboratory is reflective of the geographical spread of the population with the disease. The World Health Organisation's (2011) abbreviated report 'Use of glycosylated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus' states that the conditions for processing of blood for the HbA1c test are less stringent than for glucose, meaning that it may be easier to transport and store blood for the HbA1c test (World Health Organisation. 2011). This protocol outlines two scenarios which should be assessed: testing both within an accredited laboratory and at the point-of-care, conducted by a doctor.

## Co-administered and associated interventions

The applicant suggests that using HbA1c testing for the diagnosis of diabetes will lead to fewer plasma glucose tests and oral glucose tolerance tests (GTT), due to the relative simplicity and convenience of the HbA1c test compared to the other tests. The HbA1c test requires no patient preparation, whilst both fasting plasma glucose and GTT require patients to fast, and GTT involves a preparatory diet for 72 hours prior to the test as well as having to take the glucose load, which can be unpalatable to some and cause side effects. However it is not expected that using the HbA1c test for diagnosis will change the management of diabetes in patients diagnosed using the method. When HbA1c testing is delivered at the point-of-care, testing and receipt of results may occur within the same visit, resulting in one fewer general practitioner consultations compared to laboratory-based HbA1c testing.

## Listing proposed and options for MSAC consideration

### Proposed MBS listing

The proposed listing is for four new items for quantitation of HbA1c (glycosylated haemoglobin) performed for the diagnosis of diabetes (Table 1). Tests conducted in a NATA accredited pathology laboratory, are proposed to sit alongside the HbA1c test for management of diabetes (Category 6: Pathology Services), MBS item 66551. Tests conducted by a doctor at the point-of-care are proposed to sit within Category 2: Diagnostic Procedures and Investigations, and do not require NATA accreditation. PASC preferred two items be defined within each category:

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<sup>1</sup> Australian Diabetes Society/Royal College of Pathologists of Australasia/Australasian Association of Clinical Biochemists HbA1c committee, public consultation submission

- initial testing, which would be limited to one test per year for an asymptomatic patient, with repeat testing allowed if the patient is symptomatic and the first test result is negative, and
- confirmatory testing, which would be limited to patients in which the initial test is positive.

Due to these proposed limitations, it is not possible to amend the existing HbA1c testing item for management of diabetes, as this has different limitations (four times per year, per patient). The applicant has recommended a fee the same as the existing HbA1c item.

The applicant has also proposed that in the existing item for HbA1c, the term 'glycosylated' is replaced with 'glycated', better reflecting current terminology.

Table 1: Proposed MBS item descriptor for HbA1c testing for diagnosis of diabetes

Category 6 – Pathology Services Group P2- Chemical	
MBS xxxxx	Quantitation of HbA1c (glycated haemoglobin) performed for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines Fee: \$16.80 Limit: one per person, per year if the patient is asymptomatic, but would allow a repeat test if the patient is symptomatic and the first test result is negative.
Category 6 – Pathology Services Group P2- Chemical	
MBS xxxxx	Confirmation of HbA1c (glycated haemoglobin) quantitation performed for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines Fee: \$16.80 Limit: one per person, per year upon an initial positive test
Category 2 – Diagnostic Procedures and Investigations	
MBS xxxxx	Quantitation of HbA1c (glycated haemoglobin) performed on an analyser accredited in a recognised external Quality Assurance program for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines Fee: \$16.80 Limit: one per person, per year if the patient is asymptomatic, but would allow a repeat test if the patient is symptomatic and the first test result is negative.
Category 2 – Diagnostic Procedures and Investigations	
MBS xxxxx	Confirmation of HbA1c (glycated haemoglobin) quantitation performed for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines

Fee: \$16.80

Limit: one per person, per year upon an initial positive test

The proposed intervention is for the diagnosis of diabetes mellitus, essentially type II diabetes. Diabetes is a common chronic disease in Australia and contributes to mortality and morbidity through microvascular (eg retinopathy, neuropathy) and macrovascular (eg stroke, heart disease) complications, and can result in blindness, kidney failure and limb amputation. Effective therapy can reduce the complications associated with diabetes, and the earlier this therapy is initiated, the better the outcomes for the patient (Holman et al 2008). Thus case detection of diabetes at the earliest stage is recommended (Colagiuri et al 2009a).

There are NHMRC guidelines for practitioners to follow for the case detection of diabetes, and these guidelines suggest that case detection should be done on an opportunistic basis (most commonly in GPs rooms)(Colagiuri et al 2009a). Individuals who are judged to be at risk, either through a score of  $\geq 12$  on the AUSDRISK assessment tool, or because they belong to one of the following population groups with a known higher risk:

- people with impaired glucose tolerance or impaired fasting glucose;
- women with a history of gestational diabetes mellitus;
- women with a history of polycystic ovary syndrome;
- people presenting with a history of a cardiovascular disease event (e.g. myocardial infarction, stroke); and
- people on antipsychotic medication,

are recommended to be tested for diabetes (Colagiuri et al 2009a).

