Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1797 – Vibration-Controlled Transient Elastography (VCTE™) for identifying advanced fibrosis in patients with metabolic dysfunction-associated fatty liver disease

Applicant: **Health Technology Analysts Pty Limited**

Date of MSAC consideration: **27 November 2025**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application requesting public funding for a diagnostic test vibration-controlled transient elastography (VCTE™), delivered by FibroScan® devices, to detect advanced liver fibrosis (AF) in people with metabolic dysfunction-associated fatty liver disease (MAFLD) was received from the Health Technology Analysts Pty Limited by the Department of Health, Disability and Ageing. The ADAR used the terms VCTE and FibroScan interchangeably, while VCTE™ was primarily used in the Public Summary Document (PSD).

The ADAR proposed using VCTE™ as a follow-up to FIB-4 testing when risk of advanced liver fibrosis remains inconclusive, positioning it for use in both primary and specialist care settings.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC did not support public funding of Vibration-Controlled Transient Elastography (VCTE™) for identifying advanced liver fibrosis in patients with metabolic dysfunction-associated fatty liver disease (MAFLD). MSAC considered that the evidence presented did not demonstrate that the use of VCTE in patients with MAFLD would result in changes in clinical management and improve health outcomes. MSAC further considered that much of the evidence that was presented for other aspects of clinical effectiveness, such as test accuracy, was indirect, non-comparative and of low generalisability and applicability to the proposed testing scenario. MSAC noted that while procedure related safety concerns were negligible, there was a lack of evidence presented on potential safety issues relating to the clinical implications of false positive or false negative results. MSAC noted the high prevalence of MAFLD and the likely financial implications.

MSAC considered the use of an inappropriate comparator (abdominal ultrasound) and the limited evidence of improved clinical management resulted in the economic modelling and financial impact being highly uncertain. MSAC also considered that while the application positioned the use of VCTE in patients with MAFLD as a risk assessment tool, there is potential risk for it to be used inappropriately for monitoring liver fibrosis or for risk assessment or monitoring in other conditions which have not been supported by MSAC.

Consumer summary

This is an application from Medical Technologies Australia Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of a liver scan called "Vibration-Controlled Transient Elastography (VCTE)", which is used to detect liver damage, called "advanced fibrosis". The scan is for people with a condition called "metabolic-associated fatty liver disease (MAFLD)" and who have a score on the fibrosis index score of greater than 1.3.

MAFLD is caused by a build-up of fat in the liver. This can cause the liver to swell (inflammation) and become scarred (fibrosis) and hard. Advanced liver fibrosis can lead to cirrhosis - where the liver has developed scarring and damage. Cirrhosis can lead to serious problems like fluid buildup, infections, and liver failure. In some cases, people with cirrhosis need a liver transplant. MAFLD is also associated with an increased risk of developing diabetes, heart attack and stroke. Currently, MAFLD is managed mainly through lifestyle changes such as diet and exercise. There are currently no medicines available in Australia to specifically treat MAFLD.

VCTE is a non-invasive and painless test that uses soundwaves to detect how stiff the liver is. A probe is placed on the abdomen, similar to performing an ultrasound, and produces a numerical score called a liver stiffness measurement, shown in kilopascals (kPa). The liver stiffness measurement can suggest the degree of liver fibrosis, with higher results suggesting more severe fibrosis.

In this application, VCTE is proposed to be funded in the specialist setting where it is currently used by liver specialists, and also in the primary care setting, such as general practitioner (GP) clinics, so that GPs can work out whether patients need referral to a liver specialist. To work out whether someone needs VCTE™, people with MAFLD first need their fibrosis index score to be calculated. The fibrosis index score is calculated from the results of blood tests and works out whether someone might be at risk of liver fibrosis. People with fibrosis index scores of more than 1.3 would be recommended to have VCTE. Of those people tested with VCTE, those with a liver stiffness measurement less than 8 kPa could be ruled out from having advanced liver fibrosis. People with VCTE results of 8 kPa or higher may be at higher risk of advanced liver fibrosis and should be referred to a liver specialist for further assessment.

The applicant claimed that VCTE is a risk assessment tool that can be used in primary care settings (e.g. GP clinics) to identify people with MAFLD who may have advanced liver fibrosis. However, MSAC considered that the liver stiffness measurement cut-off of 8 kPa was too low and would lead to many people with normal livers being told they are at high risk of advanced liver fibrosis (also known as false positive results). This could mean that many people would be referred to a specialist unnecessarily, because they do not actually have advanced liver fibrosis. The application stated that using VCTE would lead to a decrease in unnecessary specialist referrals, but MSAC considered that the suggested cut-off of 8kPa could actually lead to more unnecessary referrals. MSAC was concerned about this, as more people visiting specialists when they do not need to, could be both costly and harmful. This potential harm was not explored in the application.

MSAC was also concerned that there was no evidence that having a VCTE scan would change the medical treatment of people with MALFD. MSAC considered that this also means that there is no evidence that having a VCTE scan would improve the health of people with MALFD.

MSAC could not determine whether using VCTE was good value for money. This was partly due to the issues with the clinical evidence mentioned above. MSAC could not advise the government about how much it would cost the MBS if VCTE were funded. MSAC noted the high number of people with MAFLD in Australia, and that funding VCTE was therefore likely to have large financial implications.

Consumer summary
MSAC considered that if this application is resubmitted, it would need to show evidence that using VCTE improves people's health. MSAC also noted that MAFLD is just one form of liver disease that can lead to advanced fibrosis (scarring) where VCTE can be used, and so for the purpose of equity, if the application is resubmitted it might be appropriate to include people with other forms of liver disease. This would mean extra evidence would be needed to show the benefits of using VCTE in these other liver conditions, as well as in MAFLD. **MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing** MSAC did not support listing VCTE to detect advanced liver fibrosis in people with MAFLD on the MBS. The clinical evidence did not show that VCTE improves the medical treatment of people with MAFLD, nor that it would improve their health. MSAC was concerned that there may be harms that were not addressed in the application. MSAC could not determine if the test was good value for money.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this application from Medical Technologies Australia Pty Ltd was for the MBS listing of Vibration-Controlled Transient Elastography (VCTE™/FibroScan®) to detect advanced fibrosis in people with metabolic-associated fatty liver disease (MAFLD), stratified by a previous fibrosis-4 (FIB-4) index score >1.3.

This was the first time that MSAC considered this application; however, MSAC recalled 2 similar previous applications:

- Application 1366 (2016; Transient Elastography at 50Hz for the diagnosis of Liver Fibrosis in patients with confirmed Hepatitis B or confirmed Hepatitis C). MSAC did not support this application because there was no compelling evidence that it improves patient outcomes by changing treatment decisions for either Hepatitis B or Hepatitis C.
- Application 1446 (2020; Hepascore test to diagnose and monitor liver fibrosis severity in chronic liver disease). MSAC did not support this application mainly because MSAC considered Hepascore had limited clinical utility over existing tests and is unlikely to improve clinical management or health outcomes for patients with chronic hepatitis B or C.

MSAC noted and welcomed consumer input from 7 organisations, 3 consumers and 5 health professionals, which was mostly supportive of public funding for VCTE for identifying advanced fibrosis in patients with MAFLD, although some feedback did not support the application in its current form.

MSAC noted that VCTE is an ultrasound-based technology that uses soundwaves to measure stiffness in the liver. It is safe, non-invasive and can be delivered by a technician. VCTE generates a single numerical measurement called a liver stiffness measurement (LSM), which is then assessed against LSM thresholds to either 'rule-in' or 'rule-out' whether a patient is at high risk of advanced fibrosis. This application proposes that, for people in primary care who have a FIB-4 score >1.3, a single LSM (measured by VCTE) threshold is used to both rule-in and rule-out referral to a specialist on the basis of risk of advanced fibrosis. If the LSM is <8 kPa, the patient is categorised as low risk, and would remain in primary care. If the LSM is ≥8 kPa, the patient is considered high risk and would be referred to a specialist for further management.

MSAC noted that VCTE may be performed in the clinic, rather than patients being referred to an imaging provider, although noted that the number of machines in primary care is currently very

small, across both GP clinics and community-based health centres. MSAC also considered that because the machine is costly, GP practices are unlikely to purchase the machine, meaning that access in primary care would remain limited.

MSAC noted the application initially proposed 2 PICO sets (population 1 for VCTE in primary care and population 2 for VCTE in specialist care), and that the proposed outcomes related to change in management were:

- time to test and accessibility
- equity of access and patient adherence
- reduced referrals to a specialist for population 1
- reduction in use of liver biopsy for population 2.

MSAC noted PASC's advice that a single population including all patients with MAFLD and a FIB-4 score > 1.3, regardless of the care pathway, would be appropriate, and that outcomes should include patient-related outcomes and the consequences of misclassification. MSAC noted that the applicant-developed assessment report (ADAR) did not incorporate this advice, as it included 2 PICO sets (although with a single proposed MBS item for use in both populations), and did not address patient-related outcomes or misclassification.

MSAC noted that the pre-MSAC response justified the use of abdominal ultrasound (US) as the comparator, stating that in the absence of an MBS-funded second-line non-invasive test, abdominal US is regularly used in practice by GPs for patients with suspected liver disease after an indeterminate FIB-4 result. However, MSAC agreed with ESC that US is not an appropriate comparator for VCTE, noting that US does not assess liver fibrosis severity and is not MBS-supported for use as a liver fibrosis test. MSAC considered that the clinical place of standard abdominal US is before FIB-4 scoring, not as a second-line test for liver fibrosis.

MSAC noted the proposed MBS item descriptor and considered that it required clear wording regarding restrictions on scope and frequency, to which the applicant had agreed in the pre-MSAC response. MSAC also considered that there was a high chance of unintended use in patients other than those with MAFLD, particularly in people with other liver diseases that can lead to cirrhosis, including those proposed in application 1366 which MSAC previously did not support. MSAC also considered that the proposed fee may be too high based on the short time required for the procedure and that a range of health professionals can be trained to perform the scan.

MSAC noted that the ADAR did not explicitly define the clinical claim, but referenced improvements to clinical outcomes. The ADAR stated that 'use of VCTE by GPs and liver specialists leads to superior effectiveness, and superior in terms of efficient use of healthcare resources to diagnose advanced fibrosis in patients with MAFLD [*sic*]'.

The clinical evidence presented was based on a linked evidence approach. MSAC noted there were no data presented on safety, but considered safety concerns related to the procedure itself were negligible. However, MSAC considered that test related safety due to misclassification had not been addressed, and the consequences of false positive and false negative results were not explored in the ADAR. MSAC noted from the evidence presented, which used a higher rule-in threshold than proposed in this application, that misclassification rates were high – for instance, the reported sensitivity rate of 66% would imply that more than 30% of patients tested would be misclassified as negative. The pre-MSAC response argued that 'in primary care, false positives lead only to specialist review and not to inappropriate treatment'. However, MSAC disagreed and considered that patients receiving a false positive result may be referred unnecessarily for specialist review, with implications for cost and safety. MSAC considered that the impact of misclassification should have been further explored in the ADAR.

Regarding clinical effectiveness, MSAC noted that while linked evidence was provided regarding diagnostic and prognostic accuracy there were several issues with this evidence.

In particular, MSAC noted that the evidence for diagnostic accuracy used a tertiary population with VCTE thresholds different to the ADAR's proposed threshold, making applicability to the primary care population considered in this application unclear. MSAC also considered that the issue of predictive values was not adequately addressed in the pre-MSAC response. MSAC noted that the data informing predictive values was based on a tertiary population which would have a different (likely higher) prevalence of liver fibrosis compared to a primary care population, and therefore the predictive values quoted in the ADAR were unlikely to be applicable to the primary care setting (due to the impact of prevalence on predictive values).

MSAC noted that there was no evidence presented in the ADAR to support changes in treatment decisions or clinical outcomes. MSAC considered that for investigative technologies it is the subsequent choice of clinical management that generates health outcomes, not the test results themselves, as implied in the ADAR.

MSAC noted that the single LSM threshold of 8 kPa was based on expert consensus guidelines, but was not supported by evidence in the literature. The evidence largely used 2 separate rule-in and rule-out LSM thresholds, with a rule-in threshold higher than 8 kPa. MSAC suggested that, per the evidence, incorporating a higher rule-in threshold, such as 12 kPa, may be more appropriate. MSAC considered that this was particularly relevant to primary care, where prevalence of liver fibrosis is low, and therefore using a lower threshold to identify patients at high risk of advanced liver fibrosis will lead to more patients being incorrectly identified as "high risk" (i.e. the false positive rate will be higher). MSAC noted that, during the applicant hearing, the applicant's representative stated that the proposed 8 kPa threshold was effectively being used only as a rule-out threshold, and was selected as a 'safe' cutoff; the applicant noted that patients referred to specialist care on the basis of an LSM ≥ 8 kPa would return to primary care if specialist assessment determined they did not have advanced liver fibrosis. However, MSAC considered that the proposed 8 kPa threshold would lead to excessive false positives, particularly in the primary care population, and unnecessary specialist referrals. MSAC considered that, since MAFLD was a slow-progressing disease, a higher cutoff that reduced false positive results would be preferred and would not negatively affect patient outcomes.

MSAC queried the Hayward et al. (2022) data, which demonstrated that 75–80% of participants were seen by a specialist regardless of whether or not they had VCTE. MSAC noted that although this trial appeared relevant for the application by demonstrating that VCTE resulted in a shorter time to diagnosis of severe liver disease, there did not appear to be a difference in referral pathways, contrary to what was claimed in the ADAR. At the hearing, the applicant's representative agreed with this interpretation, but clarified that the trial was designed to ensure that all participants were referred to a specialist at some point and was not designed to detect differences in referral pathways.

MSAC considered that the longitudinal accuracy evidence provided in the ADAR had poor applicability, as it did not assess the proposed sequential triage testing, management impact, or use the single 8.0 kPa LSM rule-in/rule-out threshold. In the hearing, the applicant's representative defended this approach, stating that the single threshold was sufficient to be used as a risk stratification tool. However, MSAC considered that the approach and in particular the lack of evidence regarding change in health outcomes did not provide MSAC with sufficient information to determine the appropriateness of public funding for VCTE.

MSAC noted that the application was for a device-specific listing. However, MSAC considered that there was no evidence presented in the ADAR to support an MBS item specifically for FibroScan/VCTE. MSAC noted the department's preference for device agnostic MBS items and to

align with this preference, the proposed technology could be defined as transient elastography (TE). In the hearing, the applicant's representative argued that only VCTE has validated thresholds and longitudinal data to support its use. The applicant noted that use of shear wave elastography (SWE) is not standardised, there are no validated universal cut-off values, and concerns about inter-vendor variability. While MSAC noted this argument, it considered that an item specifying TE would be more appropriate, also noting PASC advice that, if a device-specific item was pursued in the ADAR, evidence to justify limiting the test to a proprietary technology would need to be provided.

MSAC noted that the pre-MSAC response argued that the lack of comparative effectiveness or safety data relative to the standard of care (SoC) was common for long-term conditions where outcomes evolve slowly over years, and referred to the Mozes (2022) study for diagnostic accuracy. However, MSAC disagreed, stating that a linked evidence approach could be used to compare effectiveness and safety, and that the diagnostic accuracy data provided by Mozes (2022) is limited by its lack of comparative data.

MSAC acknowledged that, for some patients, the value of knowing that they might have advanced liver fibrosis may help them to better adhere to SoC lifestyle interventions. However, MSAC noted the lack of effective therapies specifically for MAFLD, leading MSAC to consider that currently, use of VCTE does not change patient management or outcomes. That is, management of patients with MAFLD, irrespective of fibrosis stage, primarily consists of lifestyle modifications and education, which appears unlikely to change with or without an LSM measured by VCTE.

MSAC noted that the economic evaluation was a cost-consequence analysis with test accuracy and cost per correct diagnosis as outcomes. The costs per correct diagnosis were consistently lower for VCTE than SoC, and were, in primary and specialist care respectively:

- $218.74 and $204.98 for VCTE
- $451.04 and $392.22 for SOC.

However, MSAC considered these results to be highly uncertain, because:

- There was no evidence presented to demonstrate a correct diagnosis would change clinical management or improve health outcomes.
- The US comparator was inappropriate and resulted in uncertain flow-on effects in the model. It was assumed that, in the comparator arm, 15% of patients with fibrosis-suggestive US findings would undergo a liver biopsy compared to only 5% of those with an increased liver stiffness as assessed by VCTE. However, these proportions were based on expert opinion and not further justified in the ADAR. The cost offsets associated with US, because it is an inappropriate comparator, will therefore not be realised.
- The model outputs indicated that there may have been issues with the model itself, the choice of outcomes, or the model assumptions. The ADAR nominated cost per correct diagnosis as a primary outcome, and indicated that a lower cost per correctly diagnosed patient is a positive outcome, which would be expected to correlate with improved testing accuracy. However, a sensitivity analysis showed that increased sensitivity of VCTE led to a higher cost per correct diagnosis.
- Assumptions used in the model were unjustified – for example, differing rates of liver biopsies in both arms favouring VCTE and the lack of a failure rate for VCTE.

MSAC noted that the financial impact was calculated using a mixed epidemiological and market-based approach, and the cost to the MBS was:

- $3,641,063 in year 1, increasing to $9,123,754 in year 6 in primary care
- $24,022,800 in year 1, decreasing to $10,885,142 in year 6 in specialist care.

MSAC considered these costs to be highly uncertain, because:

- Key assumptions, such as the uptake estimate (90% for patients who have a high FIB-4 score), are based on expert opinion only.
- The population size for testing is highly uncertain.
- Cost offsets may be overestimated (particularly given the cost offsets from the inappropriate use of US as a comparator).
- The total financial impact is estimated to be a cost saving in primary care, which is uncertain given concerns with model.

