Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1366 – Transient Elastography at 50Hz for the diagnosis of liver fibrosis in patients with confirmed Hepatitis B or C.

Applicant: **Medical Technologies Australia Pty Ltd**

Date of MSAC consideration: **MSAC 66th Meeting, 30-31 March 2016**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, see at www.msac.gov.au

1. Purpose of application and links to other applications

An application requesting a new Medicare Benefits Schedule (MBS) listing for transient elastography (TE) at 50Hz for the diagnosis of liver fibrosis in patients with confirmed hepatitis B or C was received from Medical Technologies Australia Pty Ltd.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the comparative safety, clinical effectiveness and cost-effectiveness, MSAC did not support public funding for TE at 50Hz for the diagnosis of liver fibrosis in patients with chronichepatitis B (HBV) or chronic hepatitis C (HCV). While MSAC accepted that TE is being used by hepatologists as part of routine practice, the evidence that it improves patient outcomes by changing treatment decisions for either HBV or HCV is negligible. MSAC remained unconvinced by the economic modelling and is concerned about the potential for use in other liver conditions, and for monitoring of treatment responses in HBV and HCV, resulting in substantial additional costs and no clear health gains.

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

MSAC noted that TE, supplied as a device with the requested characteristics in Australia using the brand name Fibroscan®, is a non-invasive method of measuring the stiffness of liver tissue which in turn provides an indication of the level of fibrosis (liver scarring). It can be used in conjunction with other clinical information to assess the level of fibrosis in people with HBV or HCV. While not currently subsidised via the MBS, TE is available in Australia, mainly through public hospitals.

MSAC noted that there are around half a million Australians with chronicHBV (~225,000 people) or HCV (~230,000 people). In recent years, new antivirals to treat HCV have become available on the Pharmaceutical Benefits Scheme (PBS) and that these new medicines are able to cure most people with the condition. MSAC noted that, in contrast, medicines to treat HBV do not cure the condition but aim to slow progression of the disease, and once treatment for HBV is begun, it is lifelong.

MSAC noted that, both chronic HBV and chronic HCV cause liver damage including fibrosis. At its most severe, fibrosis occurs throughout the liver (cirrhosis). The METAVIR system is a way to grade the severity of fibrosis.

MSAC noted that since the preparation of the application for TE, new consensus recommendations from the Hepatitis C Virus Infection Consensus Statement Working Group for the management of HCV (hereafter the 2016 consensus statement) were published and new curative antivirals for treating HCV were listed on the PBS.

MSAC considered that the most appropriate comparator for TE was clinical assessment rather than liver biopsy. Although liver biopsy is an appropriate reference standard for the assessment of analytical validity, it is invasive, associated with a risk of complications and is not routinely done. Clinical assessment is inherently complex and involves all the clinical and laboratory tests (used in combination) routinely performed in patients with HBV or HCV as detailed in the consensus recommendations.

MSAC agreed that TE was reasonably accurate in detecting cirrhosis as a standalone test when compared with liver biopsy. A number of meta-analyses reported on the diagnostic accuracy of TE alone compared with liver biopsy. In HBV, sensitivity ranged from 67% to 86% and specificity ranged from 76% to 89% for detection of cirrhosis. In HCV, sensitivity ranged from 83% to 89% and specificity ranged from 90% to 95% for cirrhosis. When compared with liver biopsy, the accuracy of TE in identifying HBV patients with significant fibrosis requiring treatment (METAVIR score ≥ 2), sensitivity ranged from 71% to 84% and specificity ranged from 72% to 84% for detection of significant fibrosis. In HCV, sensitivity for significant fibrosis ranged from 70% to 79% and specificity ranged from 80% to 86%.

MSAC noted that, evidence comparing the diagnostic accuracy of TE with clinical assessment relied on four observational studies of varying quality. Only one of these studies compared the ability of TE and TE plus ultrasound to detect significant fibrosis (Wang et al, 2009). It found TE alone was better than ultrasound, but the performance of TE plus ultrasound (area under the receiver operating curve [AUROC] 0.87, 95% CI 0.83 to 0.90) was similar to TE alone (AUROC 0.82, 95% CI 0.78 to 0.87).