The proposed HbA1c test for the diagnosis of diabetes will be used in this same population, and will be used in place of the plasma glucose test and where necessary, the GTT. The Applicants suggest one possible exception to this, the population subgroups with haemoglobinopathies or red cell turnover disorders. It has been suggested that HbA1c testing may not be as accurate in this subgroup (International Expert Committee 2009; World Health Organisation. 2011), and the existing test strategies will remain in place for these subgroups. PASC has requested that population subgroups in whom HbA1c testing is unsuitable be explicitly considered in the assessment of evidence. The assessment of evidence would need to define the characteristics of such patient types, and give advice on how such patients should be investigated, including whether to restrict the current



diagnostic strategy to these subgroups alone. Subgroups suggested by IVD Australia include:<sup>2</sup>

- patients with suspected impaired glucose tolerance or impaired fasting glucose
- women with a history of gestational diabetes
- women with polycystic ovary syndrome
- patients on antipsychotic medication
- patients who resist venipuncture
- patients with haemoglobinopathies or red cell turnover disorders
- patients with limited access to HbA1c testing due to remoteness

While the HbA1c test is proposed to replace plasma glucose test and GTT in the diagnosis of diabetes, the test has not been designed to diagnose related conditions such as glucose intolerance and impaired fasting glucose.

### **Clinical place for proposed intervention**

The proposed intervention will form part of case detection in diabetes. Currently case detection, according to NHMRC guidelines, is performed through a three stage process of risk assessment and two blood tests (one plasma glucose test followed by confirmatory tests, either: another plasma glucose test on a separate occasion; or, a glucose tolerance test). In some patients, a third test may be required (if the initial plasma glucose test suggests diabetes, and the follow-up plasma glucose test is equivocal, then the patient should have a GTT). The diagnostic algorithm of current practice based on the NHMRC Guidelines diagnostic pathway {Colagiuri, 2009 #1} is described in Figure 1. The addition of HbA1c testing in patients with confirmed diabetes to assess severity is not part of the NHMRC case detection Guidelines {Colagiuri, 2009 #1} however, it is recommended in the NHMRC blood glucose control guidelines that HbA1c measurements be used to assess long term blood glucose control {Colagiuri, 2009 #15}. It is therefore reasonable that an initial HbA1c test would be performed in those patients diagnosed by the current case detection methods, which would not be required if the patient has undergone the HbA1c test as part of diagnosis.

The applicant proposes that fewer general practice consultations will be required if the HbA1c test is used for diagnosis. This is based on the need for the patient to return to the doctor to receive test results at least twice under current arrangements (after the diagnostic plasma glucose test and confirmatory test/s); the patient may need to revisit the general practitioner (GP) more times if the first results are equivocal. The applicant has also suggested that once the diagnosis is made, the patient needs to have a HbA1c test to