MSAC did not support MBS listing of VCTE™/FibroScan® to detect advanced fibrosis in people with MAFLD for the following reasons:

- There is a lack of evidence to support the clinical claim or a change in health outcomes due to use of VCTE. The evidence was drawn from tertiary populations, the VCTE threshold proposed for clinical decision making differed from the evidence, and the proposed testing strategy and outcomes were not supported by real-world evidence. MSAC considered the evidence provided to support a change in referral patterns was insufficient to suggest improved health outcomes, and there was no evidence provided for change in patient management.
- There was no comparative evidence presented.
- An inappropriate comparator (US) was used, affecting the validity of the economic evaluation and financial impact.
- The ADAR did not explore the impact of misclassifying liver fibrosis status on patient safety. The net benefit/harm across the entire proposed population is unknown.
- The economic model is unreliable for decision making. MSAC considered the cost offsets relating to the comparator will not be realised, given that US is an inappropriate comparator, and that the estimated total utilisation was based on expert opinion only.

MSAC advised that if this matter were to be reconsidered a resubmission should include the following:

- Evidence from the primary care population that shows changes in clinical management that lead to improved clinical outcomes due to VCTE testing, noting that lifestyle modification is standard for all MAFLD patients regardless of liver fibrosis status and there are currently no therapies available in Australia specifically to treat MAFLD.
- Evidence supporting the proposed testing strategy (FIB-4 followed by VCTE).
- Clinical evidence to support the claim of proprietary VCTE/FibroScan superiority over other devices that deliver transient elastography.
- Quantifying the effects of different LSM thresholds (such as a 12 kPa rule-in threshold) for VCTE that aligns with thresholds identified in the literature as being more appropriate for risk stratification. This would reduce the number of false positive results. While MSAC acknowledged that the 8 kPa threshold for VCTE aligns with expert consensus, this is not supported by the available evidence and the HTA process requires that the highest-quality evidence is used.
- Evidence on, and discussion of, misclassification rates and the consequences of false positives and false negatives.
- Discussion of appropriate FIB-4 cutoffs across different age groups (such as FIB-4 of 2.0 in adults aged >65 years), given that interpretation of FIB-4 values varies with age.
- A cost-utility analysis for the economic evaluation would be strongly preferred in order to take account of changes in health outcomes from improved risk stratification.

- To address issues of patient equity, consideration of other types of liver disease where VCTE technology could be beneficial, noting that evidence of improved patient outcomes would also be required for these other types of liver disease.

4. Background

The Medical Services Advisory Committee (MSAC) previously evaluated transient elastography (TE) under Application 1366 in March 2016. This application, submitted by Medical Technologies Australia Pty Ltd, sought a new Medicare Benefits Schedule (MBS) listing for TE at 50Hz to diagnose liver fibrosis in patients with confirmed chronic hepatitis B or C. Although MSAC acknowledged TE's safety and convenience over biopsy, it concluded that TE does not offer sufficient incremental benefit to justify public funding under the MBS. MSAC acknowledged that TE was being used in routine clinical practice by hepatologists, but it found little evidence that TE use leads to changes in treatment decisions or improved patient outcomes for patients with chronic hepatitis B (HBV) or hepatitis C (HCV).

MSAC also previously evaluated Hepascore under Application 1446 in November 2020. Hepascore, a serum-based fibrosis panel, is recognised in MAFLD consensus guidelines as a second-line test following FIB-4 for liver fibrosis assessment in patients with chronic HCV or chronic HBV. MSAC concluded that Hepascore offered limited additional clinical value over existing tests and was unlikely to meaningfully improve patient management or health outcomes for HBV or HCV. Furthermore, MSAC identified significant flaws in the economic model, rendering it unreliable for funding decisions. MSAC also noted that the proposed MBS fee was lower than the current charge by pathology providers, potentially leading to out-of-pocket expenses for patients.

Table 1 provides an overview of key concerns identified by MSAC in applications 1366 and 1446, with evaluation comments on how these concerns may apply to 1797.

Table 1 Summary of key matters of concerns regarding applications 1366 and 1446.

Component	Matter of concern	How the concern is relevant to current ADAR per the evaluation
PSD 1366		
TE's diagnostic value was unclear when compared to routine clinical assessment, not biopsy.	"MSAC considered that the most appropriate comparator for TE was clinical assessment rather than liver biopsy... MSAC noted that evidence comparing the diagnostic accuracy of TE with clinical assessment relied on four observational studies of varying quality... substantial uncertainty remained about the relative diagnostic accuracy of TE compared with the combination of tests as used in current clinical practice." (PSD 1366, pp.2-3).	Not applicable because population is different
Evidence came from tertiary settings; in primary care (intended setting), false positive results may be higher due to lower disease prevalence.	"MSAC noted that because all four studies comparing TE with clinical assessment were conducted in high-risk patients in tertiary care settings, the positive predictive value of TE could be lower if it is used in lower risk settings where the prevalence of significant fibrosis and/or cirrhosis may be lower." (PSD 1366, pp.2-3)	Primary diagnostic evidence (Mozes 2022) in secondary care setting only. Diagnostic evidence in primary care setting unclear from ADAR.

Component	Matter of concern	How the concern is relevant to current ADAR per the evaluation
Treatment decisions for Hepatitis B (HBV) are based on viral load, not fibrosis stage, limiting TE's clinical utility.	"MSAC noted that the presence or absence of cirrhosis had little impact upon a patient's ability to access medicines to treat HBV. The aim of HBV treatment is control — it is not curative. Patients can access PBS-subsidised treatment for HBV whether they have cirrhosis or not because access is dependent upon viral DNA load. If a patient has cirrhosis, then levels of HBV DNA must be detectable while patients without cirrhosis must have elevated levels of HBV DNA as well as elevated liver enzymes and/or a liver biopsy." (PSD 1366, p. 3)	Not applicable because population is different
Economic modelling was unconvincing: cost-effectiveness was poor under most scenarios.	"MSAC noted that there was considerable uncertainty around the economic modelling presented in the application." "In the version of the model in which TE was used for initial diagnosis only, the incremental cost-effectiveness of adding TE to clinical assessment was not acceptable (ICER of $112,992 per QALY gained)." (PSD 1366, p.4)	Not applicable as 1797 ADAR has a different economic model
Cost of TE service was high, and broader, unsupported use (e.g., for fatty liver disease) may lead to budget underestimation.	"MSAC considered that the proposed fee for each TE service was high." "MSAC was concerned about the potential for TE to be used in other liver conditions (fatty liver disease, alcoholic liver disease). This could mean that the financial estimates of the use of TE provided to MSAC… would be substantial underestimates." (PSD 1366, p.4)	1797 ADAR proposed a fee of $58.85 per VCTE, based on fee for nurse practitioner attendance item 82210 ($58.85) compared to $55.65 in Application 1366 (based on cost of MBS item 55014 at March 2016). The ADAR did not address the use of VCTE in different populations.
PSD 1446		
Limited clinical utility: Hepascore would be used in addition to—not instead of—existing tests (e.g. APRI, FibroScan®), and has low positive predictive value requiring confirmatory testing.	"MSAC considered that there was limited clinical need for an additional test... Hepascore would be an additional test (not a replacement test)... a positive result... would likely be confirmed with additional testing due to Hepascore's low positive predictive value." (PSD 1446, p.2)	VCTE proposed as second line test after FIB-4, and would likely occupy same clinical space as Hepascore, for which MSAC had considered there to be limited clinical need.
Inadequate evidence: No clear data showing Hepascore improves clinical management or health outcomes. Meta-analyses lacked transparency; prognostic validation (e.g., Huang 2020) was misinterpreted.	"A lack of evidence on how Hepascore would affect clinical management such as enabling earlier diagnosis of cirrhosis and reducing complications..." "The presentation of a meta-analysis that could not be replicated..." "MSAC considered this was not an accurate claim, as Huang (2020) evaluated liver-related outcomes... not the ability of Hepascore to predict liver health outcomes..." (PSD 1446, p.3)	Primary diagnostic evidence (Mozes 2022) in secondary care setting only. Diagnostic evidence in primary care setting unclear from ADAR.
Comparative performance uncertain: Alternative tools like APRI offer similar diagnostic value and are routinely available.	"MSAC noted that the AST to platelet ratio index (APRI)... has similar specificity to Hepascore at a threshold of 2..." "MSAC noted that although Hepascore was frequently used in Western Australia, this was not reflective of other parts of Australia." (PSD 1446, p.2)	FIB-4 is used instead of APRI and is not considered as part of comparator in 1797

Component	Matter of concern	How the concern is relevant to current ADAR per the evaluation
Uncertain economic case: The economic model had unrealistic assumptions, used low-quality inputs, and underestimated real-world testing patterns and costs.	"Several implausible assumptions such as the assumption that only 10% of misdiagnosed patients would be retested." "Many were based on clinical experience while others were sourced from poor quality studies..." "... did not reflect clinical practice as most patients would receive all three interventions." (PSD 1446, p.3)	Not applicable as 1797 ADAR has a different economic model
Equity concerns: Proposed fee ($40.50) was well below actual patient cost ($83.90), risking affordability and access disparities.	"MSAC raised concerns about the likely out-of-pocket costs for consumers... applicant stated that PathWest requires an up-front payment of $83.90, but the applicant's proposed fee is $40.50." "MSAC considered that this would be unaffordable for many patients and may increase inequity." (PSD 1446, p.4)	No actual patient costs were presented in the 1797 ADAR. However, in the ADAR it was noted that patients may currently pay privately between $200-$300 for VCTE testing. Given the proposed MBS fee of $58.85 for VCTE, there may be similar equity concerns around affordability and out-of-pocket costs.

ADAR = Applicant Developed Assessment Report; APRI = Aminotransferase-to-platelet ratio index; AST = Aspartate Aminotransferase; DNA = Deoxyribonucleic acid; HBV =Hepatitis B Virus; ICER = incremental cost effectiveness ratio; MSAC = Medical Services Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PSD = Public Summary Document. QALY = quality adjusted life years; TE = Transient Elastography; VCTE = Vibration-Controlled Transient Elastography
Source: PSD 1336, PSD 1446.

5. Prerequisites to implementation of any funding advice

VCTE™ by FibroScan® at 50Hz is registered on the Australian Register of Therapeutic Goods (151894) as an 'External non-invasive ultrasound elastography device for measuring elasticity of organs such as the liver'. The elastography 'applicator' is listed under 206567. The device is classified by the Therapeutic Goods Administration as a medical device Class IIa and is considered low-medium risk.

6. Proposal for public funding

The proposed MBS item descriptor for VCTE in primary and specialist care, as outlined in Table 2, was not fully aligned with the recommendations of the PICO Confirmation Advisory Sub-Committee (PASC).

Table 2 Proposed item descriptor for VCTE in primary/specialist care

Category 1 – Professional attendances
MBS item XXXX Vibration-Controlled Transient Elastography at 50 Hz performed by a suitably trained health professional for the assessment of liver fibrosis in patients with metabolic dysfunction-associated fatty liver disease, following an indeterminate or high FIB-4 test score (≥1.3) Available once per patient in a 36-month period
Fee: $58.85

Abbreviations: MBS, medical benefits scheme

PASC advised limiting VCTE use to once every 36 months, unless a prior LSM is ≥8 kPa in which case no further VCTE is required, to ensure its use as a triage tool rather than for ongoing monitoring (1797 Ratified PICO Confirmation, Table 8, p. 38). However, the ADAR considered that such a restriction could inadvertently prevent re-evaluation in patients whose risk status may change over time. The MBS item descriptor proposed in the ADAR (Table 2) includes the frequency restriction (limiting VCTE to once every 36 months) but removed the condition that the service is only for patients with no prior LSM ≥8 kPa, reintroducing the possibility that the proposed item could be used for ongoing monitoring. Regarding other considerations for retesting in the proposed clinical management algorithm, the commentary considered it unclear whether there would be any difference in clinical management between patients with LSM ≥8 kPa and, for example, a patient with LSM ≥10 kPa. If there is no difference in clinical management of these patients, then retesting patients who have a prior test result of LSM ≥8 kPa would have no clinical utility and would simply incur more costs, as well as any potential safety risks and misclassification risks for the patient, for no benefit.

While PASC queried the training required to perform VCTE, for the GP workforce in particular, and noted consultation feedback that VCTE may be best conducted by specialists (1797 Ratified PICO Confirmation, p. 20), the ADAR emphasised the low training requirements and standardised interpretation guidelines. However, the commentary noted published evidence that operator experience significantly influences measurement validity, highlighting the need for substantial practical experience despite low formal training requirements.

Under the proposed item descriptor, all patients with a FIB-4 test score ≥1.3 would be eligible for testing, in both primary and secondary settings. In line with PASC advice that the use of standard validated FIB-4 cutoffs for the eligible population was appropriate, different FIB-4 thresholds were not proposed for different subgroups. The proposed thresholds are aligned with the GESA consensus statement, which PASC also considered to be appropriate.

As discussed in Table 1, the commentary noted that, given the 1797 ADAR's claim that patients currently face an out-of-pocket cost of between $200-300 for privately funded VCTE, patients would still face substantial out-of-pocket costs for VCTE even if delivery of the service were subsidised by the MBS. The same issue of inequity previously identified by MSAC in Application 1446 would apply. However, the department notes that the current out-of-pocket costs and fees set in the private system likely incorporate private practices recouping the cost of purchasing the VCTE device from their patients over time.

The fee for the proposed item ($58.85) was based on providing the scan only, without the bundled consultation elements originally proposed by the applicant. This is in line with PASC's

advice (1797 Ratified PICO Confirmation, p. 37-38). The fee was based on nurse practitioner attendance item 82210 ($58.85) for a consultation lasting at least 20 minutes.

The ADAR proposes MBS funding exclusively for VCTE by FibroScan®, and excludes other methods of elastography. PASC raised concerns about this brand-specific approach, advising that the use of a broader term (e.g. “transient elastography” or “elastography”) may be more appropriate, unless clear evidence supports VCTE’s superiority over alternatives. The ADAR referred to guidelines to defend the decision to limit to VCTE specifically, and in their comments on the ratified PICO, the applicant stated that other elastography technologies were excluded from the application due to the gap in clinical evidence and the lower diagnostic accuracy of alternative methods compared to VCTE (1797 Ratified PICO Confirmation, p. 41). However, no evidence was presented in the ADAR to demonstrate this lower accuracy.

A rapid literature search during the evaluation confirmed that VCTE is a widely used tool for fibrosis staging in MAFLD or non-alcoholic fatty liver disease (NAFLD) and chronic liver disease. However, other elastography modalities such as 2D-Shear Wave Elastography (SWE) and point Shear Wave Elastography (pSWE) demonstrate comparable diagnostic performance and may be more suitable in patients with obesity or where VCTE access is limited. Endoscopic ultrasound-guided SWE (EUS-SWE) shows promise in technically challenging cases, and magnetic resonance elastography (MRE) is highly accurate, although is reserved for specialist use due to cost and access limitations. Cassinotto 2020[1] validated the application of VCTE thresholds to 2D-SWE, supporting their clinical interchangeability. Other studies identified by the ADAR (including Tacke 2024 and Cassinotto 2021) also reported that 2D-SWE performs equivalently to VCTE and may be preferable in certain populations. The commentary considered that this supports PASC’s advice that restriction of MBS listing to VCTE may not be clinically justified.

7. Population

The ADAR proposed the use of VCTE™ in patients with a confirmed MAFLD diagnosis. In the ADAR, VCTE is to be used following FIB-4 testing for those with an indeterminate risk of AF, positioning it as a risk assessment tool in both primary and specialist care settings. Currently, no elastography technologies or direct serum fibrosis tests (including Hepascore and ELF) are publicly funded in Australia. The ADAR also proposed two separate populations, one for primary or specialist care and one for specialist care only (Table 3), depending on FIB-4, with two separate PICO sets (Table 4). As discussed above, the proposed item descriptor suggests that VCTE would be available for patients in primary care with FIB-4 >2.7 which would be inconsistent with what the ADAR proposes but consistent with PASC’s advice.

Table 3 FIB-4 Index score and associated AF risk for patients with confirmed MAFLD

FIB-4 Index score	Advanced fibrosis risk	Eligible for VCTE	Management	PICO Set
<1.3	Low	No	Primary care	-
1.3-2.7	Indeterminate	Yes, primary care or specialist care†	Primary or specialist care	PICO Set 1 & 2
>2.7	High	Yes, specialist care	Specialist care	PICO Set 2

†VCTE conducted in specialist care if no access to VCTE in primary care setting
Abbreviations: VCTE, vibration-controlled transient elastography
Source: Table 13 of the 1797 ADAR.

[1] Cassinotto et al. Agreement Between 2-Dimensional Shear Wave and Transient Elastography Values for Diagnosis of Advanced Chronic Liver Disease. Clin Gastroenterol Hepatol. 2020 Dec;18(13):2971-2979.e3

In the PICO consideration, PASC noted that VCTE may have broader clinical utility for medical conditions other than MAFLD. While the application's focus on MAFLD was justified based on disease burden and existing validation, PASC highlighted a potential equity issue, noting that patients with other liver diseases (e.g. chronic HBV and HCV) might be disadvantaged by a funding model restricted to patients with MAFLD only. The commentary noted that the item may be used outside of the proposed population, similar to MSAC's concerns in Application 1366 regarding use of TE for conditions such as fatty liver disease or alcoholic liver disease, outside the proposed population of chronic HBV and HCV (see Table 1).

Although the ADAR presented two separate PICOs for the use of VCTE in primary care and specialist settings, the proposed role of VCTE in the ADAR is limited to use as a tool following FIB-4 testing (Table 4). PASC advised that a single PICO would be appropriate for this purpose (1797 Ratified PICO Confirmation, p. 38 & Table 9, pp. 40-41). The justification provided by the ADAR for maintaining two distinct PICOs (differences in the use of VCTE in primary and specialist care, clinical consequences and the need for separate economic evaluations to capture these nuances) was inconsistent with the stated purpose of the intervention. Its intended use in stratifying risk of AF does not clearly warrant separate PICO frameworks.

Regarding the inclusion of both "indeterminate and high" FIB-4 results, PASC advised that the single population should include all patients with FIB-4 ≥1.3, in both GP and specialist settings, with the intervention limited to the scan itself. However, the ADAR's presentation (particularly in the dual-PICO framework and the economic model) appears to have focused only on indeterminate FIB-4 results in GP settings, while implicitly considering patients with high FIB-4 scores as requiring specialist referral. This divergence has created ambiguity in interpretation, and clarification is warranted to ensure alignment with PASC's advice that a single item and single PICO are sufficient to capture the proposed role of VCTE following FIB-4 testing.