MSAC noted a trend towards improved diagnostic accuracy in the detection of cirrhosis was reported by three studies. However, this did not reach significance for the two studies which compared TE alone with TE plus ultrasound (Wang et al, 2009; Chen et al, 2012). The third study compared TE alone (AUROC 0.88, 95% CI 0.81 to 0.94) with TE plus ultrasound plus platelets (AUROC 0.91, 95% CI 0.86 to 0.97), but significance testing was not reported (Kim et al, 2009). A fourth poor quality study (Gobel et al, 2015) compared the sensitivity and specificity in detecting cirrhosis of TE alone (sensitivity 91%, specificity 44%) with TE plus ultrasound (sensitivity 96%, sensitivity 51%), TE plus platelets (sensitivity 94%, specificity 49%) and ultrasound combined with physical examination (sensitivity 88%, specificity 62%).

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. Furthermore, MSAC noted the limited evidence base meant that substantial uncertainty remained about the relative diagnostic accuracy of TE compared with the combination of tests as used in current clinical practice.

MSAC was unable to establish to what extent, if any, TE changes clinical management in HBV or HCV, particularly in the context of the multiplicity of other investigations routinely undertaken as part of a patient's ongoing assessment.

MSAC noted that the clinical algorithm included in the application preceded recent changes in the management of HCV and the PBS listing of the new curative antivirals. The algorithm in the application suggested that people with HCV and significant fibrosis would be treated while those without significant fibrosis would not be treated. However, the 2016 consensus statement recommends treatment be considered in all people with chronic HCV. Improved health outcomes for patients with chronic HCV will be driven by uptake of the new curative antivirals and MSAC was not convinced that the availability of TE on the MBS will impact upon access to these medicines. While the PBS restrictions require information on whether a patient does or does not have cirrhosis to be provided at the time of application, the approach to treatment (as per the 2016 consensus statement) does not vary according to whether or not a patient has cirrhosis. The only exception to this is for the combination of sofosbuvir + daclatasvir in people with genotype 3 HCV infection, used for 12 weeks if a patient does not have cirrhosis and 24 weeks if they do. It was noted that the basis for the difference in the duration of treatment was uncertain. Furthermore, MSAC noted that TE was only one of many tests that could be done to determine whether a patient has cirrhosis including physical examination and clinical history, blood tests and serum markers, ultrasound and other non-invasive tests. Given this, MSAC concluded that there is negligible evidence that the use of TE in people with HCV will lead to important changes in treatment or improve clinical outcomes.

MSAC also 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 (see PBS restrictions for lamivudine, entecavir, tenofovir and peginterferon). Therefore the decision to treat HBV relies largely upon viral loads and serum markers. As for HCV, MSAC noted that TE was only one of many tests that could be done to determine whether a patient has cirrhosis. Given this, MSAC concluded that there is no compelling evidence that the use of TE in people with HBV will meaningfully improve their clinical management or improve their clinical outcomes.

MSAC accepted that TE is able to provide some prognostic information and was able to predict complications such as liver cancer, cirrhosis and portal hypertension.

MSAC considered that a consequence of any MBS listing would be to extend the use of TE is beyond the public hospital sector where it is already available, to include the private sector, and from the specialist setting to include the GP setting. As stated above, MSAC noted all of the evidence on the diagnostic accuracy of TE was collected in high risk patients receiving specialist or hospital care. Patients being managed by GPs are more likely to be lower risk patients and as a result, the positive predictive value of TE (i.e. the likelihood that a person with a positive test has the disease) will be lower than in tertiary care settings. This may mean

that the number of people falsely identified by TE as having cirrhosis or significant fibrosis (false positives) will be higher in the primary care setting than was seen in studies conducted in tertiary care. However, MSAC also considered that there were considerable financial barriers to the use of TE by GP practices, given the high purchase ($107,000–$180,000) and maintenance costs of the machine ($11,400 per year).

MSAC accepted that TE is a safer, more acceptable and more convenient method to measure fibrosis than liver biopsy. No adverse effects associated with the use of TE were reported in the evidence before the committee.