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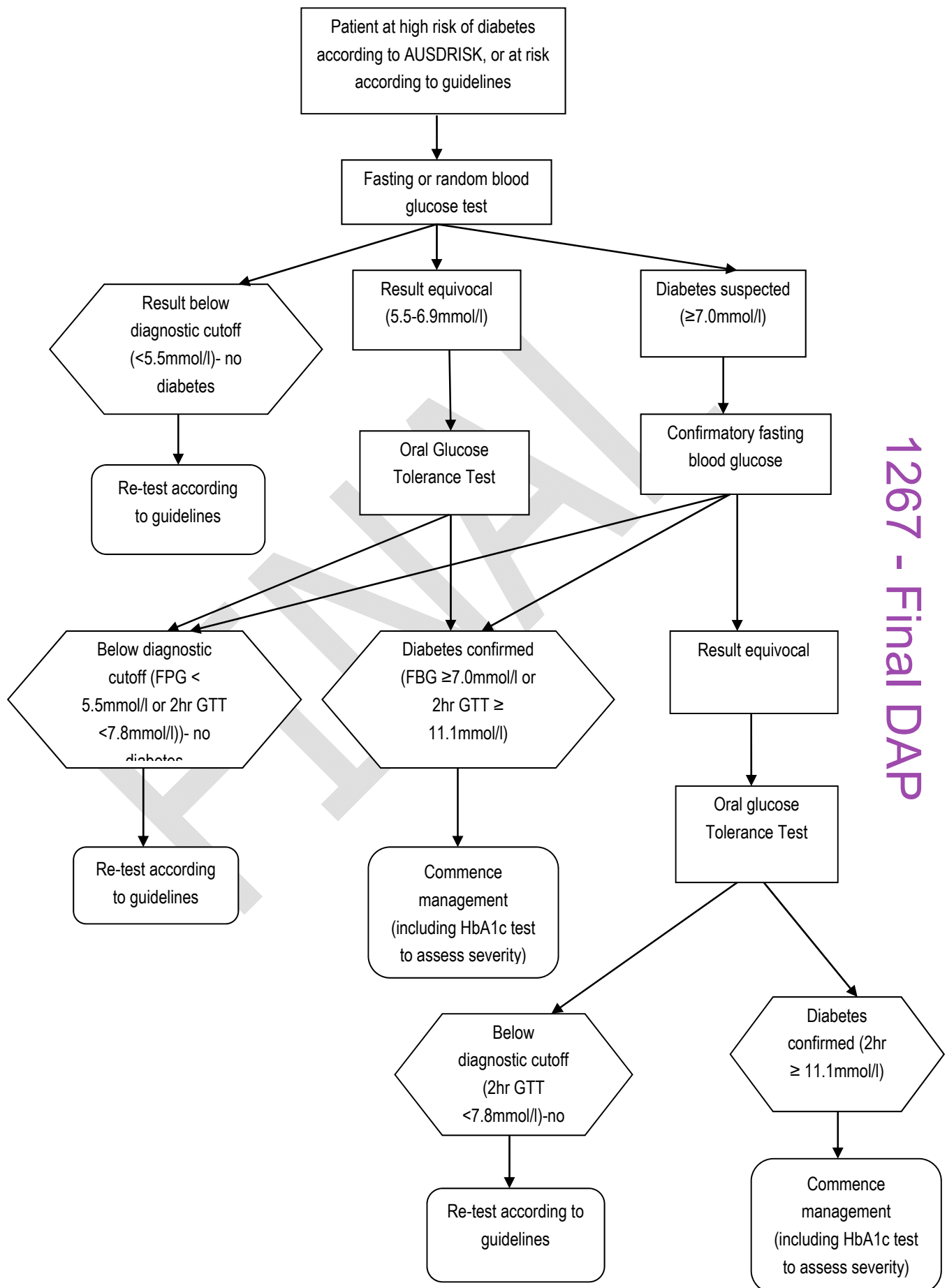
<sup>2</sup> IVD Australia, public consultation submission

assess severity and enable the practitioner to implement an appropriate management plan. The applicant claims that fewer return visits to the practitioner will be required if HbA1c is used as the diagnostic test, as it diagnoses and assesses severity in the one test, enabling the practitioner to enact management on the confirmatory test return visit. This could result in cost savings for the MBS by reducing the number of consultations. Where HbA1c testing is conducted at the point-of-care, the number of consultations may be reduced further, as testing and receipt of results may occur within the same visit. Figure 2 shows the diagnostic pathway as proposed by the applicant using HbA1c as the diagnostic test.

The diagnostic pathway will rely on the guidance given to practitioners by groups such as the Australian Diabetes Society (or new NHMRC Guidelines) should the HbA1c test become available for the diagnosis of diabetes. This will be particularly important if a patient has one HbA1c test in the diagnostic range and the confirmatory test in the no diabetes range; the applicant has suggested a 'two out of three' rule (ie two tests positive for diabetes out of three) to overcome this issue (this will have cost ramifications). This also applies to the current diagnostic regimen and this is dealt with within the Guidelines (Colagiuri et al 2009a).