This ambiguity is compounded by uncertainty about the intended role of VCTE, as presented in the ADAR. VCTE is interchangeably referred to in the ADAR as a tool for risk stratification of AF, and a tool for diagnosis and monitoring of AF, leaving its exact role unclear. This lack of distinction within the ADAR undermines alignment with the PICO, limits the transferability of evidence, risks double-counting benefits in the economic model, and raises concerns for MSAC regarding misclassification, inappropriate test use, and difficulties in defining targeted MBS items. In contrast to the ADAR, the GESA guidelines appear to support VCTE use for determination of risk of AF only, rather than diagnosis of AF.

The ambiguity is further compounded by the absence of a clear VCTE threshold. The commentary considered that a universal cut-off (e.g. 8.0 kPa) may not be appropriate for both primary and specialist settings: in primary care, lower thresholds may prioritise sensitivity to avoid missed cases, while in specialist care higher thresholds may be required to balance specificity and clinical utility. In summary, VCTE cut-offs should be setting-specific, reflecting differences in patient risk profile, intended purpose of testing, and acceptable trade-offs between sensitivity and specificity.

Table 4: PICO criteria for assessing VCTE for patients with MAFLD in primary and specialist care

Component	PICO 1	PICO 2
Population	Patients diagnosed with MAFLD	
<Prior tests>	• Diagnosis of MAFLD (≥5% hepatosteatosis; and at least one of the following (1) overweight; (2) type 2 diabetes mellitus [T2DM]; or (3) metabolic dysfunction†. • Fibrosis-4 (FIB-4) score (requiring assessment of AST, ALT and platelet count).	
Intervention	VCTE in primary care	VCTE in specialist care
Comparator	SOC which may include liver ultrasound, other non-funded tests for the diagnosis of advanced fibrosis, and/or referral to specialist care (where appropriate).	
Outcomes	**Effectiveness** • Diagnostic accuracy (sensitivity, specificity, positive and negative predictive values) in comparison to liver biopsy (reference standard) • Diagnostic accuracy in comparison to SOC • Prognostic accuracy **Change in patient management** • Reduced referrals to specialist care (Only PICO 1) • Time to test and accessibility • Equity of access and patient adherence • Reduction in use of liver biopsy (Only PICO 2) **Economic Outcomes** • Health care resources • Cost-effectiveness • Total Australian Government health care costs	
Systematic review questions: Test performance 1. What is the diagnostic accuracy of VCTE compared to the reference standard liver biopsy in identifying advanced fibrosis in patients who have MAFLD? 2. What is the diagnostic accuracy of VCTE compared to SOC as a second-line test to identify patients with advanced fibrosis in primary and specialist care? Change in management 3. Does the availability of new information from a VCTE test result in a change in management to the patients (Impact on specialist referrals, HCC surveillance, diabetes management, lifestyle intervention) 4. Does VCTE enable better time to access to care and patient adherence? Health outcomes (to be assessed if there is a change in diagnosis, timing of diagnosis or treatment, or patient behaviour; health outcomes inferred to be non-inferior if no changes) 5. How do the changes in management, resulting from the use of VCTE in primary and specialist care impact health outcomes for patients with MAFLD? Cost-effectiveness What is the cost-effectiveness of the use of VCTE in primary and specialist care compared to the current SOC in managing MAFLD patients		

Abbreviations: Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; FIB-4, Fibrosis- 4; MAFLD, metabolic dysfunction-associated fatty liver disease; SOC, standard of care; VCTE, vibration-controlled transient elastography.
†Noting that this includes those with a FIB-4 score > 2.7, in line with PICO Confirmation Advisory Sub-Committee (PASC) advice that it is reasonable to include this group of patients in the proposed population.
Source: ADAR, table 1

PASC advised that the evaluation should demonstrate evidence along the full linked evidence chain, showing how VCTE use leads to changes in clinical management and, ultimately, patient outcomes. PASC also highlighted the need to assess safety (e.g., misclassification risks), equity, and to ensure that economic modelling was grounded in demonstrated clinical benefit.

In contrast, while the ADAR suggested general benefits such as reduced specialist referrals and improved access, the evidence provided was insufficient to satisfy the linked evidence approach. Specifically, evidence for change in management was limited to referral pathways only, and there was no evidence review of the final link from change in management to improved health outcomes. Similarly, the ADAR did not address potential harms or safety concerns. Thus, while the ADAR sought to evaluate the utility of VCTE in assessing advanced fibrosis in patients with MAFLD, it did not fully address the evidentiary scope and outcome requirements set out by PASC.

The ADAR did not provide sufficient linked evidence to support claims of change in management. Key limitations included use of ineligible populations (Tulleners 2024 -included a substantial proportion of patients with FIB-4 <1.3, who would not be eligible for second line VCTE under the proposed item descriptor), absence of studies of sequential testing with FIB-4 followed by VCTE (Tulleners 2024, Hayward 2022), lack of an appropriate comparator (Hayward 2022), and application of non-aligned VCTE thresholds (Mozes 2022). While some studies suggested potential effects on referral patterns, no evidence review linked these changes to improved patient outcomes. Collectively, these gaps left the linked evidence chain incomplete and prevented conclusions about the incremental benefit of VCTE.

The ADAR assessed VCTE's clinical value primarily through improved diagnostic accuracy and timeliness following FIB-4, assuming this would inform management decisions. It did not directly evaluate downstream health outcomes, instead suggesting that earlier identification could potentially reduce future complications. From an HTA perspective, this approach is incomplete—by implying superior outcomes without directly linking evidence to health benefits, the ADAR does not fully meet the MSAC guidelines detailed in Technical Guidance 9 (Assessment framework).

8. Comparator

The ADAR identified standard of care (SOC) as an appropriate comparator, but in practice, the actual components of SOC may vary. In the primary care setting, the ADAR stated that SOC may involve referral to a specialist, or continued management within the primary care setting without referral or second line testing with ultrasound. SOC may also include the use of other non-funded tests. In specialist settings, the ADAR stated that SOC may include liver ultrasound, ongoing clinical management, and the use of other non-reimbursed diagnostic tests for advanced fibrosis.

The choice of 'standard of care' (SOC) as the most suitable comparator was in line with PASC advice. However, PASC also stated that ultrasound alone (as proposed in the original application) was not a suitable comparator second-line test due to its inability to detect fibrosis (1797 Ratified PICO Confirmation, p. 21). This aligns with the GESA MAFLD Consensus Statement, which does not recommend ultrasound as a second-line test, and with MBS rules that restrict ultrasound use to morphological imaging rather than elastography. Nevertheless, ultrasound was the primary component of the comparator in the ADAR's economic evaluation, which was inappropriate.

The 2024 Australian MAFLD Consensus Statement recommends a technology-agnostic approach to second-line testing following indeterminate FIB-4 results, including VCTE, SWE, Hepascore, or ELF – indicating that these are all clinically valid alternatives. Accordingly, while ultrasound costs may legitimately contribute to SOC costing, its use as the primary comparator in the economic and financial estimates is inappropriate. More suitable comparators would be the other (non-funded) second-line tests recommended in the Consensus Statement.

No comparative evidence for VCTE relative to SWE or direct serum fibrosis tests was presented in the ADAR. However, as discussed in Section 6 above, a rapid literature review conducted during the evaluation suggested that the diagnostic accuracy of VCTE, 2D-SWE and pSWE all demonstrate comparable diagnostic performance for detection of AF and cirrhosis based on Cassinotto 2020.

9. Summary of public consultation input

Consultation input was welcomed from:

1797 - Vibration-Controlled Transient Elastography (VCTE™) for identifying advanced fibrosis in patients with metabolic dysfunction-associated fatty liver disease	No. of Inputs Received
Organisations (7)	
I am providing input on behalf of a consumer group or organisation. Consumer organisations are not-for-profit organisations representing the interests of healthcare consumers, their families and carers.	3
I am providing input on behalf of a medical, health, or other (non-consumer) organisation. For example, input on behalf of a group of clinicians, research organisation, professional college, or from an organisation that produces a similar service or technology.	4
Health Professionals (5)	
I am a health professional or health academic working in the area.	5
Consumers (3)	
I have the health condition that this health service or technology is for and have experience with the proposed health service or technology.	2
I am a parent, partner or another person caring for someone from the above two groups.	1
Grand Total	**15**

The organisations that submitted input were:

- LiverWELL
- Gastroenterological Society of Australia (GESA)
- The Royal Australian and New Zealand College of Radiologists (RANZCR) – The Faculty of Clinical Radiology
- Liver Foundation
- The Royal Australian College of General Practitioners (RACGP)
- Hepatitis Australia
- Australian College of Nurse Practitioners (ACNP)

Level of support for public funding

The consultation input received was mostly supportive of public funding for VCTE for identifying advanced fibrosis in patients with MAFLD, although some feedback (including that provided by RANZCR) did not support the application in its current form. The consultation input raised a number of concerns, predominately in relation to the population being too restricted and the delivery of VCTE.

Comments on PICO

- The consultation input largely agreed with the proposed populations, although a number of health professionals and GESA noted there could be benefits of VCTE in patients other than those specified in the application form, including patients with type 1 diabetes and patients with viral hepatitis. Input from a health professional noted higher threshold score of 2 (compared to 1.3) for patients aged >65 years old.

- The consultation broadly agreed with the initially proposed comparator (liver ultrasound), although GESA noted that ultrasound lacks sensitivity and specificity for liver cirrhosis diagnosis. A health professional noted that shear wave elastography (SWE) is currently available and could be an appropriate comparator but stated that SWE has issues including user variability and discrepancy in results, and that results comparatively favour VCTE in accuracy and applicability.
- There is concern that without specialist interpretation, primary care use of VCTE could lead to mismanagement due to complexity of interpreting non-invasive liver tests. A health professional has noted that current Australian clinical practice reserves interpretation of non-invasive liver tests for specialist hepatologists/gastroenterologists.

Perceived Advantages

Advantages of the serviced noted in the input included:

- VCTE is non-invasive, quick, painless, and provides immediate, quantifiable results that enhance patient understanding and engagement. A liver specialist health professional described it as “indispensable for the routine management of liver disease” and “akin to a chest X-ray for a respiratory physician.”
- VCTE might reduce the need for liver biopsies, which are invasive, costly, and carry risks such as bleeding and infection.
- The technology supports early detection and monitoring of liver disease, enabling timely intervention and lifestyle changes that reduce the risk of severe complications and improve outcomes. The Liver Foundation noted these clinical benefits as well as economic benefits such as reducing unnecessary procedures and costs.
- VCTE is portable and suitable for use in community and remote settings, potentially improving access for underserved and remote populations.
- The use of VCTE in primary care could reduce unnecessary referrals to specialists and streamline care pathways, with GESA and a health professional noting it can substantially reduce the number of people requiring referral to tertiary services.

Perceived Disadvantages

Disadvantages of the service noted in the input included:

- Access to VCTE is currently limited due to lack of devices. Feedback noted devices are concentrated in specialist centres, resulting in long wait times, especially in regional and remote areas. Feedback stated this can impose significant travel, financial and logistical burdens on those patients.
- The initial cost of purchasing VCTE devices may be prohibitive for smaller or rural clinics, with some inputs noting that the proposed funding may not be sufficient to support widespread implementation, especially in rural areas.
- There is a risk of over-reliance on VCTE without integrating it into a broader diagnostic algorithm that includes clinical scores and biomarkers with RANZCR noting that the application does not acknowledge currently widely similarly available technology in practice, such as SWE, or less available but superior technology, magnetic resonance elastography (MRE).
- The use of VCTE results requires proper training and knowledge of guidelines, and inappropriate use in primary care could lead to misdiagnosis or unnecessary testing as primary care settings currently lack the tools and infrastructure to properly evaluate liver fibrosis or cirrhosis.

Support for Implementation and Issues

- Consultation input was provided in relation to service delivery, stating that an increased number of VCTE machines would be required to support equitable access across Australia and training in the correct use of VCTE would need to be provided for specialists and nurses. GESA stated that portable VCTE mobile outreach regional services may be suitable and that these services have been used in Australia for the outreach viral hepatitis liver assessment program.
- The consultation input from health professionals and professional organisations varied from agreeing to disagreeing with the proposed item descriptor. One health professional stated the item should be restricted to specialist hepatologists and gastroenterologists as the results require specialist interpretation. RACGP stated that GPs are well placed to prevent, diagnose and manage MAFLD. RANZCR advocated for an item for non-invasive assessment of liver fibrosis that allows the use of multiple technologies including SWE and MRE. GESA disagreed with the frequency restriction stating it is not in line with the Australian GESA MAFLD consensus statement which recommends repeat assessment every 1-3 years depending on risk.
- The consultation input from health professionals and professional organisations ranged from agreeing to disagreeing with the proposed service fee, with some consultation input stating it should be higher to support the cost of VCTE machines and support small rural services. RACGP stated that the fee for GPs should be in line with other specialists as they are undertaking the same tasks.

Additional Comments

- GESA noted that VCTE in combination with platelet count (blood test) has the additional benefit of triaging the need for invasive and expensive gastroscopy to diagnose portal hypertension in people with MAFLD.
- ACNP noted that the proposed descriptor should be broadened to ensure equitable access and workforce flexibility, particularly in regional, rural, and remote Australia, where Nurse Practitioners (NPs) are often the sole health-care providers.
- Hepatitis Australia noted that expanding access to FibroScan for MAFLD will also strengthen the infrastructure and service models that benefit communities affected by hepatitis B and hepatitis C, particularly in primary care, rural and regional areas, and culturally safe settings.

10. Characteristics of the evidence base

The evidence base in the ADAR was comprised of a mix of systematic reviews, meta-analyses, prospective cohorts, and modelling studies evaluating the diagnostic and prognostic performance of VCTE™. Mozes 2022, an individual patient data (IPD) meta-analysis, served as the pivotal diagnostic accuracy study, presenting cross-sectional accuracy data for VCTE (as stand alone, without any prior testing) compared to liver biopsy as the reference standard, and statistical modelling of the sequential FIB-4 to VCTE pathway in indeterminate FIB-4 patients, albeit with high risk of bias. Mozes 2023, another IPD meta-analysis, was relied upon to provide longitudinal prognostic evidence, assessing the association between baseline VCTE and future liver-related events and mortality, but did not evaluate sequential testing, repeated testing or change over time. Both of these studies presented data from a tertiary population but not from primary care. The commentary noted that poor applicability was a common limitation with the literature identified, with most studies not assessing a sequential testing strategy of FIB-4

followed by VCTE, and/or not assessing VCTE using the LSM threshold for high risk of AF proposed by the ADAR of 8.0 kPa. This led to significant limitations in the evidence base used to inform the ADAR and is discussed further in the relevant sections below.

The commentary noted that several supporting studies were identified by the ADAR that may be relevant to the proposed research question, but the ADAR did not conduct risk of bias assessments on these studies. Studies such as Leite 2025, Gawrieh 2024, Ciardullo 2023b, and Mu 2024 contributed additional prognostic data, though none tested the proposed sequential pathway. Crossan 2019 and Stein 2023 addressed change in management, with the former modelling downstream clinical impact and cost reduction, and the latter demonstrating improved referral outcomes in a real-world setting. Evidence directly linking testing strategies to health outcomes or treatment effect variation was absent. Similarly, no studies focusing on the safety of testing, specifically the results of misclassification (false positive and negative results) were identified, nor were outcomes of misclassification discussed by the ADAR.

Reliability of VCTE was primarily supported by Vuppalanchi 2018, which reported a high proportion of reliable scans (96.1%) when a standard ratio of interquartile range/median (IQR/M) ≤ 0.30 criteria were met. However, stronger evidence from Mozes 2022 and Boursier 2013—cited in the main text but not listed in the appendix—highlighted the impact of LSM reliability on diagnostic accuracy and introduced more nuanced reliability criteria. These findings underscore the need for consistent application of robust quality standards to avoid overestimating test performance.

The ADAR evaluated VCTE's clinical value mainly on the basis of improved diagnostic accuracy, with the assumption that this would guide management decisions in patients with MAFLD. However, it did not assess downstream health outcomes directly, instead inferring that earlier detection of fibrosis could reduce future complications. From an HTA perspective, this is insufficient, as it implies improved outcomes without demonstrating evidence of actual health benefits, and therefore does not fully align with the MSAC guidelines detailed in Technical Guidance 9 (Assessment framework).

Table 5 Key features of the included evidence

Criterion	Type of evidence supplied	Extent of evidence supplied	Overall risk of bias in evidence base
Pivotal diagnostic accuracy study included in main body			
Accuracy and performance of the test (cross-sectional accuracy)	Mozes 2022 partially present diagnostic accuracy for sequential approach for indeterminate range of FIB-4 (1.3-2.7)	k=1 n=5,735	High [a]
Pivotal longitudinal accuracy study included in main body			
Prognostic evidence (longitudinal accuracy)	Mozes 2023 assessed prognostic accuracy of VCTE and FIB-4 individually at baseline but did not assess serial testing, repeated testing or longitudinal diagnostic accuracy	k=1 n=2,518	High [b]
Change in patient management	Tulleners 2024 assessed outcomes from a primary care program which used VCTE as part of the liver care pathway. Hayward 2021 used VCTE after FIB-4/NFS; no outcomes reported. Sarkar Das 2024: limited support [c]	k=2 n=259	Moderate
Supporting longitudinal accuracy studies included in appendix			
Prognostic evidence (longitudinal accuracy)	Leite 2025: VCTE prognostic for liver, CV, and mortality outcomes in T2D/MASLD (2 VCTEs used). Sequential approach not assessed. Gawrieh 2024: Serial VCTEs assessed; change in LSM associated with outcomes. No sequential testing.	k=2 n=1,691	NR [d]

SR = systematic review; IPD = individual patient data; k=number of studies, n=number of patients; NR = not reported; FIB-4= Fibrosis-4 Index, CDST= Clinical Decision Support Tool; VCTE= Vibration-Controlled Transient Elastography; ELF= Enhanced Liver Fibrosis test; CV=cardiovascular;T2D= Type 2 Diabetes; MASLD= metabolic dysfunction–associated steatosis liver disease; LSM= Liver Stiffness Measurement; NFS= NAFLD Fibrosis Score; IQR/M= Interquartile Range to Median ratio.

a The commentary believes Mozes 2022 had a high risk of bias due to only 37 out of 55 identified studies being included, lack of detail on how many patients were excluded, the reasons patients were excluded, incomplete reporting of baseline characteristics for patients without advanced fibrosis, use of statistical modelling only to inform accuracy of sequential strategies, and lack of detail in statistical methods for data harmonisation, pooling, and analysis.

b The commentary believes Mozes 2023 had a high risk of bias due to only 25 out of 65 identified studies being included, lack of detail regarding how many patients were excluded from study. Additionally, histological staging—the reference standard—was not centrally reviewed, introducing heterogeneity and observer bias. Outcome assessment was frequently unblinded or based on retrospective records, contributing to a high risk of bias in outcome classification.

c Hayward 2021, Sarkar Das 2024 and Mozes 2022 were included as supporting evidence.

d Studies in the appendix were not assessed for risk of bias by the ADAR

11. Comparative safety

The ADAR did not undertake a formal comparative safety evaluation of VCTE™ against the nominated comparator tests. Only limited information related to safety was identified in the ADAR.