MSAC noted that there was considerable uncertainty around the economic modelling presented in the application. As stated above, the algorithm one which the model for HCV was based was not consistent with current recommendations, and it also did not include the antivirals most recently listed in the PBS. Based on the algorithm which MSAC did not accept, the model estimated that using TE in the initial diagnosis and annual monitoring of liver stiffness would incur an average cost of $46,673 and gain 6.38 QALYs compared with $44,187 and 6.37 QALYs for clinical assessment alone resulting in an ICER of $226,560 per QALY. In sensitivity analyses, the only scenario where TE plus clinical assessment was acceptably cost-effective (ICER $11,483 per QALY gained) was if the prevalence of significant fibrosis in the patient population was increased from 53% in the base case model to 83%. 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). On the basis of this information, the modelled incremental cost-effectiveness of adding TE to clinical assessment was not acceptable.

MSAC were also unconvinced by the economic modelling for HBV as it was unclear that TE would change decisions around commencing treatment with HBV medicines as assumed for the model. While it was argued that TE could identify an additional 9% of patients with significant fibrosis (METAVIR scores $F \geq 2$) who would then commence treatment, MSAC noted that fibrosis is not the main driver for access to PBS medicines to treat HBV. Instead, access to these medicines was linked to viral load and as such it was difficult to determine how use of TE would impact upon the decision to start HBV medicines. The results of the model as designed suggested that using TE plus clinical assessment for initial diagnosis and annual monitoring dominated clinical assessment alone. There was a small gain in QALYs of 0.01 using TE plus clinical assessment instead of clinical assessment alone. This gain was due to the small improvement in the detection of significant fibrosis. 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 $148,044 per QALY gained).

MSAC considered that the proposed fee for each TE service was high. While the fee was linked to the cost of MBS item 55014 for abdominal ultrasound, MSAC felt that this was inappropriate given that the delivery of a TE service is much less complex than of an abdominal ultrasound service and does not require a skilled operator.

MSAC was concerned about the potential for TE to be used in other liver conditions (fatty liver disease, alcoholic liver disease). It may also be used for regular monitoring of liver conditions despite a lack of evidence of incremental clinical utility. This could mean that the financial estimates of the use of TE provided to MSAC (approximately $8 million to the MBS over five years) would be substantial underestimates.

4. Background

MSAC has not previously considered an application for TE.

5. Prerequisites to implementation of any funding advice

The device that delivers TE 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.

TE can be conducted by any adequately trained health professional; it does not require an ultrasound accredited professional, as it is considered a measuring technology rather than an imaging technology. However, MSAC noted policy advice that interpreting the results does require a degree of expertise, such as by a general practitioner.

6. Proposal for public funding

The proposed new MBS item is shown in Table 1. The applicant stated that the test takes 10–20 minutes and is undertaken by a suitably trained health professional. TE needs to be performed with physical examination and other tests including liver function tests, serum biomarkers, and ultrasound to assess liver structure. Furthermore, as a diagnostic procedure, a patient consultation is required to advise subsequent care based on the interpretation of the test results. Therefore, a fee for the service was claimed to be in line with other point-of-care testing services.

Table 1 – Proposed MBS item

Category 5 – DIAGNOSTIC IMAGING SERVICES
MBS XXXX Transient Elastography at 50 Hz (performed by a suitably trained health professional) for the assessment of liver fibrosis in patients with chronic hepatitis B or C Used on the liver – 1 service only in a period of 12 consecutive months - including interpretation and report **Fee:** $55.65 **Benefit:** 75% = $41.74 85% = $47.30