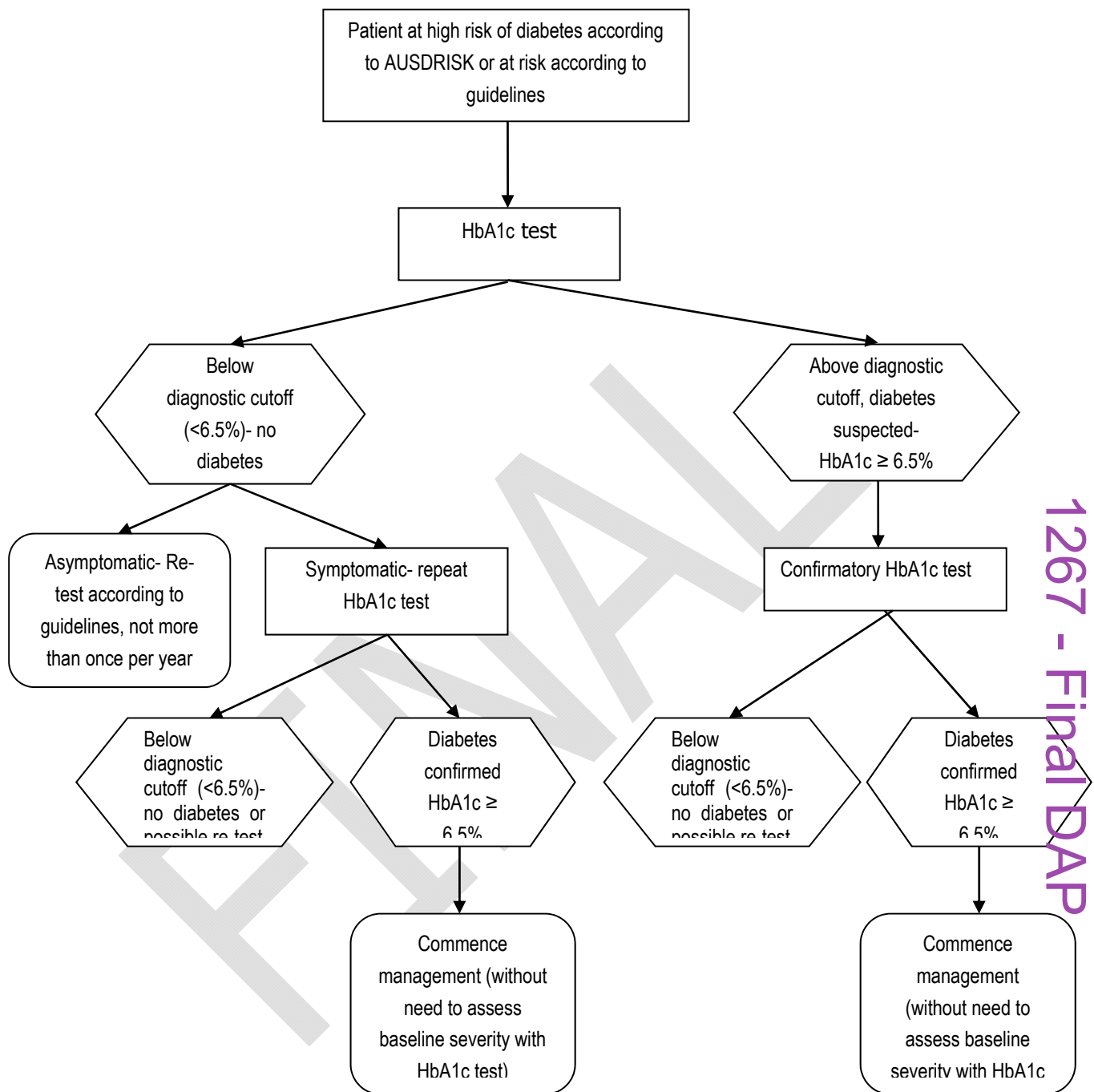
PASC noted that it is important to limit the frequency of testing, because there is the potential for a perverse incentive to more frequently order the HbA1c test, in case this identifies more patients to be eligible for the current diabetes service incentive payments (SIP) for the management of established diabetes. PASC considered that the assessment of evidence needs to provide evidence to assess the suitability of the nominated frequency of testing and also the nominated HbA1c threshold of  $\geq 6.5\%$  as being positive for diabetes.

Figure 1: Current diagnostic algorithm according to NHMRC Guidelines



1267 - Final DAP

Figure 2: Proposed diagnostic algorithm using HbA1c test for diagnosis



1267 - Final DAP

### Comparator

The correct comparators for the HbA1c test are fasting or random plasma glucose tests and oral glucose tolerance tests, where necessary (Colagiuri et al 2009a). MBS item descriptors for the comparators are listed in Table 2. According to the pathway at Figure 1 and based on the NHMRC guidelines, once a patient has been screened for diabetes risk using the AUSDRISK instrument and scored  $\geq 12$ , or if they are otherwise indicated as at risk, they should undergo a fasting or random plasma glucose test. If the results of this test indicate a

diagnosis of diabetes, then the test is repeated on another day for confirmation of the results. If the results of the first or second blood glucose test are equivocal, then the patient should undergo an oral glucose tolerance test to confirm the diagnosis. PASC noted that fasting blood glucose and the oral glucose tolerance test are time intensive tests, placing a high demand on patients, and are consequently associated with poor adherence levels. The proposed new item would be undertaken on the same patients (those identified as at risk of diabetes according to AUSDRISK or according to guidelines), in the same settings.

Table 2: MBS item descriptors for current diagnostic tests (Fees at 1<sup>st</sup> January 2013)

Category 6- Pathology Services Group P2- Chemical	
MBS 66500	<p>Quantitation in serum, plasma, urine or other body fluid (except amniotic fluid), by any method except reagent tablet or reagent strip (with or without reflectance meter) of: acid phosphatase, alanine aminotransferase, albumin, alkaline phosphatase, ammonia, amylase, aspartate aminotransferase, bicarbonate, bilirubin (total), bilirubin (any fractions), C-reactive protein, calcium (total or corrected for albumin), chloride, creatine kinase, creatinine, gamma glutamyl transferase, globulin, glucose, lactate dehydrogenase, lipase, magnesium, phosphate, potassium, sodium, total protein, total cholesterol, triglycerides, urate or urea - 1 test</p> <p>Fee: \$9.70</p>
MBS 66542	<p>Oral glucose tolerance test for the diagnosis of diabetes mellitus that includes:</p> <ul style="list-style-type: none"> <li>(a) administration of glucose; and</li> <li>(b) at least 2 measurements of blood glucose; and</li> <li>(c) (if performed) any test described in item 66695</li> </ul> <p>Fee: \$18.95</p>

In association with the diagnosis of diabetes, patients would be required to consult general practitioners. The costs associated with this should be taken into account, as the number of consultations required varies between pathways and scenarios.