The ADAR states that VCTE is "non-invasive, well-tolerated, no known direct harms. May cause anxiety or overtreatment if false positives occur." However, no supporting evidence was identified in the ADAR to support this claim. While the ADAR acknowledges that PASC recommended the assessment should address outcomes such as safety, diagnostic accuracy, changes in patient management, health outcomes, and cost-effectiveness, it similarly provided no evidence to support its related statement that "test safety, specifically the risk of misclassification or misdiagnosis of advanced fibrosis, was conceptually considered and accounted for in the assessment of financial impact."

The commentary noted that the ADAR did not consider the impact of false negative results (i.e. patients who have AF that is not detected by VCTE). This was important as exploratory modelling of testing outcomes with the proposed sequential testing compared to referral based only on a

FIB-4 threshold of 1.3 demonstrated that there would be more false negative results when sequential testing is used compared to use of FIB-4 only. This is discussed further in Section 12.

12. Comparative effectiveness

Notably, the ADAR uses the terms “diagnosis” and “risk stratification” inconsistently. In primary care, VCTE™ is presented as a triage tool for risk stratification, whereas in specialist care it is described as a diagnostic test, despite being used in practice alongside other tests. This interchangeable use creates ambiguity regarding whether VCTE is positioned in the ADAR as a diagnostic test or a risk stratification tool.

The ADAR did not present comparative effectiveness data for the proposed sequential approach—using VCTE (with an 8 kPa threshold used to classify high risk of AF) following an indeterminate FIB-4 result—against SOC, which may involve liver ultrasound, non-funded diagnostic tests (e.g., SWE, ELF) for AF, referral to specialist care where appropriate, or ongoing management without further testing.

Instead, the ADAR relied on Mozes 2022 and Mozes 2023 to support diagnostic and prognostic claims for VCTE. However, neither study compared VCTE to SOC or modelled its impact on real-world patient management following prior FIB-4 testing.

Mozes 2022 reported diagnostic accuracy outcomes including area under receiver operator curve (AUROC), sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) of VCTE alone as well as FIB-4 alone against a reference standard of liver biopsy in 5,735 patients with NAFLD, using IPD obtained from 37 separate published studies. Mozes 2022 however did present diagnostic results based on a simulated sequential testing strategy in which patients with indeterminate FIB-4 were tested with second line VCTE. However, this was not directly applicable to the ADAR’s research question as the rule-out and rule-in thresholds used for VCTE in Mozes 2022 differed to the threshold proposed in the ADAR.

The ADAR proposed a single rule-out and rule-in threshold of LSM 8.0 kPa using VCTE. That is, a patient is considered to not have AF (i.e. ruled out) if LSM was < 8.0 kPa and is considered to have AF (i.e. ruled in) if LSM was ≥ 8.0 kPa. However, the literature presented in the ADAR does not support the use of a single threshold for both rule-out and rule-in, nor support the value of the nominated threshold. The range of rule-out and rule-in thresholds identified in the systematic review conducted by Mozes 2022 for both VCTE and FIB-4 is presented in Table 6. Based on the literature identified by Mozes 2022, the rule-out and rule-in cut offs for LSM by VCTE varied substantially. Rule-out thresholds ranged from <5.9 kPa (Hsu 2019) to <10.0 kPa (Wong 2019, Papatheodoridi 2021) and rule-in thresholds ranged from >9.6 kPa (Peta 2019, Boursier 2019, Petta 2017) to >15.0 kPa (Wong 2019, Papatheodoridi 2021). The nominated threshold of 8.0kPa in the ADAR was within the reported range of values for the rule-out threshold, but lower than any of the rule-in thresholds in literature, suggesting that it would likely lead to more false positive results compared to the literature. Importantly, no literature source supported the use of a single threshold (as proposed in the ADAR) for both rule-in and rule-out.

Table 6: Non-invasive test thresholds to rule-in and rule-out fibrosis in patients with NAFLD identified by Mozes 2022

Test	Source	Rule-out	Rule-in
VCTE	**Predefined thresholds**		
	Anstee 2019	<9.0	>11.4
	Wong 2019, Papatheodoridi 2021	<10.0	>15.0 [a]
	Petta 2019, Boursier 2019, Petta 2017	<7.9	>9.6 [b]
	Thresholds from other primary studies		
	Tapper 2016	<7.9	>9.8
	Eddows 2019	<7.1	>14.1
	Hsu 2019	<5.9	>13.4
	Cassinotto 2016	<8.2	>12.5
	Papatheodoridi 2021	<8.0	<12.0

a based on de Franchis 2015 (referred to as Baveno VI in Mozes 2022)
b Based on Wong 2010
Source: Supporting Table 2, Mozes 2022

The diagnostic performance of VCTE alone (i.e. not used sequentially after FIB-4) and FIB-4 alone compared to liver biopsy as reported in Mozes 2022 is presented in Table 7. LSM by VCTE demonstrated the highest diagnostic performance, with a point estimate for the AUROC of 0.85 (compared to 0.76 for FIB-4 and 0.73 for NFS), indicating good discrimination between patients with and without AF. At the maximum Youden's Index (YI; measured as sensitivity + specificity - 1) threshold, VCTE shows balanced sensitivity and specificity (77–78%), resulting in a misclassification rate of 22%. The commentary noted this meant that, when using a single rule-out and rule-in threshold, it would not be possible to achieve both a sensitivity and specificity of above 80% (Figure 1). Mozes 2022 suggests that a rule-out threshold of 7.4 kPa and a rule-in threshold of 12.1 kPa were necessary for VCTE to have a sensitivity and specificity of 90%. However, this increase in sensitivity and specificity comes at the cost of a cohort of patients receiving indeterminate VCTE results.

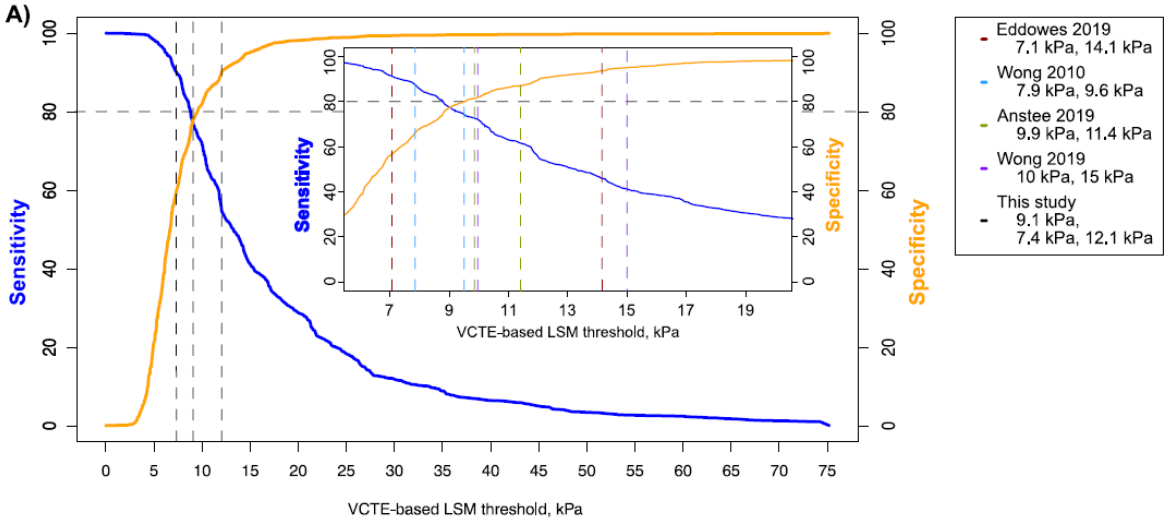
Overall, applying a single lower threshold of 8.0 kPa, compared to the 9.1 kPa threshold that maximised the Youden Index, would increase sensitivity but reduce specificity (see Figure 1), leading to more false positive results. At 9.1 kPa, sensitivity and specificity are more closely balanced, whereas at 8.0 kPa the gap between them is wider.

Table 7 Diagnostic performance of non-invasive tests for advanced fibrosis (F3–F4) in Mozes 2022

	LSM by VCTE alone (n=5,489)			FIB-4 alone (n=5,393)		
Advanced fibrosis, %	30			30		
AUROC	0.85 (0.84–0.86)			0.76 (0.74–0.77)		
	YI	90% Se	90% Sp	YI	90% Se	90% Sp
Threshold	9.1	7.4	12.1	1.44	0.88	2.31
Sensitivity, %	77 (75–79)	90 (89–91)	55 (52–57)	69 (67–72)	90 (88–91)	38 (36–41)
Specificity, %	78 (76–79)	60 (59–61)	90 (89–91)	70 (69–72)	39 (37–40)	90 (89–91)
Misclassified, %	22 (22–23)	31 (31–32)	21 (20–21)	30 (30–31)	46 (46–47)	26 (25–26)

For each non-invasive test thresholds were selected according to Youden's index (YI), and fixed at 90% sensitivity (90% Se) and 90% specificity (90% Sp). 95% confidence intervals were estimated with 500 bootstrap replicates.
Abbreviations: AUROC, area under the receiver operating curve; FIB-4, Fibrosis-4 Index; LSM, liver stiffness measurement; NFS, NAFLD (non-alcoholic fatty liver disease) Fibrosis Score; VCTE, vibration-controlled transient elastography.
Source: Table 28 of the ADAR

Figure 1: Distribution of sensitivities and specificities over the possible threshold ranges for LSM-VCTE in Mozes 2022



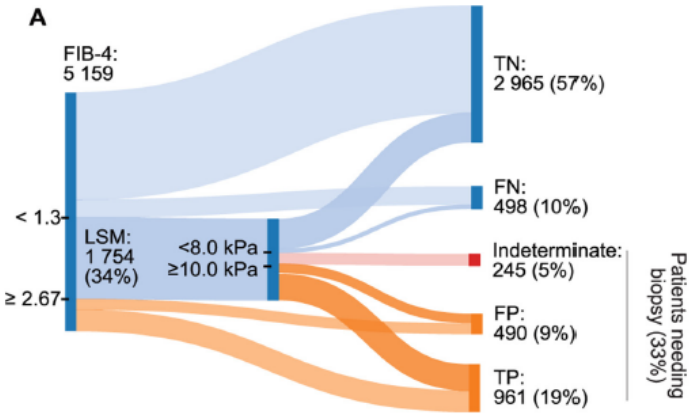
Notes: Insets show the distribution of cut-offs identified from the literature. Horizontal dashed lines are representing the minimum acceptable criteria for considering a test as having high sensitivity (≥80%) and high specificity (≥80%).
Abbreviations: LSM, liver stiffness measurement; VCTE, vibration-controlled transient elastography
Source: Mozes 2022, Figure 2A p1012

Furthermore, subgroup analyses in Mozes 2022 (ADAR Table 20) show that VCTE performance declines in patients with obesity, diabetes, and younger age—demographics highly prevalent in the MAFLD population. Use of age- or BMI-adjusted thresholds or stratified modelling may better reflect clinical practice and reduce misclassification risk.

Mozes 2022 also presented simulated results from a sequential testing strategy in which patients with indeterminate FIB-4 results were tested by VCTE. The most relevant strategy was sequential testing strategy A, in which patients with FIB-4 ≥ 1.3 but <2.67 were tested with VCTE, as the definition of indeterminate FIB-4 was reasonably aligned with the ADAR's definition (see Table 3) in the PICO 1 population. However, no analysis in the PICO 2 population (i.e. FIB-4 ≥1.3) was considered, and the rule-out and rule-in thresholds for VCTE were <8.0 kPa and ≥ 10.0 kPa, which was inconsistent with the proposed threshold in the ADAR. As such, the applicability of this analysis to the ADAR's research question was poor, and the simulated (rather than empirically observed) nature of the results may not accurately reflect accuracy seen in actual clinical practice. Nonetheless, the ADAR relied on the results of sequential testing strategy A to inform the economic evaluation.

Mozes 2022 calculated the diagnostic accuracy of sequential testing strategy A (see Figure 2) by excluding the results from the 5% of patients who had indeterminate FIB-4 and VCTE results, which may not be reflective of clinical practice as these patients must be accounted for. Using this methodology, a sensitivity of 66% (95% confidence interval [CI] 63-68) and specificity of 86% (95% CI 84-97) was reported, along with a PPV of 66% (95% CI 64-68) and NPV of 86% (95% CI 85-87%), at a prevalence of AF of 30% in the population. Of the resulting 34% of patients who required and underwent VCTE, 19% (95% CI 18-20) of those patients were misclassified following VCTE (i.e. incorrectly identified as having or not having advanced fibrosis) when liver biopsy was used as the reference standard.

Figure 2: Sankey diagrams for TP, TN, FP, FN and indeterminate groups for sequential testing (FIB-4 + LSM-VCTE) for FIB-4 >1.3 and <2.67, and LSM ≥ 8.0 kPa and <10.0 kPa in Mozes 2022



		FIB-4	LSM
< Lower cutoff	TN	2311 (44%)	654 (13%)
	FN	396 (8%)	102 (2%)
≥ Upper cutoff	TP	459 (9%)	502 (10%)
	FP	239 (4%)	251 (5%)

Abbreviations: LSM, liver stiffness measurement; VCTE, vibration-controlled transient elastography; FIB-4, Fibrosis-4 Index; TP, true positive; TN, true negative; FP, False positive; FN, false negative
Source: Mozes 2022 Figure 3A p1015

Mozes 2023 reported the outcomes from a composite endpoint (all-cause mortality, hepatocellular carcinoma, liver transplantation, or cirrhosis complications) of 2,518 patients with NAFLD, using IPD obtained from 25 separate published studies. FIB-4 and NFS (non-alcoholic fatty liver disease (NAFLD) fibrosis score) alone were nominated as comparators but were not appropriate stand-ins for SOC, limiting the validity of any comparative conclusions. The commentary noted that Mozes 2023 evaluated prognostic accuracy, not diagnostic or clinical utility. It did not model sequential testing, which severely limited its applicability, nor modelled treatment guidance or reported any changes in real-world management impact.

VCTE results in Mozes 2023 were reported using rule-out and rule-in thresholds of LSM < 10 kPa and LSM ≥ 20 kPa, respectively, which further reduced its applicability. Compared to patients with LSM <10 kPa (reference), the multivariate cox regression adjusted survival HR (95% CI) in patients with LSM ≥10 but <20 kPa and LSM ≥20 kPa were 3.12 (1.94, 5.02) and 10.65 (6.53, 17.35), respectively. Time-dependent area under the receiver operating characteristic curve (tAUC), which evaluated the prognostic accuracy of different fibrosis assessment methods used to assess histologically assessed fibrosis stage, VCTE, FIB-4, and NFS over time in predicting liver related events and all-cause mortality, were also analysed. VCTE demonstrated numerically higher tAUCs compared to histology, while FIB-4 performed similarly to histology, and NFS had slightly lower tAUCs. However, these differences were not statistically significant.

Four additional MAFLD/NAFLD studies (Leite 2025, Gawrieh 2024, Ciardullo 2023b and Mu 2024) that may help inform longitudinal accuracy were identified by the ADAR and presented in the appendix but not addressed in the main body. However, similar to Mozes 2022 and Mozes 2023, they had limited applicability as they either did not consider sequential FIB-4 and VCTE testing, or did not use the same LSM threshold as the ADAR. Of these studies, Leite 2025 and Gawrieh 2024 may be of the most interest as they reported outcomes from repeated VCTE testing, which was not considered in Mozes 2023 and complements the ADAR's results:

- Leite 2025 was a prospective cohort involving 288 patients who underwent two VCTE examinations at least two years apart. Relative percentage changes in LSM and controlled attenuation parameter (CAP) were measured and the associations with clinical outcomes, including liver-related events (LREs), cardiovascular events (CVEs), and all-cause mortality

were investigated. Over a median follow-up of 6 years, the cohort experienced 22 LREs, 28 CVEs, and 37 deaths. For LREs, baseline LSM was the strongest predictor, though increases in LSM over time also conferred independent prognostic value (HR: 1.5 [1.0–2.1] per 1-SD increment). For CVEs, both a rise in LSM (HR: 1.7 [1.3–2.3]) and a decline in CAP (HR: 1.5 [1.0–2.3]) were significantly associated with increased risk.

- Gawrieh 2024 was a prospective cohort study in which 1,403 patients had biopsy at baseline and serial annual VCTE assessments, with a mean follow-up of 4.4 years (range 0.4–9.5 years) and a median of 4 VCTE exams per patient. Progression to compensated advanced chronic liver disease (cACLD) was defined as an increase to LSM ≥10 kPa, and regression from cACLD as a drop to LSM <10 kPa. Over a mean follow-up of 4.4 years, 89 LREs occurred (annual incidence: 1.5%). Among those at risk, 29% progressed to ≥10 kPa and 44% regressed below this threshold. Patients who progressed to cACLD had significantly higher LRE rates than non-progressors (16% vs. 4%; adjusted HR (aHR): 4.0; 95% CI: 1.8–8.9). Those who regressed from cACLD had significantly lower LRE rates than non-regressors (7% vs. 32%; aHR: 0.25; 95% CI: 0.10–0.61). The study concluded that dynamic LSM changes are independently associated with LRE risk in both directions (progression and regression), supporting serial VCTE as a non-invasive surrogate for monitoring disease trajectory and clinical outcomes in NAFLD.