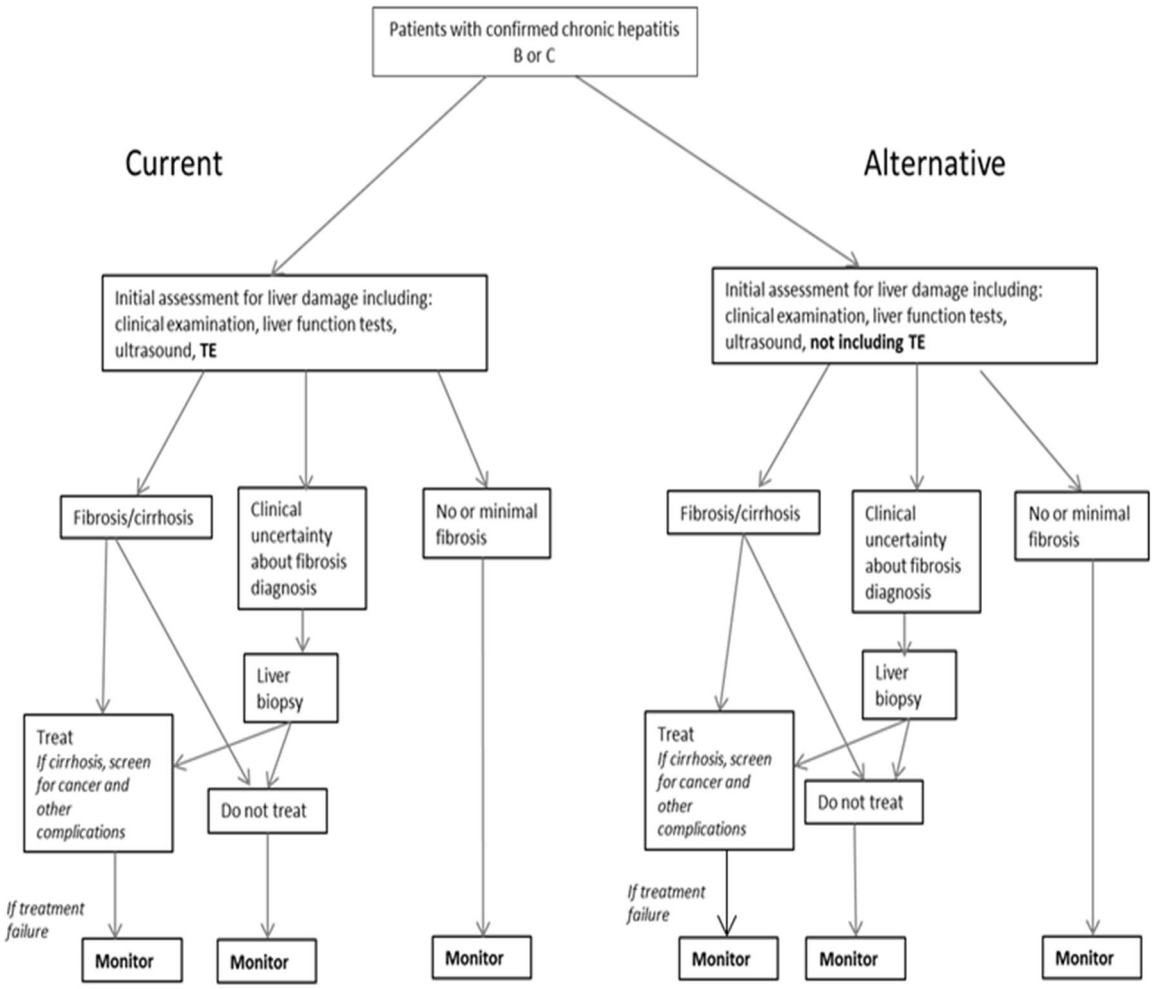
MSAC noted policy advice that the proposed service would be better placed under Category 2 of the MBS (Diagnostic Procedures and Investigations), as the technology is for measuring not imaging.

7. Summary of Public Consultation Feedback/Consumer Issues

As the procedure is currently available in public hospitals, there is a risk that moving the service to private clinics will introduce out-of-pocket expenses to patients. Consumers had no safety concerns about it being performed in a private setting.

8. Proposed intervention's place in clinical management

The proposed clinical management algorithm was:



Patients with confirmed chronic hepatitis B or C are initially assessed with clinical assessment comprising physical examination, liver function tests, and ultrasound. TE will be added to clinical assessment for the initial evaluation of liver fibrosis in this group of patients.