Following a diagnosis of diabetes, patients who are diagnosed as having diabetes by fasting blood glucose and oral glucose tolerance tests would be required to undertake a HbA1c test to assess the severity of diabetes, as part of the management of the disease (claiming MBS item 66551 for testing in a NATA-accredited laboratory, or item 73840 in a QAAMS-accredited Aboriginal and Torres Strait Islander health and medical centre).

Table 3: MBS item descriptors for associated consultations and HbA1c test for management (Fees at 1<sup>st</sup> January 2013)

Category 1- Professional Attendances	
MBS 23	
Consultation at consulting rooms	
Fee: \$36.30	
Category 6 - Pathology Serviced	
MBS 66551	
Quantitation of glycosylated haemoglobin performed in the management of established diabetes - (Item is subject to rule 25)	
Fee: \$16.80	
(QAAMS project participants only)	
MBS 73840	
Quantitation of glycosylated haemoglobin performed in the management of established diabetes - each test to a maximum of 4 tests in a 12 month period.	
Fee: \$14.55	

## Outcomes

Diagnostic accuracy will be compared between the proposed test and the current testing regime. The reference standard for determining diagnostic accuracy is retinopathy (as a diabetes-specific health outcome, which was used to determine the diagnostic cutoff). In addition to comparisons against the reference standard, the submission should also include concordance data between HbA1c testing strategy and the current diagnostic testing strategy.

Diagnostic accuracy and effectiveness:

Sensitivity, specificity, positive predictive value, negative predictive value, false positive rate, false negative rate, psychological consequences of incorrect results, need for re-testing.

Safety:

Test-related adverse events, physical or psychological harm from testing.

Other outcomes to consider, including change in management:

Currently, the diagnostic criteria in the NHMRC Guidelines are the same as those proposed by WHO and based on the 'glycaemic levels associated with a substantially increased risk of

diabetes-associated microvascular complications, particularly retinopathy, above these levels' (Colagiuri et al 2011). It is known that using HbA1c rather than using fasting plasma glucose results in fewer people being diagnosed with diabetes. The implications for this will need to be considered in the assessment, in particular:

- How many individuals are discordant for diabetes diagnosis when tested with either the proposed or current regime, that is, diagnosed using plasma glucose but not using HbA1c, or diagnosed using HbA1c but not plasma glucose?
- What are the potential ramifications for the management and follow-up of individuals who are undiagnosed by either method?
- Are there any differences in patient health outcomes (e.g. retinopathy), when diagnosed using the different strategies?

As the HbA1c test is more appealing to individuals, given its greater acceptability and no requirement for fasting or consuming a glucose load, it is possible that more people may actually be tested. Point of care testing is further convenient, allowing results to be given in the same consultation as the test is performed. This means that the number of people diagnosed with diabetes may not change, despite the HbA1c test diagnosing fewer people per number tested. In light of this, the assessment should also consider the following outcomes for each testing regime:

- Patient acceptability and satisfaction
- Patient convenience
- Test turnaround times
- Number of patients tested
- Characteristics of patients tested
- Number of patients tested per case of diabetes detected
- Number of patients tested per case of diabetes treated
- Cost of testing per case of diabetes detected
- Cost of testing per case of diabetes treated.

The HbA1c test is unable to detect impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). Should HbA1c replace the current testing regime, this subgroup of the population, who are known to be at risk of progressing to diabetes, would not be identified. This would have ramifications for retesting guidelines, where currently people with IGT or IFG are retested on a yearly basis, compared to those without diabetes who are retested 3-yearly. Therefore the assessment should also consider:

- Consequences for the population not identified as having IGT or IFG and therefore not identified as at risk of progression to diabetes.

## Summary of PICO to be used for assessment of evidence (systematic review)

Table 4 provides a summary of the PICO used to:

- (1) define the question for public funding,
- (2) select the evidence to assess the diagnostic accuracy and safety of HbA1c testing for diagnosis of diabetes, and outcomes relevant to the management of the populations diagnosed by each testing regime;
- (3) provide the evidence-based inputs for any decision-analytical modelling to determine the cost-effectiveness of HbA1c testing in the diagnosis of diabetes.