Performance degradation in real-world subgroups (e.g., people with obesity or diabetes, or younger patients) is not adequately addressed in the ADAR's modelling.

The ADAR did not provide direct evidence that the proposed sequential strategy of VCTE (single rule-out/rule-in threshold of 8.0 kPa) following an indeterminate or high FIB-4 result (≥1.3) leads to meaningful changes in clinical management compared to SOC. The cited MAFLD studies that presented evidence on change in management had limited applicability as follows:

- Tulleners 2024 compared a structured liver care pathway with community-based VCTE access and triage, and the usual care group, where patients remained on the hospital waitlist without additional intervention. However, 37/48 (77%) patients in the usual care arm in Tulleners 2024 also had VCTE, which may not be representative of current SOC. The HR for the time to diagnosis of high risk was 1.28 (95% CI 0.59 to 2.79), indicating a faster average time to diagnosis with the intervention, but failing to conclusively demonstrate a faster time. Tulleners 2024 had limited applicability as VCTE was not used as a second-line test after indeterminate FIB-4, may have been underpowered (only 97 out of planned 156 patients enrolled) and included patients with baseline FIB-4 <1.3 in the VCTE group.
- Hayward 2021 was a feasibility study of a real-world, two-step liver fibrosis assessment pathway. Step 1 was assessment via FIB-4 and NFS, and step 2 was patients with indeterminate or high results from either FIB-4 or NFS being referred to undergo VCTE. Patients with LSM <8.0 kPa were returned to primary care but those with LSM ≥ 8.0 kPa were referred to hospital liver clinics. 38/162 patients (23.5%) were referred to hepatology management clinic assessment. However, meaningful conclusions were difficult due to the lack of a comparator group or outcome tracking related to VCTE-driven decisions.
- Sarkar Das 2024 was a systematic review that reported findings from six studies, which reported adherence or completion rates of VCTE among patients who were offered the test, with a completion rate of over 90%. However, as noted by the ADAR, only six out of the 14 included studies reported VCTE adherence or completion rates. This limited reporting introduces a risk of selection bias, as studies with lower adherence or implementation challenges may have been less likely to report or be published. Additionally, it was unclear whether VCTE was part of sequential testing (i.e. stratified by FIB-4 category).

Additionally, the ADAR claimed that Mozes 2022 provided evidence that VCTE reduced the number of liver biopsies required. The commentary noted that the applicability of this finding to the proposed population is uncertain, as the LSM and FIB-4 cut-offs used in Mozes 2022 differed substantially from those proposed in the ADAR and were aimed at detecting cirrhosis rather than advanced fibrosis.

In summary, the ADAR provided insufficient direct evidence to support the use of VCTE following FIB-4 in a specific sequential pathway with a single rule-out/rule-in threshold of LSM 8.0 kPa, as most studies did not assess sequential testing, or used different thresholds for VCTE, with most studies considering a separate threshold for rule-in and rule-out based on LSM. The claim of improved change in management was based on indirect evidence and conclusions regarding incremental benefit with VCTE could not be drawn based on the evidence provided, due to the lack of a comparator or the use of an inappropriate comparator.

Clinical claim

The ADAR made the clinical claim that "VCTE performed significantly better in detecting advanced fibrosis than all serum-based tests."

The commentary considered the claim that VCTE outperforms all serum-based tests was unsubstantiated based on the available evidence, as no comparative studies against serum based tests using the LSM thresholds proposed by the ADAR were presented. Clinical guidelines instead support a technology-agnostic approach, with evidence suggesting that other forms of elastography such as 2D-SWE, or the direct serum fibrosis test ELF, performed similarly to VCTE. Limiting funding to a single proprietary device may therefore not be justified.

The ADAR also claimed that "(s)equential use of FIB-4 followed by VCTE offers improved diagnostic accuracy for detecting advanced fibrosis (≥F3), with VCTE demonstrating comparable diagnostic accuracy with liver biopsy (reference standard) at dual cut-off thresholds."

The commentary considered that this claim was not adequately supported. Although Mozes 2022 was cited to support the diagnostic accuracy and biopsy-reduction potential of a FIB-4 to VCTE strategy, its design and analysis do not align with the ADAR's proposed pathway and had poor applicability. Mozes 2022 presented results from a sequential strategy via a simulation model rather than reporting results from actual testing, applied different VCTE thresholds to the ADAR and had a high risk of bias. The literature did not, as a whole, appear to support the use of a single rule-out/rule-in threshold for VCTE due to poor sensitivity/specificity.

The ADAR also claimed that "VCTE provides similar prognostic insight into future liver-related events (LREs), including hepatocellular carcinoma (HCC) and mortality compared to the reference standard."

The commentary considered that this claim was not adequately supported. The evidence presented to support claims against HCC and mortality was Mozes 2023, a retrospective IPD meta-analysis. However, Mozes 2023 did not evaluate the sequential use of FIB-4 followed by VCTE, nor did it apply the LSM threshold of 8.0 kPa as proposed by the ADAR. Although it meets technical criteria for prognostic accuracy, it lacks evaluation of test-guided management, treatment impact, or longitudinal diagnostic performance. The study does not model real-world triage, track serial measurements, or assess test substitution or biopsy reduction. As such, it cannot substantiate claims about VCTE's clinical utility or diagnostic superiority in the proposed MAFLD pathway.

The ADAR further claimed that "(t)he use of non-invasive sequential testing with VCTE and FIB-4 leads to change in management decisions for patients with MAFLD, including accurate disease

staging, earlier testing, better patient adherence, streamlined referral patterns and increased resource efficiency."

The commentary considered that this claim was not adequately supported. The studies cited in support of the ADAR's proposed FIB-4 followed by VCTE pathway do not provide directly applicable evidence. Tulleners 2024 did not evaluate VCTE as a second-line test after indeterminate FIB-4; Hayward 2021 lacked a comparator and outcome tracking; and Sarkar Das 2024 did not assess sequential testing or clinical utility. None of the studies were specific to the proposed FIB-4 subgroups of >1.3 and <2.7 or FIB-4 >2.7, and none demonstrated VCTE-driven changes in management or outcomes.

13. Economic evaluation

The key features of the economic model in the 1797 ADAR are presented in the table below.

Table 8 Summary of the economic evaluation

Component	Description
Perspective	Australian Health Care System Perspective
Population	Patients with diagnosed MAFLD in both primary (general practice and community settings) and secondary care (hepatology practices)
Prior testing	FIB-4 test
Comparator	SOC, including: Primary care: ultrasound (MBS item 55036) Secondary care: ultrasound (MBS item 55036), percutaneous liver biopsy (MBS item 30409)
Type(s) of analysis	Cost-Consequence analysis
Outcomes	Cost per correctly diagnosed patient Number of correct final diagnoses Number of high-risk patients incorrectly diagnosed as low risk
Time horizon	Time to reach a diagnosis and assign a risk category of liver disease
Computational method	Decision analytic model in EXCEL
Generation of the base case	Modelled cost-consequences analysis presented separately for primary and secondary care settings
Health states	Not applicable
Cycle length	Not applicable
Transition probabilities	Derived from diagnostic outcomes (TP, TN, FP, FN) of the proposed diagnostic strategy FIB-4 index, followed by VCTE vs a comparator – ultrasound in primary care and secondary care
Discount rate	Not applicable
Software	Excel

FIB-4=Fibrosis-4 Index, TP=true positive; FN=false negative; TN=true negative; FP=false positive.

Contrary to the proposed comparator of SOC (see Table 4), the only diagnostic method in primary care evaluated in the ADAR economic model was ultrasound. As discussed previously in Section 8, the commentary considered this to be inappropriate, as ultrasound has a limited ability to detect fibrosis, and PASC considered it to be an inappropriate test comparator. The GESA consensus statement recommends morphological liver ultrasound, covered by MBS item 55036, as the first-line test prior to VCTE™. Patients in both the intervention and comparator arms should have had this scan done prior to VCTE. The GESA consensus statement and clinical management algorithms do not include additional ultrasound after VCTE. As such, VCTE is unlikely to impact the number of abdominal ultrasounds billed to the MBS.

MBS item 55036 is used as a unit cost, with the implication that VCTE would reduce ultrasound costs to MBS. In the economic model, it was assumed that in primary care 90% of patients in the comparator arm underwent an ultrasound, and in specialist care 100% patients in the comparator arm underwent an ultrasound. Ultrasound is also conducted in the intervention arm

in both settings where 10% of patients with a finding suggestive of fibrosis by VCTE will proceed with ultrasound (this assumption is informed by clinical experts). Including ultrasound in the comparator arm for most patients at the unit price of MBS item 55036 likely biased the economic evaluation in favour of VCTE, as it overestimated the costs in the comparator arm at this point. The ADAR nominated cost per correctly diagnosed patient as a primary outcome. The commentary noted that, presumably, the ADAR suggests that a lower cost per correctly diagnosed patient is a positive outcome, which should be correlated with improved testing. However, in the model, if the sensitivity of VCTE is improved, the cost per correctly diagnosed patient actually increases in the PICO 1 population due to an increase in the number of true-positive cases and the increased cost associated with (necessary) specialist visits. This suggests that the outcome measure may not be the most appropriate, and the results of the economic evaluation presented in the ADAR may not be informative, and/or the ADAR's assumptions may be inappropriate.

Other similar computational issues were noted during the evaluation which may point to the lack of robustness of the economic model. For example, if the distribution of FIB-4 results from Mozes 2022 was used as a sensitivity analysis (the ADAR's base case relied on Anstee 2024), the 'Number of high-risk patients incorrectly diagnosed as low risk' in the PICO 1 population becomes negative, which lacks face validity.

Avoiding unnecessary liver biopsies (estimated by the reduction in the proportion of false-positive results with VCTE compared to ultrasound) was cited as one of the advantages of a two-tier NIT, with another related benefit being a reduction in specialist referrals. Cost of a liver biopsy seems to be a decisive factor in the short term. The degree of reduction in the number of referrals to a hepatologist, but ultimately, to liver biopsy in hospital, would determine some cost-savings to offset the additional cost of a second-tier test. Some assumptions of the model seem to confirm this tendency. It is assumed that in the comparator arm, 15% of patients with fibrosis-suggestive ultrasound findings undergo a liver biopsy however, only 5% of those with an increased liver stiffness as assessed by VCTE (the intervention arm) undergo a liver biopsy. The parameter estimates are based on expert advice, not supported by the evidence and bias the outcomes in favour of VCTE.

The commentary also noted that none of the economic evaluation outcomes were considered patient-relevant, thus being inconsistent with PASC's preference that cost-effectiveness would be measured in terms of health outcomes, rather than test outcomes. The commentary reviewed economic evaluations identified in the literature and confirmed that some of them, including at least three high-quality cost-utility analyses (CUA), assessed patient-relevant outcomes. PASC considered that a CUA would be desirable but noted that a cost-effectiveness analysis (CEA) was acceptable based on the clinical claim. One example of a health outcome measurable in a CEA would be cost per case of cirrhosis or liver cancer averted. However, PASC also considered that any changes to the number of referrals to specialists based on risk stratification in the primary care setting should be captured in the economic evaluation.

There were also some unjustified assumptions in the model structure; in primary care, non-attendance estimated at 10% in both the ultrasound in the comparator arms and VCTE in the intervention arm is. The diagnostic outcome for this proportion of patients is defined as "incorrect diagnosis", but this assumption is unjustified and biases the outcome (cost per correct diagnosis) in favour of VCTE. The model did not include the FibroScan® failure rate, estimated at 5% by NICE (2021-2022) and at 15.8% by Gruneau (2023), where a failed VCTE scan is defined as indeterminate or unreliable results when fewer than 10 valid shots are obtained. This omission also introduced a bias in the outcomes.

The commentary noted that there is a fundamental mathematical problem with all two-tier diagnostic tests where the first NIT produces non-binary results. In the case of FIB-4 with a dual cutoff [1.3-2.67] (or [1.3-3.25] as in the model), these are AF risk negative <1.3 or AF risk positive ≥2.67 or an indeterminate risk of AF [≥1.3; <2.67]. According to the structure of the ADAR model, the population being tested with VCTE is a subgroup of the MAFLD population with FIB-4 indeterminate results and higher values, as per the ratified PICO.

However, there is a conceptual problem with estimating the prevalence of AF in this subgroup. By definition, the proportion of true positives (or true negatives) is unknown. Facing the conceptual nature of the "indeterminate" as in the non-binary outcomes of FIB-4, it is likely that a reliable estimate of AF prevalence in the indeterminate FIB-4 subgroup, which is unknown by definition, could not be obtained without a reference standard – a histological tissue sample. Nevertheless, the ADAR attempted to empirically estimate the prevalence of AF in the FIB-4 indeterminate subgroup by employing data from three disparate publications (Armstrong 2012, McPherson 2010 and Anstee 2024), each with applicability issues with respect to the target population as defined in the Ratified PICO, as explained below. The exercise does not seem to have produced a valid estimate of the AF prevalence in the indeterminate FIB-4 subgroup. Conventionally, for a given sensitivity and specificity of a test, a Bayesian revision theorem is applied, where the Bayesian prior is set equal to the prevalence of a condition in the population, which is unknown for the subgroup with indeterminate test results. The prevalence of AF in the "indeterminate" subgroup cannot be estimated by probabilistic means, but it can be calculated, with some degree of precision, from observations in the individual patients' test results, provided each of these results is validated with a histological sample and assuming that liver biopsy is a reference standard. The most prominent source of such data is a meta-analysis by Mozes 2022, which was relied upon by the ADAR to inform the accuracy of VCTE. However, as discussed above, Mozes 2022 had poor applicability to the proposed research question as the VCTE thresholds differed from that proposed in the ADAR, and sequential strategy A in Mozes 2022 did not report results for FIB-4 >1.3 only to inform the comparator arm for Population 2. As such, the diagnostic accuracy results for VCTE applied in the model were not applicable to the ADAR's proposed VCTE thresholds and the results of the economic analysis based on these diagnostic accuracy results were uncertain.

There were also issues with assumptions regarding the inputs used in the economic model. For example:

- McPherson 2010 was used to inform the sensitivity and specificity of FIB-4 testing for both the rule-in and rule-out thresholds; however, McPherson 2010 assessed the accuracy of FIB-4 with a rule-in threshold of 3.25, whereas the ADAR proposed a rule-in threshold of 2.67. As such, the diagnostic accuracy for FIB-4 in the economic model was unlikely to represent the accuracy in the clinical setting as proposed in the ADAR;
- Anstee 2024, which primarily enrolled patients in primary care was used to inform the distribution of FIB-4 in the population for both PICO 1 (primary care) and PICO 2 (secondary care) even though distributions from Mozes 2022, which mainly included patients in secondary care, were available; and
- Armstrong 2012, which reported a prevalence of 7.6% of AF in MAFLD patients in the primary care setting, was used for both primary and secondary care settings. In comparison, Mozes 2022 reported a prevalence of 30% in the secondary/specialist care setting.

These issues increased the uncertainty associated with the results presented by the ADAR economic model.

Table 9 and Table 10 present the results of the ADAR model for the PICO 1 and PICO 2 populations, respectively. However, the commentary considered that these results were likely uncertain, biased in favour of VCTE and may not be informative for the multitude of reasons discussed above.

Table 9 Results of the economic analysis presented in the ADAR in PICO 1 (Primary care)

	FIB-4 +VCTE	Ultrasound	Increment
Outcomes			
Correct diagnosis	0.73	0.55	0.18 (33%)
High-risk patients incorrectly diagnosed as low risk	0.04	0.08	-0.04 (-45%)
Unnecessary specialist referrals	0.11	0.26	0.16 (-60%)
Specialist referrals	0.19	0.32	0.12 (-39%)
Costs			
Ultrasound	$8.84	$112.23	-$103.39 (-92%)
VCTE	$52.97	$0.00	$52.97 (NA)
GP	$38.57	$38.57	$0.00 (0%)
Specialist	$58.32	$96.12	-$37.81 (-39%
Total cost	$158.69	$246.92	-$88.23 (-36%)

FIB-4 = Fibrosis-4, VCTE= Vibration-Controlled Transient Elastography
Source: Tables 54 and 56 of the ADAR

Table 10 Results of the economic analysis presented in the ADAR in PICO 2 (secondary/specialist care)

	FIB-4 +VCTE	Ultrasound	Increment
Outcomes			
Correct diagnosis	0.83	0.60	0.23 (39%)
High-risk patients incorrectly diagnosed as low risk	0.05	0.12	-0.06 (-55%)
Liver biopsies	0.01	0.05	-0.04 (-75%)
Costs			
Ultrasound	$9.82	$124.70	-$114.88 (-92%)
VCTE	$58.85	$0.00	$58.85 (NA)
Liver biopsy	$2.58	$10.43	-$7.85 (-75%)
Specialist	$98.95	$98.95	$0.00 (0%)
Total cost	$170.20	$234.08	-$63.88 (-27%)

FIB-4 = Fibrosis-4, VCTE= Vibration-Controlled Transient Elastography
Source: Tables 55 and 57 of the ADAR

The Commentary designed an exploratory cost-consequences analysis (CCA) comparing the combination of FIB-4 and VCTE versus FIB-4 alone (assumed to be a comparator - current practice). The latter reflects the recommendation that further tests are required for individuals with indeterminate to high-risk scores (e.g. FIB-4 test score ≥1.3) (EASL 2021).

For its CCA exercise, the Commentary employed the evidence sequential strategy A from Mozes 2022 to inform the diagnostic accuracy of FIB-4 followed by VCTE (see discussion in Section 12). Comparative effectiveness and Figure 2). Acknowledging that this was inaccurate due to the use of a rule-in LSM threshold of ≥ 10.0 kPa instead of ≥ 8.0 kPa as proposed by the ADAR, this still represented the closest source of data available. The diagnostic accuracy of the comparator of FIB-4 ≥1.3 was back-calculated during the evaluation. The diagnostic outcomes used to inform the CCA exercise are presented in Table 11. It was assumed for the illustrative modelling exercise that the proportions of true/false positives and true/false negatives from Mozes 2022 correspond to a single LSM cutoff at 8 kPa, implying that there are no indeterminate VCTE results.