The METAVIR system is commonly used to grade the severity of liver fibrosis on a scale from 0 to 4. In general, significant liver fibrosis, defined as METAVIR score $F \geq 2$, would require treatment, but no treatment is required for zero or minimal fibrosis (i.e. METAVIR score $F \leq 1$). Screening for cancer and other liver complications is warranted with cirrhosis (i.e. METAVIR score $F = 4$). When there is further clinical uncertainty about fibrosis diagnosis, a liver biopsy would be taken to confirm the findings.

Patients with treatment failure or those untreated with an initial TE result indicating an intermediate risk of cirrhosis will be monitored annually with TE plus clinical assessment. The degree of hepatic fibrosis can be inferred from the liver hardness. The shear wave velocity is directly related to the tissue stiffness, with a higher velocity equating to higher tissue stiffness, corresponding to increasing severity of fibrosis. Ten validated measurements are required, with the median value taken as the final result, which is expressed in units of kilopascals (kPa).

9. Comparator

Two comparators were proposed by the applicant:

1. Clinical assessment without TE
2. Liver biopsy.

In keeping with the Protocol for this application, other non-invasive tests were not considered as comparators in this assessment including:

- indirect blood tests (e.g. aspartate aminotransferase-to-platelet ratio index and the Fibrosis4 scores);
- direct markers of fibrosis (e.g. haptoglobin, Fibrotest); and
- other imaging technologies (e.g. acoustic radiation force impulse imaging and 3D magnetic resonance elastography).

MSAC considered that the most appropriate comparator for TE was clinical assessment without TE rather than liver biopsy.

10. Comparative safety

TE is an ultrasound-based non-invasive test that has been reported to be painless, rapid and easily performed by trained staff (Crossan, Tsochatzis et al. 2015; Kemp, Levy et al. 2015). There have been no reported adverse events associated with TE use (Crossan, Tsochatzis et al. 2015; Kemp, Levy et al. 2015).

TE is considered by surveyed patients to be a more acceptable and more convenient method of measuring fibrosis than liver biopsy. TE is associated with greater comfort and no feelings of anxiety compared to biopsy. The surveyed patients perceived TE as a fast procedure with shorter test duration and short wait for the test result compared with liver biopsy (Kan, Marquez Azalgara et al. 2015).

11. Comparative effectiveness

Four prospective cohort studies evaluated the diagnostic accuracy of TE with clinical assessment in the detection of liver cirrhosis (Kim, Kim et al. 2009; Wang, Changchien et al. 2009; Chen, Liang et al. 2012; Gobel, Schadewaldt-Tummers et al. 2015). The four studies were observational and their quality varied. TE with clinical assessment appeared to be superior to clinical assessment alone. However, the addition of clinical assessment (mainly ultrasound) to TE does not significantly improve the diagnostic accuracy of TE alone (Wang et al., 2009, Chen et al., 2012).

With liver biopsy as a reference, TE alone has proven accuracy in the diagnosis of liver fibrosis/cirrhosis in patients with chronic hepatitis B or C. There is strong evidence from a number of meta-analyses to support the diagnostic accuracy of TE with a range of cut-offs for each liver disease and fibrosis level. In patients with hepatitis B, the cut-offs for significant fibrosis ranged from 6 to 9 kPa with 84% sensitivity and 84% specificity, and 8 to 18 kPa for cirrhosis with sensitivity and specificity of 86% and 89%, respectively (Tsochatzis, Gurusamy et al. 2011; Chon, Choi et al. 2012; Crossan, Tsochatzis et al. 2015; Xu, Su et al. 2015). In hepatitis C, the cut-offs for significant fibrosis ranged from 5 to 10 kPa with 79% sensitivity, and 86% specificity whereas when the cut-offs were from 9 to 17 kPa for cirrhosis, TE had 90% sensitivity and 91% specificity (Tsochatzis, Gurusamy et al. 2011; Steadman, Myers et al. 2013). The accuracy of TE is adversely affected by food; and

therefore, patients undergoing this test should fast for at least two hours (Arena, Lupsor Platon et al. 2013; Berzigotti, De Gottardi et al. 2013).