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Table 4: Summary of PICO to define research questions that assessment will investigate

Patients	Intervention	Comparator	Reference standard*	Outcomes to be assessed
People at high risk of diabetes, as determined by the AUSDRISK screening tool or according to NHMRC guidelines	HbA1c test, followed by confirmatory HbA1c test if first result indicated diabetes, or repeated if symptomatic patient has negative result <i>Scenarios:</i> 1. Test analysed in an accredited laboratory 2. 'Point of care' test analysed in clinical setting	Fasting blood glucose or random blood glucose, followed by a confirmatory fasting blood glucose if diabetes suspected or an oral glucose tolerance test if first result indefinite	Retinopathy	Safety Diagnostic accuracy Change in patient management Cost-effectiveness Patient-relevant health outcomes (including retinopathy and other diabetes complications) Patient satisfaction and acceptability Patient convenience Test turnaround times Number of patients tested Characteristics of patients tested Number of patients tested per case of diabetes detected Number of patients tested per case of diabetes treated Cost of testing per case of diabetes detected Cost of testing per case of diabetes treated.
<p><b>Questions</b></p> <ol style="list-style-type: none"> <li>Does HbA1c testing in an accredited laboratory have similar diagnostic accuracy to the current testing strategy for diagnosis of diabetes mellitus?</li> <li>Does HbA1c testing performed at the point of care have similar diagnostic accuracy to the current testing strategy for diagnosis of diabetes mellitus?</li> <li>How does HbA1c testing performed in an accredited laboratory compare with testing performed at the point of care, in regards to analytical validity, reliability, costs, and practical issues of implementation, including quality assurance issues?</li> <li>Given that HbA1c detects fewer people in the diagnostic range, what are the ramifications for diabetes management?</li> <li>Is there any health benefit to patients in being diagnosed by HbA1c compared to being diagnosed by the current testing strategy for diagnosis of diabetes mellitus?</li> <li>How suitable are the nominated frequency of testing and the nominated HbA1c threshold of <math>\geq 6.5\%</math> as being positive for diabetes?</li> </ol>				

\*NB: In the absence of good quality evidence comparing the HbA1c testing strategy and the comparative testing strategy against the reference standard, PASC determined that the HbA1c testing strategy should be compare the concordance between the two testing strategies.

### Clinical claim

The applicant's clinical claim relates to the practical aspects of HbA1c in relation to the other diagnostic tests. The applicant claims that testing HbA1c for the diagnosis of diabetes will be more efficient and acceptable to patients as it requires no preparation, can be undertaken at any time of the day and has no side effects apart from the possible side effects of taking blood (which are also part of the risk for standard blood glucose testing). This is in

comparison to current diagnostic tests which require fasting and, for those needing a GTT, a time commitment, preparatory diet, several blood drawings and possible side effects from the glucose load such as nausea. The applicant claims that because of the convenience of the HbA1c test, it is likely to result in fewer plasma glucose tests and fewer GTT being conducted. The applicant also claims that using the HbA1c test will result in fewer general practice consultations as the procedure for diagnosis is streamlined, enabling diagnosis of diabetes and assessment of severity in the one test.

The applicant has not made a clinical claim on the safety and effectiveness of the proposed test in comparison to the reference standard. Given that the proposed test is not intended to change the management of diabetes, but to streamline its diagnosis, the application has been interpreted as a non-inferiority comparison (see Table 5).

PASC noted that should the cost per patient tested using the HbA1c-based diagnostic strategy exceed that of the existing diagnostic strategy, evidence of an improvement in health outcomes for the population tested would be needed to generate to calculate an incremental cost-effectiveness ratio, enabling MSAC to consider whether the increase in costs is justified.

Table 5: Classification of an intervention for determination of economic evaluation to be presented

		Comparative effectiveness versus comparator				
		Superior		Non-inferior	Inferior	
Comparative safety versus comparator	Superior	CEA/CUA		CEA/CUA	Net clinical benefit	CEA/CUA
					Neutral benefit	CEA/CUA*
					Net harms	None <sup>^</sup>
	Non-inferior	CEA/CUA		CEA/CUA*	None <sup>^</sup>	
	Inferior	Net clinical benefit	CEA/CUA	None <sup>^</sup>	None <sup>^</sup>	
		Neutral benefit	CEA/CUA*			
Net harms		None <sup>^</sup>				

Abbreviations: CEA = cost-effectiveness analysis; CUA = cost-utility analysis

\* May be reduced to cost-minimisation analysis. Cost-minimisation analysis should only be presented when the proposed service has been indisputably demonstrated to be no worse than its main comparator(s) in terms of both effectiveness and safety, so the difference between the service and the appropriate comparator can be reduced to a comparison of costs. In most cases, there will be some uncertainty around such a conclusion (i.e., the conclusion is often not indisputable). Therefore, when an assessment concludes that an intervention was no worse than a comparator, an assessment of the uncertainty around this conclusion should be provided by presentation of cost-effectiveness and/or cost-utility analyses.