Table 11: Diagnostic outcomes from Mozes 2022 sequential strategy A

	FIB-4 <1.3; ≥2.67 only no VCTE, n (%)	VCTE > 8kPa in indeterminate subgroup, n (%)	FIB-4 <1.3 only, no VCTE (calculated during evaluation), n (%)
True negatives (TN)	2311 (0.47)	654 (0.13)	2311 (0.47)
False negatives (FN)	396 (0.08)	102 (0.02)	396 (0.08)
True positives (TP)	459 (0.09)	502 (0.10)	1063 (459+102+502) (0.22) [a]
False positives (FP)	239 (0.05)	251 (0.05)	1144 (239+654+251) (0.23) [b]
Subtotals	**3405 (0.65)**	**1509 (0.30)**	**-**
Total excluding indeterminate VCTE results	**4914 (0.95)**		**-**
Total with recalculated FIB-4 results	-		**4914 (1.00)**
VCTE Indeterminate outcome	-	**245 (0.05)**	-
TOTAL SAMPLE	**4914+245=5159 (1.00)**		

FIB-4, Fibrosis-4 Index; FN = false negative; FP = false positive; kPa = kilo pascal; TN = true negative; TP = true positive; VCTE = vibration-controlled transient elastography
Source: Fig 3A, Mozes (2022)
a Calculated as TP of FIB-4 ≥2.67 plus TP of VCTE > 8 kPa plus FN of VCTE > 8 kPa
b Calculated as FP of FIB-4 ≥2.67 plus FP of VCTE > 8 kPa plus TN of VCTE > 8 kPa

Table 12 shows the parameters and diagnostic outcomes used in the CCA, based on the results recalculated results from Mozes 2022, excluding the 5% indeterminate VCTE results.

Table 12 Diagnostic outcomes used for evaluation cost consequence analysis

outputs	Proposed algorithm: Patients with FIB-4 <1.3 remain in primary care; patients with [FIB-4 <1.3; ≥2.67] are referred to VCTE [> 8kPa]	Current practice: Patients with FIB-4 <1.3 remain in primary care; patients with FIB-4 ≥1.3; are referred to specialist care
% tested FIB-4 indeterminate	(1509+245) / 4914 = 31%	Not applicable
% patients correctly diagnosed (TP+TN)	(2311+459+654+502) /4914 = 80%	(2311+1063)/ 4914 = 69%
% patients incorrectly diagnosed (FP+FN)	(396+239+102+251) /4914 = 20%	(396+1144) / 4914 = 31%
%. of specialist referrals (TP+FP)	(459+239+502+251) / 4914 = 30%	(1063+1144) 4914= 45%
% of unnecessary referrals to specialist (FP)	(239+251) / 4914 = 10%	1144 / 4914 =23%
%. of missed AF (FN)	(396+102) / 4914 = 10%	396 / 4914 = 8%

FIB-4, Fibrosis-4 Index; FN = false negative; FP = false positive; kPa = kilo pascal; TN = true negative; TP = true positive; VCTE = vibration-controlled transient elastography

The CCA conducted during the evaluation showed that, compared to a strategy in which all patients with FIB-4 > 1.3 are referred to specialist care, the proposed two-tier diagnostic algorithm of FIB-4 and VCTE for indeterminate results will result in more correctly diagnosed patients, fewer incorrect diagnosis (overall) and fewer unnecessary referrals, all of which are positive outcomes and likely to improve efficiency and deliver positive health outcomes. However, there are also more missed diagnoses with the two-tier diagnostic strategy (which is plausible as fewer patients end up being referred), which raises an ethical question of whether increased efficiency in the cohort should be obtained at the expense of a minority who may be worse off.

Unit costs from the ADAR model were adjusted for the most recent MBS prices and applied to the outputs in Table 12. The costs of physical assessment and blood investigations are common to both alternative strategies and their diagnostic input is assumed to have been captured in the FIB-4 score. Patients were assumed to be diagnosed with MAFLD (NAFLD) at the baseline as determined by ultrasound with the corresponding cost included in the total cost per patient. The role of a subsequent ultrasound in AF assessment is unclear and should be excluded for the reasons described above. The CCA assumes that ultrasound follows VCTE investigations in 10% of patients for reasons aside from the diagnosis of AF. Table 13 shows the results of the CCA conducted during the commentary.

Table 13 Results of the Commentary cost-consequences analysis

costs	Proposed algorithm: patients with FIB-4 <1.3 remain in primary care; patients with [FIB-4 score between 1.3 and 2.67] are referred to VCTE [> 8kPa]	Current practice: Patients with FIB-4 <1.3 remain in primary care; patients with FIB-4 ≥1.3; are referred to specialist care	Incremental cost
Two GP visits (initial and post-test) assumed 100%	$87.80	$87.80	-
Cost of FibroScan test attendance assumed 100%	$18.07	$0.00	$18.07
Cost of ultrasound after VCTE assumed 10%	$3.77	$N/A	$3.77
Cost of specialist attendance	$92.26	$140.33	-$48.07
Cost of liver biopsy (33% according to Mozes 2022)	$19.82	$30.15	-$10.33
Total costs			
Total cost per patient	**$349.43**	**$385.98**	**-$36.56**
Cost per correct diagnosis	**$437.36**	**$562.16**	**-$ 124.80**

Total cost per patient was not much different between the strategy that combines FIB-4 and VCTE and the strategy based on a FIB-4 test with a single cutoff [1.3]. The incremental cost (savings) was $36.56. However, the cost per correct diagnosis is considerably less in the strategy that combines FIB-4 and VCTE; the incremental cost (savings) is $124.80 per correct diagnosis, which is explained by the difference in diagnostic accuracy between the two strategies.

The CCA was repeated for the cohort that includes 5% of patients with indeterminate VCTE results, by increasing the proportions of patients with true positive, false positive and false negative VCTE results. The cost per correct diagnosis in the proposed FIB-4, as proposed by the VCTE strategy, was not very sensitive to the inclusion of the small proportion of patients with indeterminate VCTE results, changing by -2 to 9%.

14. Financial/budgetary impacts

The ADAR adopted a mixed approach to inform VCTE™ utilisation and the financial implications of listing VCTE on MBS. This hybrid approach combines epidemiological reasoning with market-based assumptions for VCTE test capacity.

The ADAR's assumption that GPs could perform 10 VCTE scans per day (2,600 annually) across redacted machines in primary care, equating to redacted scans per year, lacks a clear rationale. This estimate does not account for the realities of GP workload, competing consultation demands, or the low likelihood that GP practices would operate VCTE devices given their high capital cost and limited patient volumes. It is also unlikely that GPs will perform VCTE themselves, given the requirements for training and practical experience, and competing consultation workload. VCTE is more realistically delivered in specialist or diagnostic service

settings, with most GPs referring patients for testing. Accordingly, the projected primary care capacity is likely overstated and does not accurately reflect real-world practice. The exception in primary care may be the limited number of GPs who work in special interest clinics, have a scope of practice very similar to that of a specialist, and therefore would be expected to provide more than 10 scans per day.

The budget impact model assumed an uninterrupted flow of patients who seem to begin the diagnostic pathway by undertaking the initial FIB-4 test in primary care, followed by VCTE as a confirmation test if results the FIB-4 results are indeterminate. Specialist care is reserved exclusively for patients who have already been identified as being at high risk (FIB-4 >2.67).

Epidemiological data were utilised to estimate the number of patients likely to take up VCTE for AF risk classification purposes. It was informed by three data sources:

A) The expected NAFLD rates from the study of the NAFLD disease burden in Australia, which estimated a projected disease growth over the 2019–2030 period (Table 1, Adams, 2020). These rates applied to the projected total Australian population (ABS Population projections, Table B9) to estimate the NAFLD population from 2026 to 2031. The commentary notes however, that the number of patients was not relied upon to inform the number of patients being tested with VCTE.

B) The number of liver ultrasound services (MBS Item 55036) that were conducted in Australia in 2019-2024 and their linear extrapolation to 2026-2031; This was assumed to be equal to the number of patients diagnosed with MAFLD.

C) The number of patients eligible for VCTE in primary care (i.e. those with an FIB-4 score between 1.3 and 2.67) was obtained by applying the proportion of patients with indeterminate FIB-4 outcomes from Anstee 2024 (29.65%) to the number of ultrasound services in each of the years 2026-2031 (from B). The number of patients eligible for VCTE in secondary care was obtained by applying the proportion of patients at high risk of AF (i.e. FIB-4 score > 2.67; 4.35%) to the number of ultrasound services in each of the years 2026-2031 (from B). Both proportions were obtained from the UK study, which reported the distribution of a large cohort of individuals with obesity and T2D with respect to their FIB-4 outcomes (Anstee 2024).

There are the following areas of uncertainty in estimating the size of the population eligible for VCTE:

1. The ADAR did not identify any data source to estimate the MAFLD population; therefore, all data inputs were sourced from the NAFLD evidence, the population that overlaps with the MAFLD population but is not identical to it.
2. The GESA consensus statement recommended liver ultrasound as the first-line test to diagnose hepatic steatosis in people at high risk of MAFLD. However, a number of alternative diagnostic methods are available in Australia (e.g. MRE or magnetic resonance spectroscopy, biomarkers, and CAP using FibroScan) (GESA, p.13) and as such, ultrasound may not capture all diagnostic methods for MAFLD.
3. Ultrasound is a non-specific investigation used for diverse abdominal conditions which include but are not limited to the MAFLD population. Moreover, the implicit assumption that all ultrasounds produce a positive outcome for hepatic steatosis is in direct contradiction with the assumed 65% specificity of ultrasound (rather than 100%) in the ADAR economic model. Moreover, some patients may claim more than one MBS item 55036 per year. Using the number of MBS item 55036 as the proxy for the number of

patients with positive MAFLD diagnosis likely significantly overestimates the number of MAFLD patients.

4. The linear extrapolation of the observed ultrasound services was not performed correctly, as it first calculated the rates of change in the services from each given year to the next and then simply averaged the rates across the 2018-2024 years for which the data were available. This resulted in an average annual growth rate of 3.15%. This rate was then applied to calculate the future services beginning in 2025. It can be observed that the number of ultrasound services fluctuated over the period from 2018 to 2024, increasing in some years and decreasing in the others. The trend does not appear linear; the extrapolation has likely produced a biased estimate of the diagnosed MAFLD population. Notwithstanding other deficiencies in estimating the eligible population, a method of moving averages would be more appropriate. The direction of the bias and the size of the under- or overestimate are difficult to determine since the service is not specific to the MAFLD condition.
5. The large population-based UK study (Anstee 2024) was conducted in the population with type 2 diabetes and/or obesity. Although patients with NAFLD were not excluded, this population is not the same as defined in the ratified PICO. The application of the FIB-4 score distribution from Anstee 2024 as a risk stratification input may introduce a systematic bias in financial calculations, unless it can be demonstrated that the distribution is relatively stable across subgroups with metabolic dysfunction-associated steatotic liver disease and type 2 diabetes. Anstee 2024 estimated 66% of the population with T2D and obesity in the low (FIB-4 <1.30), 29.65% in the indeterminate (FIB-4 1.30–2.67) and 4.35% in the high FIB-4 (>2.67) risk categories. The commentary noted that these proportions were used in the ADAR's economic evaluation. The financial estimates were sensitive to the selected values of a dual cutoff and to the underlying prevalence of advanced fibrosis. But even for the same upper and lower cutoffs, there is variation in the published estimates of the proportions of patients in the risk-stratified subgroups. For example, Mozes 2022 estimated 34% of patients with indeterminate risk and 13% in the high risk category, with the latter more than twice the size of the high risk subgroup in the Anstee 2024 cohort.

In both the primary care (FIB-4 indeterminate) and specialist care (FIB-4 high risk) subgroups, the annualised testing volume was calculated under assumption and potential overestimation of MAFLD patients regardless of setting being regularly tested, once every three years, i.e. the number of tests each year equalled the number of MAFLD patients divided by three.

The problem with estimating the size of the MAFLD population in general, and the size of the subgroup of patients at risk of AF in particular, is well recognised in the international literature. To reduce uncertainty on the local level, the funding authorities have resorted to feasibility studies. One UK study estimated the size of the primary care population that would benefit from VCTE at 9%, the figure included diabetics and patients with known hazardous alcohol use (e.g. Harman 2015). The population size suggested in the ADAR appears to be overestimated. More relevant is the actual inclination in MAFLD patients to undergo the full diagnostic procedure, given that fibrosis is a slow-progressing disease. The ADAR recognised this issue by assuming that only 90% of patients with FIB-4 indeterminate outcome would proceed to VCTE. The commentary could not independently validate the figure, but it appears to be an overestimate of the actual demand for VCTE tests.

The second part of the financial model involves estimating the total testing capacity in Australia, and then assigning testing to primary or secondary care based on assumed capacity, with the

assumption that capacity in primary care must be exhausted before testing in secondary care was conducted. According to the sponsor, there are currently only redacted GP-owned FibroScan® devices. Together with redacted other machines in community-based and Aboriginal health centres, FibroScan devices in primary care account for only 10% of the total number of FibroScan devices in Australia. The annual growth in FibroScan devices is assumed to favour primary care at 20% versus specialist care at 2%, reducing the initial (as of 2026) imbalance of redacted primary care device to redacted devices in specialist care to redacted to redacted in 2031. The model assumes immediate full utilisation without any rollout plan. The commentary noted that the number of FibroScan machines as well as the claimed increase in FibroScan devices in primary care could not be independently verified.

The ADAR assumes each VCTE machine in primary care performs 10 tests per weekday (2,600 annually), while in specialist settings, throughput is limited to 3 tests/day (780 annually). The commentary could not independently validate this fourfold discrepancy, and this difference was not justified in the ADAR. There was a discrepancy in the number of tests assumed to be performed per day in the primary care setting. In the financial calculations spreadsheet, 2,600 tests per year were used; however, in Table 64 (parameter values), the annual capacity per VCTE machine in primary care was reported as 4,160 tests based on daily throughput.

The commentary considered that number of tests per machine in the ADAR in the primary care setting may be overestimated. The FibroScan submission to NICE (2021 and 2022) assumed that a single FibroScan device is used for between 500 and 1,000 patients per year per primary care network (PCN), where the average size of the PCN is 48,000 patients (data from 2020) or in 2,500 to 5,000 patients per year across 5 PCNs. In this submission the target population included patients with alcoholic liver disease and hepatitis C and B. However, the NICE assessors suggested that this throughput may not be achievable across the National Health System (NHS) meaning that the projected uptake would not be financially viable.

The key to the ADAR financial model is the assumption that testing first occurs in the primary care setting, and any tests that cannot be accommodated in primary care will “overflow” to secondary care. The magnitude of this overflow was estimated as the difference between the annual (increasing at 20% annual growth) testing capacity of VCTE in primary care and the size of the population with indeterminate FIB-4 results as estimated in the epidemiological part of the model. For example, in 2026, redacted machines in primary care were assumed to produce redacted tests, while the size of the FIB-4 indeterminate test subgroup of the MAFLD population is 348,181 patients who require 116,060 tests after adjusting for the follow-up test, which is conducted once every 3 years. The overflow of 69,260 tests is then redirected to the specialist care, provided there is “a given access”. Specialist care has an overcapacity of redacted machines with an annual throughput of 780 potentially delivering redacted tests while the need of the subgroup with high risk of AF (by FIB-4 test) is estimated at 17,010. The total number of tests performed at specialist care is calculated at 86,270 (17,010 plus the overflow of 69,260 from primary care) which still indicates an extra unutilised, at least by the target population, capacity of 40,090 tests. Nevertheless, while the “overflow” is gradually shifted back to primary care machines, which continue to grow at 20% per year, the number of machines in specialist care also grows, albeit at a much smaller rate of 2%. The proportion of primary and secondary care testing affects the financial estimates, as the ADAR assumes that testing was cheaper in the primary care setting due to GP fees being lower than specialist fees, and liver biopsies were avoided.

The flow of eligible patients through the diagnostic management pathway was not presented with respect to the proposed services (VCTE tests) versus current practice (inappropriately assumed to be ultrasound as the key comparator test to be substituted). This was also an issue with the

choice of comparator in the economic model. In patients with abnormal LFTs or non-specific abdominal symptoms, ultrasound remains clinically necessary, regardless of VCTE access.

The modelled diagnostic outcomes in the intervention (VCTE) and the comparator (ultrasound) arms (Section 13) are used indirectly, to inform the "downstream savings", which consist of a reduction in specialist appointments and liver biopsies avoided. Here, a "downstream" effect relates not to the patients' progression through the stages of liver disease, but to the financial implications of a sharp increase in the number of FibroScan devices in primary care. Given the uncertain results of the economic model, the financial impact which relied on these inputs was also uncertain. Moreover, the commentary noted that specific claims around diagnostic outcomes which were supposedly based on the economic model could not be verified. For example, a false negative rate of 2% was reported but this could not be verified. As such, the diagnostic parameters which informed the "downstream savings" should be considered uncertain.

Nevertheless, the ADAR translated the difference in proportions of incorrect diagnoses (FN and FP) between the comparator (FIB-4 + ultrasound) and the intervention (FIB-4+VCTE) arms (Section 13) into the incremental cost offsets. These are then included in the financial model to reduce the net cost to MBS. The estimated cost offsets were due to assumptions in:

- Reduction in the follow-up specialist consultations (90%), assuming that all FibroScan devices are placed at the point-of-care, and results are instantly available and interpreted by GPs in the course of the initial presentation. It should be noted that the requirement for patients to fast for at least two hours before VCTE may conflict with the claim that the test can be conveniently performed at the first visit. In practice, patients who have eaten recently would be unable to undergo the test immediately, potentially necessitating a return appointment and reducing the efficiency and accessibility of care.
- Reduction in ultrasound services in primary and specialist care, with VCTE replacing 80% of ultrasounds. However, as discussed above, PASC did not consider morphological ultrasound to be an appropriate comparator and MBS item 55036 (used by the ADAR in the cost offsets) is not covered by the MBS for elastography.
- Reduction in liver biopsies (10%) in specialist care. This was based on expert advice that, in current practice, 15% of patients with fibrosis-suggestive ultrasound findings undergo a liver biopsy, whereas only 5% of patients with increased liver stiffness, as assessed by VCTE undergo a liver biopsy.
- Reduction in the proportion of false positive outcomes by 60% when ultrasound is substituted with VCTE. Translated into a corresponding reduction in unnecessary specialist visits.