Two studies have investigated the accuracy of TE in monitoring liver fibrosis in patients who are not on antivirus treatment (Crisan, Radu et al. 2012; Christiansen, Mossner et al. 2014). TE was performed at least once yearly and more frequently when necessary. In the study by Crisan et al (2012), untreated patients yielded constant values of fibrosis or a slight increase in follow-up. The study confirms the accuracy of TE and liver tests for the assessment of fibrosis at baseline and at follow-up in treated or untreated patients with chronic hepatitis C patients. Another study by Christiansen et al (2014) evaluated liver stiffness monitoring with TE overtime in patients with chronic hepatitis B or C. The study found that a TE cut-off of 17 kPa correctly classified 96% as having cirrhosis with 92% sensitivity and 95% specificity. There are no clear guidelines on the frequency of TE monitoring although most of the included studies performed annual assessments. Christiansen et al. (2014) and Kemp et al. (2015) recommend more frequent monitoring when the repeated liver stiffness scores are between 7 to 9 kPa and when there are other comorbidities.

TE is an effective predictive and prognostic test in patients with chronic hepatitis B or C. One prospective cohort study compared the performance of TE plus clinical assessment in predicting the development of hepatocellular carcinoma in patients with chronic hepatitis B (Chon, Jung et al. 2012). It showed that in predicting hepatocellular carcinoma, TE had a slightly higher accuracy compared with TE plus clinical assessment (0.789 vs 0.788, respectively), but this was not statistically significant.

A number of large prospective studies and two meta-analyses demonstrated the effectiveness of TE alone as a non-invasive approach to predict chronic liver complications including cirrhosis, portal hypertension, oesophageal varices, liver cancer and mortality (Shi, Fan et al. 2013; Singh, Fujii et al. 2013). In these studies, TE was also performed at least once yearly and more frequently when necessary; however, none of the studies compared the outcome of various monitoring frequencies (e.g. annually versus every other year).

12. Economic evaluation

A cost-utility analysis was presented. Due to the different treatment pathways involved in hepatitis B compared with hepatitis C, two separate Markov cohort models were constructed with annual cycles for both models. Each model had two stages: 1) a decision tree for diagnostic accuracy of tests, and 2) Markov chains for long-term treatment effects for fibrosis. The tests compared in the models were TE plus clinical assessment, clinical assessment, and liver biopsy. The starting age of the cohort was 40 years and the model duration was until the age of 90. The main inputs in each model were the sensitivity and specificity of the tests, prevalence of liver fibrosis stages, transition probabilities between fibrosis stages (i.e. F1-F4), probability of hepatocellular carcinoma, treatment effectiveness, mortality of liver complications and age-related mortality, utility scores of the various liver fibrosis stages, and the costs of diagnosis and treatment. The key results are presented in Tables 2 and 3.

Table 2: Key results of hepatitis C economic evaluation

Scenario	Test	Mean LY[a]	Mean Costs	Mean QALYs	Inc Costs	Inc QALYs	ICER
TE plus clinical assessments for diagnosis and monitoring	Biopsy	33.68	$39,596	5.01	-	-	-
-	**CA**	**33.59**	**$44,187**	**6.37**	**$4,594**	**1.36**	**$3,388**
-	TE+CA	33.62	$46,673	6.38	$2,486	0.01	$226,560
TE plus clinical assessments for diagnosis only	CA	33.68	$30,476	6.09	-	-	-
-	**Biopsy**	**33.59**	**$30,822**	**6.10**	**$346**	**0.02**	**$14,208**
-	TE+CA	33.62	$34,784	6.15	$3,962	0.04	$112,992

TE = transient elastography; CA = clinical assessment; Inc = incremental; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; LY = life years
[a] Undiscounted
Bold = the cost-effective option of the three options.

For patients with chronic hepatitis C, the economic model estimated that patients would live for an average of approximately 34 years irrespective of annual monitoring. TE plus clinical assessment for the initial diagnosis and annual monitoring of liver stiffness would incur an average cost of $46,637 and gain 6.38 QALYs compared with $44,187 and 6.37 QALYs for clinical assessment alone resulting in an ICER of $226,560 per QALY gained. TE plus clinical assessment was not cost effective compared to clinical assessment alone.