<sup>^</sup> No economic evaluation needs to be presented; MSAC is unlikely to recommend government subsidy of this intervention

## Outcomes and health care resources affected by introduction of proposed intervention

### Outcomes for economic evaluation

Considerations for the economic evaluation include: the number of HbA1c tests required to confirm a diagnosis of diabetes (two according to the applicant); the costs of the tests; and, the number of GP consultations required to make the diagnosis (reviewing test results and ordering confirmatory tests). Depending on the data available, it may be appropriate to measure quality-adjusted life years or another relevant indicator of quality of life.

PASC noted that the cost-effectiveness analysis would need to address a number of issues, including:

- the consequences for a shift in the spectrum of the disease for which treatment is initiated (noting that fewer patients are diagnosed early with the proposed pathway compared to the current diagnostic strategy, and the proposed strategy does not detect related conditions such as glucose intolerance and impaired fasting glucose);
- the change in health outcomes would only occur in the proportion of patients for which there would be a different diagnostic conclusions leading to a different treatment decision;
- given the progressive nature of diabetes, which means that subsequent HbA1c testing in the following years might exceed the proposed diagnostic threshold, the proposed intervention might only delay the diagnosis so the change treatment and treatment outcomes would be limited to that caused by the delay.

### Health care resources

Given that the populations selected for testing for diabetes are the same using both the proposed test and the comparator, the initial GP visit where diabetes risk is assessed is the same in both groups so is not considered as a difference in resources. The differences come by way of the tests themselves and the return visits to the GP to get results and receive orders for further tests.

Subsequent to the diagnosis of diabetes, the management of patients is expected to be the same between diagnostic pathways, with one exception. Those patients who are diagnosed without the use of HbA1c test would undergo the HbA1c test to assess severity of disease, prior to commencing treatment. Patients diagnosed using the Hba1c test would not be required to undergo this test separately, as assessment of severity occurred during the diagnosis phase. This would be associated with an additional patient episode initiation fee and GP consultation. Indigenous patients having their diabetes managed in Remote Health Centres with QAAMS registration are able to access HbA1c testing by point of care analysers

(MBS item 73840), so would have the additional fee for the test, but would not require the additional consultation to receive the results.

Table 6: List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
<b>Resources provided to deliver proposed intervention at an accredited laboratory</b>										
- Patient episode initiation fee	Pathology	Laboratory		1	6.00					6.00
- HbA1c test	Pathology	Laboratory		1	16.80					16.80
- GP consultation for results	GP	Outpatient		1	36.30					36.30
- Patient episode initiation fee if confirmatory test required	Pathology	Laboratory		1	6.00					6.00
- Confirmatory HbA1c test if required	Pathology	Laboratory		1	16.80					16.80
- GP consultation for results (initiate management)	GP	Outpatient		1	36.30					36.30
<b>Resources provided to deliver proposed intervention at point-of-care</b>										
- HbA1c test	GP	Outpatient		1	16.80					16.80
- Confirmatory HbA1c test if required	GP	Outpatient		1	16.80					16.80
- GP consultation for confirmatory results (initiate management)	GP	Outpatient		1	36.30					36.30
<b>Resources provided to deliver comparator (blood glucose followed by confirmatory tests, as below)</b>										
- Patient episode initiation fee <sup>3</sup>	Pathology	Laboratory		1	6.00					6.00
- Blood glucose test	Pathology	Laboratory		1	9.70					9.70
- GP consultation for results and order of confirmatory test	GP	Outpatient		1	36.30					36.30
<b>EITHER:</b>										
- Patient episode initiation fee	Pathology	Laboratory		1	6.00					6.00
- Confirmatory blood glucose test	Pathology	Laboratory		1	9.70					9.70
<b>OR:</b>										
- Patient episode initiation fee	Pathology	Laboratory		1	6.00					6.00

<sup>3</sup> Patient episode initiation items (Group P10 of the Pathology Services Table) fees range from \$2.40 to \$17.70 depending on the circumstances of collection. For the purposes of this DAP, a fee of \$6.00 is used.

1267 - Final DAP

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
- Oral glucose tolerance test	Pathology	Laboratory		1	18.95					18.95
ALL:										
- GP consultation for results of confirmatory blood glucose test or GTT	GP	Outpatient		1	36.30					36.30
Resources provided in association with comparator in those diagnosed (test performed in accredited laboratory)										
- HbA1c test for severity	Pathology	Laboratory		1	16.80					16.80
- Patient episode initiation fee	Pathology	Laboratory		1	6.00					6.00
- GP consultation for severity results and initiation of management	GP	Outpatient		1	36.30					36.30
Resources provided in association with comparator in those diagnosed (test performed at point-of-care)										
- HbA1c test for severity	Pathology	Laboratory		1	16.80					16.80