The assumptions for cost-offset calculations were uncertain, as they relied on diagnostic data with limited applicability (see Section 12. Comparative effectiveness), were based solely on clinician opinion and lacked support from observations in real-world practice, and were contingent on the outcomes of an uncertain economic model (see Section 13). Economic evaluation). Overall, the cost-offsets were likely uncertain and overestimated, specifically due to the inclusion of ultrasound in the offset.

The financial implications for the MBS resulting from the proposed listing of VCTE as a confirmation test for indeterminate and high FIB-4 results, as presented in the ADAR, are summarised in Table 14 (PICO 1 population: primary care) and Table 15 (PICO 2 population: secondary/specialist care).

Table 14: Net financial implications of VCTE testing in primary care to the MBS

Parameter	2026	2027	2028	2029	2030	2031
Estimated use and cost of the proposed health technology						
Number of eligible patients	116,060	119,718	123,491	127,383	131,398	135,539
Number of services of VCTE in primary care given capacity	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Cost to the MBS (with appropriate copayments excluded)	$3,641,063	$4,399,958	$5,279,950	$6,335,940	$7,603,128	$9,123,754
Change in use and cost of other health technologies						
Change in use of specialist referrals avoided	$8,568,612	$10,282,334	$12,338,801	$14,806,562	$17,767,874	$21,321,449
Change in use of additional ultrasounds avoided	$4,668,768	$5,602,522	$6,723,026	$8,067,631	$9,681,157	$11,617,389
Net change in costs to the MBS (with appropriate copayments excluded)	$11,251,773	$13,502,128	$16,202,553	$19,443,064	$23,331,676	$27,998,012
Net financial impact to MBS	**-$7,610,710**	**-$9,102,169**	**-$10,922,603**	**-$13,107,124**	**-$15,728,548**	**-$18,874,258**

Source: ADAR, Section 4.4

Table 15: Net financial implications of VCTE testing in secondary/specialist care to the MBS

Parameter	2026	2027	2028	2029	2030	2031
Estimated use and cost of the proposed health technology						
Number of people eligible for VCTE	17,010	17,546	18,099	18,669	19,258	19,865
Number of services redirected to specialist care due to testing capacity limits in primary care	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Cost to the MBS (with appropriate copayments excluded)	$24,022,800	$22,647,084	$20,720,289	$18,204,660	$14,976,017	$10,885,142
Change in use and cost of other health technologies						
Change in use of additional ultrasounds avoided	$8,606,315	$8,090,942	$7,402,005	$6,502,567	$5,348,239	$3,885,678
Change in use of return specialist appointments avoided	$6,829,149	$6,420,199	$5,873,523	$5,159,816	$4,243,851	$3,083,302
Change in use of liver biopsy avoided	$337,988	$348,640	$359,628	$370,962	$382,653	$394,713
Net change in costs to the MBS (with appropriate copayments excluded)	$13,407,435	$12,630,814	$11,589,883	$10,228,344	$8,478,532	$6,259,139
Net financial impact to the MBS	**$10,615,366**	**$10,016,270**	**$9,130,407**	**$7,976,317**	**$6,497,485**	**$4,626,003**

Source: ADAR, Section 4.4

The ADAR estimates that, due to an increase in the number of tests in primary care, the number of specialist referrals and testing in secondary care will decrease, leading to an overall cost

saving. The commentary considered these financial estimates to be highly uncertain, the primary reason being that the number of MAFLD may be overestimated, uptake of both FibroScan by primary caregivers as well as number of tests conducted in primary care setting may be overestimated, the concept of overflow may not be justified, and the cost offsets may be overestimated.

Given the numerous conceptual, methodological and calculational problems with the ADAR financial model, the sensitivity analyses in parameter variation was not considered informative for MSAC.

15. Other relevant information

As discussed in Table 1, the commentary noted that, given the 1797 ADAR's claim that patients currently face an out-of-pocket cost of between $200-300 for privately funded VCTE, patients would still face substantial out-of-pocket costs even if the delivery of VCTE were subsidised by the MBS. The same issue of inequity previously identified by the MSAC in Application 1446 would apply.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- No comparative effectiveness or safety data were presented against the management options in standard of care (SOC). The applicant-developed assessment report's (ADAR's) nominated comparator of SOC includes liver ultrasound (US), other non-funded tests for the diagnosis of advanced fibrosis, and/or referral to specialist care (where appropriate). However, no comparative effectiveness or safety data were available for the proposed triage strategy (i.e. Vibration-Controlled Transient Elastography [VCTE] performed as a second-line test following FIB-4 testing).
- Furthermore, ESC considered that US is a prior test for the proposed population, not a subsequent test as proposed in the ADAR. ESC noted that anatomical US does not assess liver fibrosis severity and US is not MBS-supported for elastography. ESC therefore considered US does not constitute part of SOC following FIB-4 testing and is not suitable for inclusion in the SOC comparator. ESC noted that the inappropriate positioning of US in the SOC comparator had many flow-on effects throughout the application.
- The ADAR proposes that a single liver stiffness measure (LSM) threshold (8 kPa) be used to both rule-out and rule-in a patient being at risk of advanced fibrosis (AF) when measured by VCTE. ESC noted that this was inconsistent with the clinical evidence provided, in which the large majority of studies used separate thresholds for rule-out and rule-in, due to the relatively poor diagnostic performance of a single threshold. This affected the applicability of the evidence to the proposed strategy. ESC considered that the cost-effectiveness of using different thresholds or adopting a higher rule-in VCTE threshold as per the literature could be explored (e.g. >10 kPa or >12 kPa), acknowledging that different thresholds may influence whether some patients are misclassified.
- There was a paucity of data directly applicable to the proposed primary care population, and additionally, data directly comparing the proposed triage strategy (FIB-4 followed by VCTE in patients who require a second test) with the current strategy (FIB-4 followed by

SOC) were lacking. The pre-ESC response claimed that tertiary population data should apply to the proposed primary care population. ESC noted none of the identified studies were directly applicable to the proposed intervention (most did not use the single threshold of 8.0 kPa for VCTE and/or did not involve sequential triage strategies) within the proposed population (studies primarily did not select patients for VCTE based on FIB-4 score). ESC considered that the diagnostic accuracy and predictive values of tests would be different in low-prevalence vs higher-prevalence populations. ESC considered that additional evidence in primary care populations should be provided by the applicant to demonstrate diagnostic accuracy in the populations proposed to be tested.

- Longitudinal accuracy evidence provided in the ADAR had poor applicability, as it did not assess the proposed sequential triage testing, management impact, or use the single 8.0 kPa LSM rule-in/rule-out threshold. ESC noted there was a lack of evidence demonstrating clear changes in management attributable to VCTE beyond referral pathways. The pre-ESC response reiterated that the studies demonstrating a change in referral pathway support the use of VCTE and that improved clinical outcomes can be inferred; however, ESC disagreed and advised that evidence on change in health outcomes (not referral pathways) as a result of VCTE testing is needed.
- The effect of misclassification following FIB-4 and VCTE testing was not addressed. The net health benefit/harm of VCTE across all patients tested (including patients with true positive, false positive, true negative and false negative results) was not addressed. ESC considered that the rate of false positive results would be high, and this was not addressed in the ADAR. ESC considered that the analysis could be revised to include the effect of misclassification at both the FIB-4 and VCTE testing stages, with a focus on the consequences of false positive results. ESC noted that the GESA consensus recommendations for metabolic dysfunction-associated fatty liver disease (MAFLD) references a study which proposed that the lower FIB-4 cutoff for the indeterminate range should be raised from 1.3 to 2.0 in the population aged>65 years, to improve specificity, which reduces with increasing age. ESC considered that it would be informative to capture the impact of this increased FIB-4 threshold for the >65 years population in the economic and financial modelling, as this older population would benefit from adjusting FIB-4 thresholds in line with the evidence, to reduce misclassification rates.
- ESC noted that the application requested a technology and device-specific listing. ESC considered that it is possible that VCTE is superior to shear wave elastography (SWE) per the applicant's claim in the pre-ESC response, but that this would need to be supported by evidence, of which none was provided.
- ESC noted that the role of VCTE is unclear in the ADAR, i.e. whether it is a tool for diagnosis and monitoring of AF or a tool to stratify a patient's risk of AF. ESC considered that it is positioned as a risk stratification tool, but the applicant should clarify this.

Economic issues:

- ESC advised that US should be removed from the economic model and the financial analysis. The comparator in the economic model included FIB-4 + US, along with GP or specialist attendance, but did not incorporate any other non-funded AF tests. As previously noted, ESC considered that US is a prior test in the proposed populations and is not suitable as either a standalone comparator or as part of the proposed SOC comparator.
- The outcomes in the model are focused only on test accuracy and cost per correct diagnosis. ESC considered that the model should be expanded to include long-term and downstream outcomes – such as change in management, reduced disease progression, liver-related morbidity and mortality, cases of cirrhosis or liver cancer averted and quality-adjusted life-years (QALYs) – to better demonstrate meaningful patient benefit and therefore economic value of funding the proposed intervention.

- ESC noted the exploratory analysis conducted during the evaluation, which compared the sequential strategy of FIB-4 testing followed by VCTE versus FIB-4 testing only. ESC noted the results of the exploratory analysis and considered that the application should proceed with evidence-based VCTE thresholds and present data on misclassification.

Financial issues:

The financial estimates were likely to be highly uncertain as:

- ESC noted that the financial estimates were generated using a mixed epidemiological and market-share approach, and that key assumptions rely on expert opinion only, including the relative utilisation of VCTE in primary versus specialist care settings.
- Cost offsets are uncertain. ESC considered that the financial impact should be re-specified, including and excluding cost offsets due to the use of MBS item 55036 for abdominal US as SOC. ESC considered that, to address the uncertainty, the applicant could demonstrate the effect of removing all cost offsets — that is, from 60% to 0% in specialist care, as well as conduct a sensitivity analysis on reduced referral rates.
- ESC considered that the use of MBS item 55036 (abdominal ultrasound) for the utilisation estimates was highly uncertain, as the item is not specific to patients with MAFLD. ESC therefore considered that utilisation was likely overestimated.

Other relevant information:

- The MBS item descriptor proposed in the ADAR allows for testing once every 3 years for all patients. ESC noted that the proposed descriptor allows the possibility that the proposed item will be used for ongoing monitoring and could result in use of the item outside its proposed scope of diagnosis only and exceeding the uncertain utilisation estimates.
- ESC noted the ethical issue raised by the commentary of whether efficiency in the cohort (as determined by the commentary's exploratory economic analysis) should be prioritised over some patients being worse off (due to increased numbers of missed cases).

ESC discussion

ESC noted that this application from Health Technology Analysts Pty Ltd was for Medicare Benefits Schedule (MBS) listing of Vibration-Controlled Transient Elastography (VCTE™) for detection of advanced fibrosis in people with metabolic dysfunction-associated fatty liver disease (MAFLD) stratified by a prior FIB-4 (fibrosis-4 score) of >1.3.

ESC noted that MSAC has not considered this application before, but has previously considered other relevant applications. ESC noted MSAC considered and did not support MSAC Application 1366 (2016) (Transient Elastography at 50Hz for the diagnosis of Liver Fibrosis in patients with confirmed Hepatitis B or confirmed Hepatitis C) in primary care settings. ESC noted that MSAC considered that, because the evidence provided was from tertiary settings, the positive predictive value (PPV) provided may not be applicable to the proposed primary care settings, where the PPV is likely to be lower (due to the lower prevalence of liver fibrosis in primary care compared to tertiary care settings). MSAC also considered that the proposed fee was high, and there was a high risk of the proposed item being used in populations and for uses outside those proposed in the application. ESC also noted MSAC considered and did not support MSAC Application 1446 (2020) (Hepascore test to diagnose and monitor liver fibrosis severity in chronic liver disease). ESC noted MSAC did not consider the evidence from tertiary populations could be generalised to the proposed healthcare settings (primary care and specialist settings). There was a lack of evidence on how Hepascore would influence clinical management, such as enabling earlier diagnosis or reducing complications.

ESC noted and welcomed the public consultation input from consumers, health professionals and organisations for this application. ESC noted the feedback was of mixed support for the application. ESC noted that the Royal Australian and New Zealand College of Radiologists (RANZCR) was not supportive of the application because it does not acknowledge other similar technology that is widely available. Other feedback suggested that VCTE interpretation was challenging and best restricted to specialists. ESC also noted that although the application claimed the technology would be beneficial for First Nations people, the application did not adequately address how the needs of First Nations people, who have higher prevalence of obesity and liver conditions than non-First Nations people, would be addressed by funding of VCTE.

ESC noted that the applicant-developed assessment report (ADAR) included 2 populations:

- Population 1 – patients with a diagnosis of MAFLD (≥5% hepatosteatosis, and at least one of overweight, type 2 diabetes mellitus [T2DM] or metabolic dysfunction), plus a FIB-4 score (requiring age, aspartate aminotransferase [AST], alanine transaminase [ALT] and platelet count) of 1.3–2.7 in a primary care setting.

- Population 2 – patients with a diagnosis of MAFLD (≥5% hepatosteatosis, and at least one of overweight, type 2 diabetes mellitus [T2DM] or metabolic dysfunction), and a FIB-4 score of >2.7 in a specialist care setting.

ESC noted that the role of VCTE is unclear in the application. ESC considered that the application must clarify the purpose of VCTE, in particular clarifying whether it is a tool for diagnosis and monitoring of AF or a tool for stratifying a patient's risk of AF. ESC considered that VCTE has been positioned by the applicant as a risk stratification tool, but this should be clarified by the applicant.

ESC noted issues with the comparator in the ADAR, where the stated comparator was standard of care (SOC), including abdominal ultrasound (US), other diagnostic tests that are not publicly funded, or ongoing management. However, no comparative effectiveness or safety data were presented against the management options in SOC following the proposed triage strategy (i.e. Vibration-Controlled Transient Elastography [VCTE] performed as a second line test following FIB-4 testing). Further, ESC noted that the comparator used for the purposes of economic and financial evaluation included only US in addition to a GP or specialist consultation. ESC considered that US is a prior test in these populations and was not appropriate for inclusion in the SOC comparator, noting that guidelines do not recommend anatomical assessment as part of fibrosis testing, and ultrasound is not MBS-supported for elastography. ESC noted that this positioning of US in the SOC comparator had many flow-on effects throughout the application, including to the proposed clinical management algorithm, in which an abdominal US was incorrectly duplicated for population 2 following VCTE.

ESC noted a number of issues with the proposed MBS descriptor, including that there is no wording to prevent the MBS item from being used as a monitoring tool, as the descriptor allows testing for patients once every 3 years, including those who have already been stratified as having high AF risk. ESC considered that although the proposed MBS item descriptor restricts the item to the MAFLD population only, in practice, there was potential for the item to be used in patients who have other causes of chronic liver disease (e.g. chronic viral hepatitis). ESC noted that no risk mitigation strategy had been presented to prevent use outside of the intended MAFLD population. ESC noted that this was concerning given that MSAC had previously not supported use of VCTE in people with viral hepatitis (MSAC Application 1366). ESC also considered the proposed fee of $58.85 to be too high, noting that the procedure only takes 4–10 minutes and can be performed by a technician. ESC noted that the fee for the nurse practitioner attendance item 82205 is $31.05 for consultations lasting 6 to less than 20 minutes, and considered that a fee less than this would be more appropriate. ESC noted the possibility that out-of-pocket costs for patients could be high because of the establishment costs

associated with VCTE. However, ESC considered this to be unlikely since in the current referral pathway and model of care, many of these procedures are bulk-billed using MBS consultation items or performed at no additional cost when morphological ultrasound is provided (under both referred and non-referred MBS items).

ESC noted that the ADAR used a linked evidence approach. ESC noted the commentary's analysis that the linked evidence provided for changes in the steps of the primary care pathway had the following issues: imbalances in baseline characteristics favouring one arm of the study; no assessment of VCTE as a second-line test following a FIB-4 result; and the evidence supporting VCTE's role in reducing unnecessary specialist referrals was a single arm study only. The linked evidence for change in management in the specialist care setting was based on reducing the number of liver biopsies, however the commentary noted that the evidence provided did not match the 8 kPa single threshold proposed by the ADAR. ESC further noted that no evidence was provided to support the claim that use of VCTE results in a change in treatment decisions or health outcomes, apart from changes in referral pathway. ESC acknowledged that the commentary noted that in contrast to the ADAR, the current GESA MAFLD consensus statement does not designate VCTE as the only standard second-line test following initial blood-based assessments (e.g. FIB-4) and instead recommends different liver elastography methods (such as VCTE or SWE) or direct serum fibrosis tests (such as Hepascore or ELF) as suitable second-line options for indeterminate FIB-4 results. ESC noted that the PASC-ratified PICO included several health outcomes for change in patient management, however most of these were excluded from the ADAR. ESC also noted that the option of continued management without further testing was omitted without explanation. ESC considered that MSAC may accept that a reduction in liver clinic referrals is beneficial, but that this alone is inadequate evidence of improvement in health outcomes. ESC noted that it is not the tests themselves that generate health outcomes, but rather the subsequent choice of clinical management. ESC also noted that there were no comparative data available for any stage of the linked evidence approach.

ESC noted that no comparative data were provided to evaluate safety: however, it considered that procedure-related safety concerns are minimal, as VCTE uses a non-invasive technique. However, ESC considered that test-related safety issues due to misclassification had not been addressed in the ADAR, such as undertreatment for patients with false-negative results, or overtreatment or referral for unnecessary liver biopsies for patients with false-positive results.