Table 3: Key results of hepatitis B economic evaluation

Scenario	Test	Mean LY	Mean Costs	Mean QALYs	Inc Costs	Inc QALYs	ICER
TE plus clinical assessments for diagnosis and monitoring	**TE+CA**	**28.46**	**$67,069**	**5.76**	**-**	**-**	**Preferred**
-	CA	28.36	$67,203	5.75	$132	- 0.00	Dominated
-	Biopsy	28.33	$70,741	4.39	$3,672	-1.36	Dominated
TE plus clinical assessments for diagnosis only	**CA**	**26.81**	**$46,085**	**5.65**	**-**	**-**	**Preferred**
-	TE+CA	27.07	$48,644	5.66	$2,559	0.02	$148,044
-	Biopsy	27.49	$61,177	5.53	$13,763	-0.132	Dominated

TE = transient elastography; CA = clinical assessment; Inc = incremental; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; LY = life years (undiscounted)
Bold = the cost-effective option of the three options.

The hepatitis B modelled economic evaluation results estimated that patients would survive, on average, 28 years with annual monitoring and 27 years without monitoring. The cohort of patients diagnosed and annually monitored with TE plus clinical assessment would incur an average cost of $67,069 and gain 5.76 QALYs, making this test superior to liver biopsy or clinical assessment alone.

13. Financial/budgetary impacts

The financial impact was calculated for the next five years taking into consideration the prevalent population of chronic hepatitis B or C and the assumed numbers of new cases of significant fibrosis diagnosed with TE every year. By listing TE, the MBS was estimated to incur costs of approximately $8 million over the next five years. Table 4 summarises the key financial estimates for the MBS.

Table 4: Results of the financial estimates over next five years

	2016	2017	2018	2019	2020
HEPATITIS B					
Eligible population					
Australian population estimate	24,359,761	24.781,121	25,201,317	25,619,895	26,037,356
Proportion with chronic hepatitis B	236,290	240,377	244,453	248,513	252,562
Proportion engaged in care	30,718	31,249	31,779	32,307	32,833
Estimated number of TEs					
Annual scans on F≥2 fibrosis (50% have F≤1)	15,359	15,625	15,890	16,154	16,417
MBS Costs					
TEs	$727,249	$739,820	$752,368	$764,868	$777,321
Costs associated with additional patients treated					
Incidence of hepatitis B	7,527	7,657	7,787	7,917	8,046
New cases of F ≥2 fibrosis diagnosed with TE	673	685	696	708	719
New cases of F ≥2 fibrosis diagnosed with TE and engaged in care	87	89	90	92	93
MBS costs (HCC screening)	$17,217	$17,613	$17,811	$18,207	$18,405
TOTAL MBS COSTS – Hepatitis B	**$744,466**	**$757,433**	**$770,179**	**$783,075**	**$795,726**
HEPATITIS C					
Eligible population					
Australian population estimate	24,359,761	24,781,121	25,201,317	25,619,895	26,037,356
Proportion with chronic hepatitis C	253,027	257,404	261,768	266,117	270,453
Proportion engaged in care	32,894	33,463	34,030	3,4595	35,159
Estimated number of TEs					
Annual scans on F≥2 fibrosis (50% have F≤1)	16,447	16,732	17,015	17,298	17,580
MBS Costs					
TEs	$778,765	$792,237	$805,660	$819,037	$832,389
Costs associated with additional patients treated					
Incidence of hepatitis C	11,279	11,474	11,668	11,862	12,055
New cases of F ≥2 fibrosis diagnosed with TE	1,008	1,026	1,043	1,060	1,078
New cases of F ≥2 fibrosis diagnosed with TE and engaged in care	131	133	136	138	140
MBS costs (HCC screening)	$25,925	$26,321	$26,914	$27,310	$27,706
TOTAL MBS COSTS – Hepatitis C	**$804,690**	**$818,558**	**$832,574**	**$846,347**	**$860,095**
TOTAL MBS COSTS – Hepatitis B + Hepatitis C	**$1,549,156**	**$1,575,991**	**$1,602,753**	**$1,629,422**	**$1,655,822**

MBS = Medicare Benefits Schedule, PBS = Pharmaceutical Benefits Scheme, TE = transient elastography; HCC = hepatocellular carcinoma

The addition of TE to clinical assessment was anticipated to increase the number of patients diagnosed with significant fibrosis each year by 8.9%. This would result in an increase in the number of patients screened for hepatocellular carcinoma together with additional costs for treatment incurred by the PBS. On the other hand, listing TE on the MBS would result in a cost saving to state hospital systems since they would be eligible to claim for the service provided. Table 5 summarises the estimated costs for other health budgets.