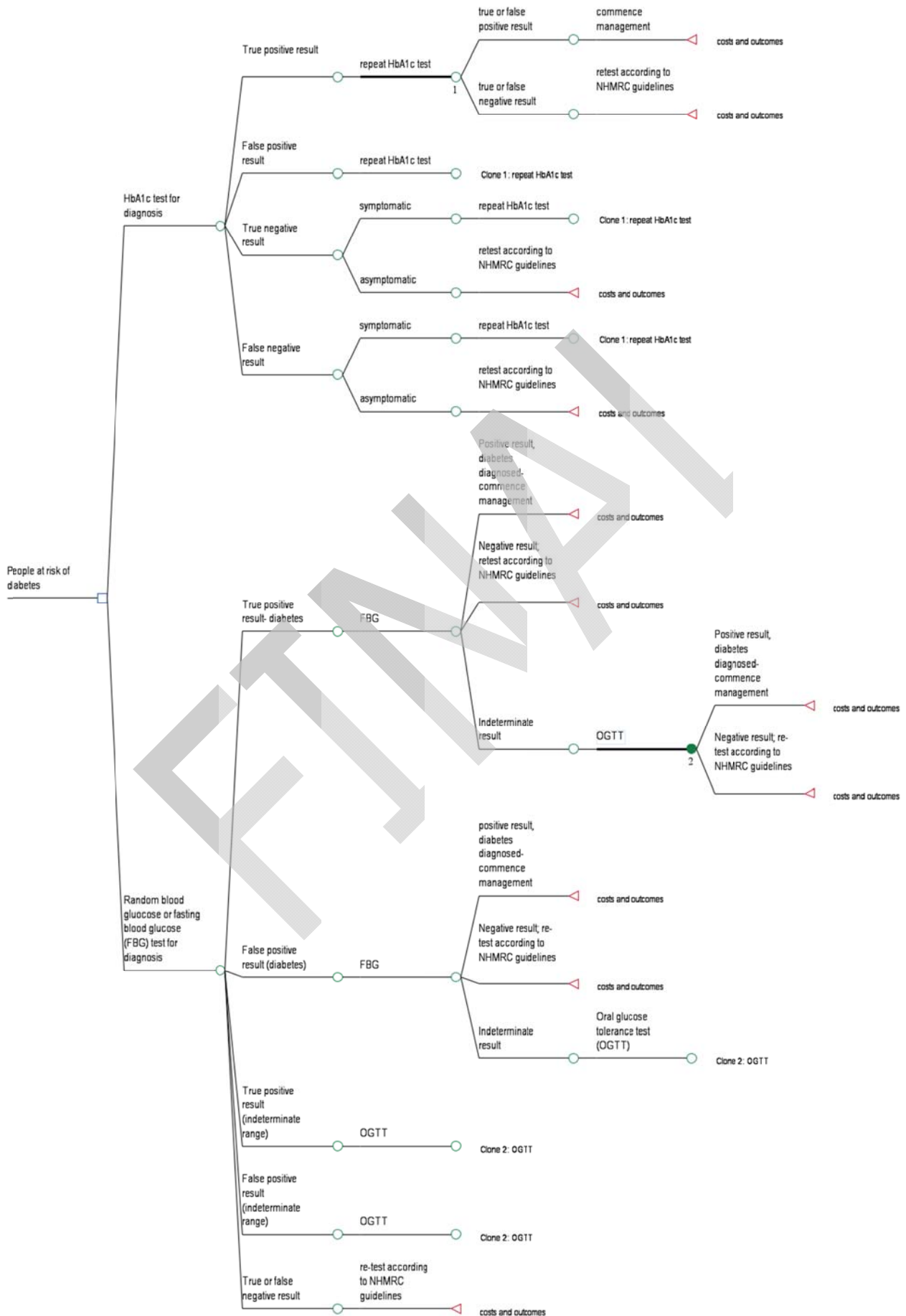
1267 - Final DAP

### Proposed structure of economic evaluation (decision-analytic)

The decision-analytic will compare the diagnostic accuracy of the proposed items (HbA1c testing) with current practice (a combination of plasma glucose testing and oral glucose tolerance testing where required). The algorithm is presented in Figure 3. PASC further requested that the scenarios of laboratory and point-of-care testing be compared in terms of analytical validity, reliability, cost and any practical issues of implementation, including the need to monitor point-of-care analyser performance.

Using HbA1c for diagnosis will not change diabetes management; it is an alternative way of diagnosing the condition, not managing it (with the exception of one fewer HbA1c tests prior to commencing management in those diagnosed). Should the diagnostic accuracy be similar to current diagnostic testing, there are several possible advantages of the HbA1c test, such as convenience and patient acceptability, which may result in more people having the test and therefore being diagnosed earlier in the course of the disease. However, it is known that fewer people are diagnosed using the HbA1c test, and this could have an effect on when management is initiated for people who go on to have a diagnosis of diabetes.

Figure 3: Decision-analytic for HbA1c for diagnosis of diabetes



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