ESC reviewed the diagnostic performance of VCTE. ESC noted that the ADAR presented a meta-analysis (Mozes et al. 2022)[2] of cross-sectional studies comparing FIB-4 and VCTE with a reference standard of liver biopsy. The meta-analysis found that the diagnostic performance of FIB-4 and VCTE was acceptable in terms of the detection of advanced fibrosis. Mozes et al. (2022) also presented modelled data on the sequential use of FIB-4 followed by VCTE, to determine if this testing strategy was sufficiently accurate (compared to liver biopsy) and could lead to the avoidance of liver biopsy in some patients. ESC noted that it showed that the sequential use (modelled data only) may reduce the need for liver biopsy. However, ESC noted the following issues raised by the commentary regarding the evidence:

- Different LSM thresholds were used compared to the ADAR and were dual, not single – for example, FIB-4 (<1.3, ≥2.67) or VCTE (<8 kPa, ≥10 kPa) and for VCTE (≥10 kPa, ≥20 kPa or ≥28 kPa). The ADAR used a single cut-off of 8 kPa.
- Patient demographics that affect accuracy were not reported, such as age, obesity and T2DM status.
- Sequential use results were modelled and did not represent real-world empirical data.
- There were some methodological concerns – 36/37 studies had high risk of bias, as

[2] Mózes FE, Lee JA, Selvaraj EA, et al. Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis. Gut. 2022;71(5):1006-1019. doi:10.1136/gutjnl-2021-324243

assessed by the commentary, due to issues such as selection bias and pairwise deletion.

In addition, ESC noted that the diagnostic accuracy was only applicable to the specialist setting (population 2), and 30% of this population had advanced fibrosis and 11% had cirrhosis. The misclassification rate was also high, which ESC considered would mostly be due to false-positive results. This means that some patients will be negatively affected by VCTE and undergo unnecessary further management, which will increase costs and unnecessarily expose patients to the adverse effects of further treatment and investigation. ESC acknowledged that the specificity of FIB-4 reduces with increasing age, as noted by the GESA Australian consensus recommendations for the assessment of MAFLD.[3] Therefore, ESC noted that the diagnostic accuracy of the proposed FIB-4 threshold of 1.3 was low in older populations over 65 years (specificity 35%) compared to a threshold of 2.0 (specificity increases to 70%), as proposed by Mcpherson et al. (2017)[4].ESC considered that it would be informative to capture the impact of this additional age-based cutoff (increasing the lower FIB-4 threshold for the indeterminate range from 1.3 to 2.0 for people aged 65 years and over) in the economic and financial modelling. ESC noted that the sequential testing strategy had a PPV of 66% and a negative predictive value (NPV) of 86% in a population assumed to have 30% prevalence of AF. ESC considered that the ADAR should have explored the diagnostic accuracy evidence for the primary care setting or in populations with low prevalence of AF (e.g. 5%, as the ADAR noted the prevalence of AF in general practice is 5-10%), as well as the effect of misclassification when modelling outcomes.

ESC noted the prognostic performance of VCTE presented by the ADAR and commentary. A meta-analysis (Mozes et al. 2023)[5] assessed the prognostic performance of VCTE only with regards to liver-related outcomes and to calculate adjusted survival outcomes. However, Mozes et al. (2023) used dual thresholds with rule-out (<10 kPa) and rule-in (>20 kPa) thresholds opposed to the ADAR's single rule-in/rule-out threshold of <8 kPa. ESC noted that in the tertiary populations presented in Mozes et al. (2023), there was limited evidence for the prognostic ability of a single, baseline VCTE in a highly selected population. However, ESC noted MSAC's advice in previous applications (such as 1366 and 1446, discussed above) that evidence from tertiary settings is not necessarily applicable to primary care. ESC further noted that Mozes et al. (2023) did not fully align with the MSAC guidelines' broader framework for longitudinal accuracy assessment, which also requires evaluating the test's incremental benefit over existing clinical risk stratification tools, assessing clinical utility and demonstrating impact on management or outcomes. ESC noted that the commentary identified 2 studies that were omitted in the ADAR – Leite et al. (2025)[6] and Gawrieh et al. (2024)[7], both prospective cohort studies – that incorporated serial VCTE measurements. ESC noted that these studies demonstrated that dynamic changes in liver stiffness were independently associated with clinical outcomes, which aligns more closely with the health technology assessment (HTA) concept of longitudinal

[3] MAFLD Consensus Statement Working Group. Recommendations for the assessment of metabolic dysfunction associated fatty liver disease (MAFLD) in primary care: a consensus statement. Gastroenterological Society of Australia (GESA), 2024. https://www.gesa.org.au/public/13/files/Education%20%26%20Resources/Clinical%20Practice%20Resources/MAFLD/MAFLD%20consensus%20statement%202024.pdf

[4] McPherson S, Hardy T, Dufour JF, et al. Age as a Confounding Factor for the Accurate Non-Invasive Diagnosis of Advanced NAFLD Fibrosis. *Am J Gastroenterol*. 2017;112(5):740-751. doi:10.1038/ajg.2016.453

[5] Mózes FE, Lee JA, Vali Y, et al. Performance of non-invasive tests and histology for the prediction of clinical outcomes in patients with non-alcoholic fatty liver disease: an individual participant data meta-analysis. Lancet Gastroenterol Hepatol. 2023;8(8):704-713. doi:10.1016/S2468-1253(23)00141-3

[6] Leite NC, Villela-Nogueira CA, Santos LV, Cardoso CRL, Salles GF. Prognostic value of changes in vibration-controlled transient elastography parameters for liver, cardiovascular and mortality outcomes in individuals with type 2 diabetes and metabolic dysfunction-associated steatotic liver disease: The Rio de Janeiro type 2 diabetes cohort. *Diabetes Obes Metab*. 2025;27(4):2024-2034. doi:10.1111/dom.16195

[7] Gawrieh S, Vilar-Gomez E, Wilson LA, et al. Increases and decreases in liver stiffness measurement are independently associated with the risk of liver-related events in NAFLD. *J Hepatol*. 2024;81(4):600-608. doi:10.1016/j.jhep.2024.05.008

accuracy. However, ESC noted that neither study evaluated the sequential FIB-4 to VCTE approach or validated the ADAR's 8.0 kPa cut-off.

ESC noted the ADAR's acknowledgement that a single VCTE LSM cut-off to determine risk of AF does not perform as well in terms of diagnostic accuracy. ESC noted that use of a single threshold was inconsistent with the clinical evidence provided, in which the large majority of studies (including Mozes et al. 2022, which was relied upon by the ADAR to inform the diagnostic accuracy of VCTE compared to liver biopsy as the reference standard) used different thresholds for rule-out and rule-in, due to the relatively poor diagnostic performance of a single threshold. For example, ESC noted the commentary's observation that the Mozes et al. (2022) and Noorian et al. (2022)[8] studies demonstrated that 2- or 3-tiered models (e.g. <7.9, 7.9–9.6, ≥9.6 kPa) provide superior sensitivity and specificity, and allow for a grey zone to manage diagnostic uncertainty, at the risk of having a proportion of patients being considered as having indeterminate outcomes. ESC noted that, in contrast, a single cut-off at 8.0 kPa avoids having this indeterminate outcome at the risk of an increased rate of misclassification. ESC also noted that both the ADAR and pre-ESC response state that the single 8.0 kPa cutoff for VCTE is supported by an expert consensus guideline. However, ESC considered that supporting clinical evidence should be presented as the primary evidence source, in addition to expert opinion. ESC considered that the incremental cost-effectiveness of using different thresholds or adopting the higher rule-in VCTE thresholds as per the literature could be explored (e.g. >10 kPa or >12 kPa), acknowledging that different thresholds would influence the proportion of patients who would be misclassified.

ESC noted the evidence presented in the ADAR and commentary regarding the proposed test's impact on the change in management. ESC noted that Tulleners et al. (2024)[9] was an Australian-based randomised controlled trial (RCT) with 2 arms: usual care versus early VCTE, where participants with MAFLD and FIB-4 ≥1.3, received a VCTE assessment and were classified as low risk (<8.0 kPa) or high-risk (≥8.0 kPa) for advanced fibrosis. ESC noted that the commentary stated the outcomes of Tulleners et al. (2024) did not demonstrate that early use of VCTE led to a change in diagnosis (and hence assumed no change in management). Additionally, although >85% of patients had FIB-4 testing, not all patients did, and some patients with FIB-4 <1.3 were included in the study. ESC considered that the study population was applicable and possibly demonstrated a trend toward earlier diagnosis, but there was still no evidence of a change in management. ESC also noted Hayward et al. (2022)[10] was a single-arm study in which patients were stratified using FIB-4 and non-alcoholic fatty liver disease [NAFLD] Fibrosis Score (NFS), with patients determined to be at low risk of advanced liver fibrosis remaining in primary care, while those at indeterminate or high risk proceeded to VCTE testing; if the resulting LSM was ≥ 8 kPa patients were then referred to a liver clinic. ESC noted that the primary outcome was identification of patients at risk for advanced liver fibrosis. ESC then noted that the commentary identified issues regarding the lack of a comparator group, that outcomes were limited to a referral pathway with no data beyond the point of referral. ESC further noted that the Mozes et al. (2022) study was also referenced as the modelling suggested that a 2-tier strategy may reduce liver biopsies. However, ESC considered that biopsies are very infrequently done in patients with MAFLD to investigate the presence of liver fibrosis, meaning that any cost offsets in practice would be negligible, and that there were no real-world data to support this modelling. ESC noted that the pre-ESC response reiterated that there is evidence that VCTE testing results in reduced

[8] Noorian S, Patel A, Ashkar C, Saab S. Identifying Advanced Fibrosis in NAFLD Using Noninvasive Tests: A Systematic Review of Sequential Algorithms. *J Clin Gastroenterol*. 2022;56(3):266-272. doi:10.1097/MCG.0000000000001517

[9] Tulleners R, Barnett A, O'Beirne J, et al. Parallel randomised trial testing community fibrosis assessment for suspected non-alcoholic fatty liver disease: outcomes from LOCATE-NAFLD. *BMJ Open Gastroenterol*. 2024;11(1):e001418. Published 2024 Dec 20. doi:10.1136/bmjgast-2024-001418

[10] Hayward KL, McKillen BJ, Horsfall LU, et al. Towards collaborative management of non-alcoholic fatty liver disease: a 'real-world' pathway for fibrosis risk assessment in primary care. *Intern Med J*. 2022;52(10):1749-1758. doi:10.1111/imj.15422

specialist referrals, however ESC considered that there were no studies presented to support a change in clinical decision making or health outcomes.

ESC noted that the economic evaluation was a cost-consequence analysis of VCTE for the identification of advanced fibrosis in individuals with diagnosed MAFLD in both primary care (general practice and community settings) and specialist care (hepatology practices) settings. ESC noted that the model outcomes are focused only on test accuracy and cost per correct diagnosis. ESC considered that the model should be expanded to include long-term and downstream outcomes – such as change in management, reduced disease progression, liver-related morbidity and mortality, cases of cirrhosis or liver cancer averted and quality-adjusted life-years (QALYs) – to better demonstrate meaningful patient benefit and therefore economic value of funding the proposed intervention.

ESC agreed with the commentary that the economic model, although based on the National Institute for Health and Care Excellence (NICE) guidelines,[11] has incorrect assumptions – namely, the model incorrectly assumes that no further testing always suggests an incorrect diagnosis (whereas this can be due to other factors such as missed appointments or scan failures). The model also incorrectly assumes that the use of a single cut-off for FIB-4 (no intermediate subgroup) is appropriate, and that US is a comparator. ESC considered that adding scan failures or missed appointments (for no further testing) is appropriate, that the model should align with PICO cut-off thresholds (FIB-4 1.3 and 2.7), and the comparator should be SOC including non-funded tests and excluding US. In addition, ESC agreed with the commentary noting that there were issues with applicability to the Australian setting (prevalence source Armstrong et al. 2021[12] which is also the reference for the GESA guidelines was a UK based study), and that the model did not differentiate between management in primary and specialist care. ESC also agreed with the commentary on uncertainty around key inputs in the economic model such as utilisation and costs of VCTE, US, GP visits and specialist visits. ESC noted the exploratory analysis conducted by the commentary during the evaluation, which compared the sequential strategy of FIB-4 testing followed by VCTE using a rule-out and rule-in threshold of < 8.0kPa and ≥ 10.0kPa in patients with FIB-4 ≥ 1.3 and < 2.67 (informed by Mozes et al. 2022). The comparator in the analysis was FIB-4 testing only (with referral if FIB-4≥1.3). ESC noted the analysis suggested that there would be fewer misclassified patients and fewer unnecessary referrals with the sequential strategy, resulting in a lower cost per correct diagnosis. However, the sequential strategy was also associated with more missed diagnoses of AF compared to FIB-4 testing only. ESC noted the results of the exploratory analysis and considered that the application should proceed with the thresholds in the evidence and present data on misclassification. ESC also considered that the commentary's reanalysis using 2-tier diagnostic tests highlighted differences to the base case and was more appropriate for informing the economic evaluation than the approach in the ADAR.

ESC noted the base case results for primary care were $218.74 per correct diagnosis for VCTE and $451.04 per correct diagnosis for SOC. For secondary care, the results were $204.98 per correct diagnosis for VCTE and $392.22 per correct diagnosis for SOC. ESC considered that the sensitivity analyses demonstrated that VCTE remained cheaper than SOC per correct diagnosis for different scenarios, such as different fibrosis prevalences and VCTE sensitivities and specificities, for both care settings. ESC noted the sensitivity analyses in the commentary, which corrected the assumptions made in the ADAR, including the use of dual LSM thresholds (aligned with the clinical evidence provided). The analyses determined that FIB-4 + VCTE resulted in 16% more correct diagnoses compared with SOC. ESC further noted that the commentary determined

[11] NICE guideline. Non-alcoholic fatty liver disease (NAFLD): assessment and management. National Institute of Health and Care Excellence (NICE), 2016 (last reviewed 2024). https://www.nice.org.uk/guidance/ng49

[12] Armstrong MJ, Houlihan DD, Bentham L, et al. Presence and severity of non-alcoholic fatty liver disease in a large prospective primary care cohort. *J Hepatol*. 2012;56(1):234-240. doi:10.1016/j.jhep.2011.03.020

that FIB-4 + VCTE was associated with a lower cost per correct diagnosis than SOC, although costs were higher than those calculated in the ADAR.

ESC noted that the financial impact was calculated using a mixed epidemiological and market-based approach. ESC noted that costs to the MBS – without considering the cost offsets due to changes in use of other health technologies – were as follows:

- In primary care: $3,641,063 in year 1, increasing to $9,123,754 in year 6
- In specialist care: $24,022,800 in year 1, decreasing to $10,885,142 in year 6.

However, ESC considered that the financial estimates and impact were highly uncertain. ESC considered the use of MBS item 55036 (abdominal ultrasound) as a proxy for the number of MAFLD patients potentially eligible for VCTE was highly uncertain and will likely overestimate the MAFLD population, as item 55036 is for any morphological assessment of the abdomen by ultrasound regardless of underlying diagnosis and is therefore not specific for MAFLD diagnosis. Furthermore, ESC noted that some patients may use the item multiple times per year, and tests other than ultrasound may be used to diagnose MAFLD. ESC also noted that the ADAR used the incorrect MBS item to calculate cost offsets, thereby making these calculations uncertain; however, it was noted that using the correct costs did not significantly alter the outcomes. ESC considered it would be informative to show the effect of removing all cost offsets and a sensitivity analysis on reduced referral rates. ESC also noted that the selection of data sources was not aligned with the proposed clinical setting and considered it introduced uncertainty to the financial impact. For example, prevalence data from a primary care population (Anstee et al. 2024)[13] were applied to the secondary care population (PICO 2), and accuracy results from McPherson et al. (2010)[14], which used a rule-in threshold of 3.25 for FIB-4, were used to inform the estimates for a rule-in threshold of 2.7 as proposed by the ADAR.

ESC also considered that there were several more concerns regarding assumptions included in the ADAR's evaluation of the financial impact:

- The ADAR calculated cost savings for the net MBS impact. While these savings assumed large drops in referrals and unnecessary tests, the number of false positive results was not well estimated.
- Some key assumptions (US/biopsy reductions, uptake rates) rely on expert opinion only, rather than robust clinical evidence. ESC expressed concern that the number of liver biopsies offset is likely to be negligible.
- Some cost offsets are based on misapplication of MBS services (for example, the US item on the MBS is for morphological assessment, which is not relevant to second-line testing for fibrosis in SOC).
- Projections are overly optimistic and inconsistent (for example, savings fall even as test use increases).

ESC considered that US should be removed from the economic model and financial analysis, and replaced with the appropriate SOC comparator.

[13] Anstee QM, Berentzen TL, Nitze LM, et al. Prognostic utility of Fibrosis-4 Index for risk of subsequent liver and cardiovascular events, and all-cause mortality in individuals with obesity and/or type 2 diabetes: a longitudinal cohort study. *Lancet Reg Health Eur*. 2023;36:100780. Published 2023 Dec 19. doi:10.1016/j.lanepe.2023.100780

[14] McPherson S, Stewart SF, Henderson E, Burt AD, Day CP. Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease. *Gut*. 2010;59(9):1265-1269. doi:10.1136/gut.2010.216077

17. Applicant comments on MSAC's Public Summary Document

The applicant thanks MSAC for considering this application for VCTE as part of sequential non-invasive testing in Australian clinical practice for patients with MAFLD, a large and high burden population that is growing. We also acknowledge the supportive consumer and clinician input, reflecting the significant clinical need for improved risk stratification and timely identification of patients with advanced liver fibrosis. While non-invasive testing practices are already being used in Australian clinical practice, the applicant considers that the absence of public funding results in inequitable and fragmented access, particularly for underserved populations.

Regarding MSAC's consideration of the presented evidence, the applicant clarifies that the submission was intended to demonstrate intermediate clinical utility (risk stratification and referral optimization), rather than to model long-term disease progression outcomes, which remain challenging to quantify in MAFLD. The applicant notes that the absence of direct evidence linking VCTE use to long-term outcomes reflects limitations of the current evidence base rather than evidence of no clinical benefit. The applicant clarifies that the proposed 8 kPa threshold was intended as a conservative referral threshold in primary care, rather than a diagnostic cut-off. In this context, false-positive results lead to further specialist assessment rather than treatment initiation, whereas the clinical consequences of missed advanced fibrosis remain the primary safety concern. The applicant notes that comparator choice of abdominal ultrasound was as a pragmatic proxy to reflect real-world diagnostic activity in the absence of a reimbursed second-line non-invasive fibrosis test, rather than as a fibrosis staging comparator.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website