Table 5: Estimated costs to other health budgets

	2016	2017	2018	2019	2020
Hepatitis B					
Total MBS costs	$744,466	$757,433	$770,179	$783,075	$795,726
PBS costs	$1,014,410	$1,037,729	$1,049,389	$1,072,709	$1,084,369
State hospital cost saving	-$727,249	- $739,820	-$752,368	-$764,868	-$777,321
Total cost of Hepatitis B	**$1,031,627**	**$1,055,342**	**$1,067,200**	**$1,090,916**	**$1,102,274**
Hepatitis C					
Total MBS costs	$804,690	$818,558	$832,574	$846,347	$860,095
PBS costs	$9,954,935	$10,106,919	$10,334,894	$10,486,878	$10,638,862
State hospital cost saving	-$778,765	-$792,237	-$805,660	-$819,037	-$832,389
Total cost of Hepatitis C	**$9,980,860**	**$10,133,240**	**$10,361,808**	**$10,514,188**	**$10,666,568**
Hepatitis B + Hepatitis C					
Total MBS cost	$1,549,156	$1,575,991	$1,602,753	$1,629,422	$1,655,822
Total PBS cost	$10,969,345	$11,144,648	$11,384,284	$11,559,587	$11,723,231
Total State hospital cost saving	-$1,506,014	-$1,532,057	-$1,558,028	-$1,583,905	-$1,609,711
Total cost of Hepatitis B + Hepatitis C	**$11,012,487**	**$11,188,582**	**$11,429,009**	**$11,605,104**	**$11,769,342**

MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme

The estimated increase to the PBS was $10,969,345 in the first year of listing. Total costs to the health system over the next five years were estimated at $57 million.

Providing 15% of the scans in a primary care setting would reduce total MBS costs from $3.055 million to $3.049 million. This decrease would be due to a slight reduction in consultation costs charged to the MBS. This would also reduce the out-of-pocket cost to patients and total state hospital cost savings of $14.238 million in the first year of listing.

14. Key issues from ESC for MSAC

- Transient elastography appears to be safe and accurate in the detection of liver fibrosis;
- It is unlikely to fully substitute conventional ultrasound due to yielding limited information;
- Liver biopsy is not a suitable comparator, as this is an undesirable initial method of testing;
- The clinical utility claims are unknown. There is no demonstration of transient elastography resulting in changes to clinical management of the patient;
- Given the high incremental cost-effectiveness ratio for Hepatitis C: MSAC may wish to limit the proposed MBS item to patients with Hepatitis B only;
- There are cost implications to other health systems due to a likely increase in the number of patients needing to be screened for hepatocellular carcinoma, plus treatment incurred by the PBS; and
- Training for use of the device is provided by the sponsor: ESC questioned whether it is plausible for the sponsor to continue providing free training to providers if uptake is high following listing on the MBS.

15. Other significant factors

Nil.

16. Applicant's comments on MSAC's Public Summary Document

The PSD references the 2016 consensus statement issued by the Hepatitis C Virus Consensus Statement Working Group. The statement was prepared by an expert panel representing the majority of medical organizations in Australia involved the diagnosis and treatment of Hepatitis. The consensus statement on page 11 states "Transient elastography, or FibroScan (EchoSens, Paris), measures liver stiffness and is the most common method used for diagnosing cirrhosis. It has been extensively evaluated and validated in people with chronic HCV infection and outperforms serum biomarkers for detecting cirrhosis. FibroScan is available in most metropolitan centres."

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website at: www.msac.gov.au.