

Population-Based Return on Investment of Deploying Transient Elastography

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Chronic liver disease and cirrhosis are leading causes of death in the United States,¹ and the spectrum of fatty liver disease (FLD) is among the most common liver conditions. FLD is characterized by the accumulation of fat in liver cells and further distinguishes between nonalcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (AFLD) depending on whether heavy alcohol use is involved. Besides the distinction of alcohol use, both types of diseases have similar diagnostic pathways.

NAFLD can progress to a more advanced form known as nonalcoholic steatohepatitis (NASH).² NASH consists of inflammation and cellular injury in addition to fat accumulation; it may progress to cirrhosis and hepatocellular carcinoma.^{2,3} A US prevalence study estimated that 85.3 million Americans had NAFLD and 17.3 million had NASH in 2016.⁴ These conditions contribute billions of dollars to the country's health care costs.⁵ In addition, NAFLD is an independent risk factor for cardiovascular disease. Hence, NAFLD and NASH are emerging as important disease states for payers to manage.

AFLD has been estimated to affect about 5% of the US population.⁶ Although it is lower in prevalence compared with NAFLD, the burden of AFLD is still significant. AFLD surpassed hepatitis C virus (HCV) as the leading indication for liver transplants in 2016,⁷ and a 2018 US population-based study demonstrated that individuals aged 25 to 34 years have experienced the fastest increasing cirrhosis-related mortality in recent years, driven entirely by alcohol-related liver disease.⁸

Despite the high prevalence and costs, most patients with FLD are asymptomatic and undiagnosed. This has led to delayed identification of advancing liver disease, which can have significant human and economic costs. In fact, the American Diabetes Association recently called for assessment of NAFLD in patients with prediabetes and diabetes who have elevated liver enzymes to address the lack of timely identification of NAFLD.⁹

With the large population at risk for these adverse outcomes due to FLD, increasing payer focus, and looming US guidelines, cost-effective and easily implemented liver assessment strategies are needed at the point of care. Vibration-controlled transient

ABSTRACT

OBJECTIVES: To evaluate the cost savings outcomes, from the payer's perspective, of deploying vibration-controlled transient elastography/controlled attenuation parameter (VCTE/CAP) machines for detecting and monitoring fatty liver disease (FLD).

STUDY DESIGN: We modeled disease transitions and costs under the current observed pathway and under an alternative pathway in which VCTE/CAP devices are adopted. Marginal savings (or costs) due to implementing the device are derived by comparing the aggregate costs between the 2 pathways. Sources of potential savings are 2-fold. First, VCTE/CAP tests result in early identification of patients with FLD (the majority are currently undiagnosed), allowing for proactive intervention and behavior change to slow the progression of disease in these patients. Second, VCTE/CAP tests can reduce the aggregate volume of some current diagnosis methods, such as liver biopsy, imaging, and laboratory work.

METHODS: Our model relied on administrative claims data consisting of 5 million commercial members and 3 million Medicare members to inform baseline statistics on disease prevalence, health care cost and utilization, and disease progression associated with different severities of liver disease. We consulted expert clinical opinion and medical literature to inform our assumptions related to device adoption and use.

RESULTS: Scenario testing demonstrated positive net savings within 2 to 3 years after device deployment. Across a 5-year time span, we estimate net savings up to \$2.64 per member per month (PMPM) for Medicare payers and up to \$1.91 PMPM for commercial payers.

CONCLUSIONS: We conclude that deploying VCTE/CAP devices is a financially advantageous solution to address the epidemic of FLD.

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elastography (VCTE) and controlled attenuation parameter (CAP) represent a potential solution. VCTE/CAP is a noninvasive screening procedure used to detect liver stiffness and fat, the 2 key identifying characteristics of FLD. In this study, we constructed an economic model to determine the potential return on investment (ROI) from deploying a VCTE/CAP-based care model to identify people with FLD in both Medicare and commercial payer settings.

METHODS

Data

Our economic model relied on administrative claims data consisting of 5 million commercial members in 2015 to 2017 from IBM's MarketScan data set and 3 million Medicare members in CMS' Limited Data Set from 2012 to 2016. These data sets were used to inform baseline statistics on disease prevalence rates, as well as health care cost and utilization associated with various levels of liver disease. Key data elements contained in each data source include member enrollment, diagnosis codes, procedure codes, and claim allowed amounts (insurance and member paid amounts).

Definitions and Member Identification

For the purpose of this model, we segmented the spectrum of FLD-related conditions into multiple severity levels: simple fatty liver, steatohepatitis and fibrosis, cirrhosis, end-stage liver disease (ESLD), and liver cancer. Disease levels were defined using the *International Classification of Diseases, Tenth Revision* diagnosis codes (see [eAppendix A](#) [eAppendices available at [ajmc.com](#)]). We identified and assigned members to disease levels based on this code list.¹⁰ Members with certain severe conditions that are likely to result in unavoidable high costs, such as cancer (non-liver-related), severe injuries or burns, and end-stage renal disease, were subsequently excluded from the analysis. [eAppendix B](#) contains the full list of exclusion conditions.

Disease Transition Probabilities

We modeled disease transition probabilities between each disease level using multistate Markov models. Claims data were summarized on a half-year basis, so the cycle length of the disease transition probabilities is half a year. We limited remission from members in levels 3, 4, and 5 because this is clinically unlikely to happen. In other words, once a patient acquires cirrhosis, ESLD, or liver cancer, the member can only remain in that level, progress to the next level, or leave the health plan.⁵ Furthermore, we require a patient to demonstrate remission of their condition in 2 consecutive periods to move down into a less severe level. These adjustments are necessary to counteract inconsistencies in medical claims coding and to reflect real-world experience

TAKEAWAY POINTS

Chronic liver disease and cirrhosis are leading causes of death in the United States. Given the high prevalence and cost of fatty liver disease (FLD), it is paramount to implement accurate, easy-to-use tests to identify individuals who are at risk for advanced liver disease. We constructed an economic model to assess the cost savings outcomes of deploying transient elastography to identify and monitor patients with FLD in a payer population. Outcomes are evaluated across multiple dimensions and scenarios, and we estimate up to \$2.64 per member per month net savings over 5 years.

- ▶ Although several papers have outlined cost-effectiveness of noninvasive diagnosis models, we are not aware of any analysis that incorporates the cost of the testing device, which is an important consideration for executives when making investment decisions.
- ▶ This is the first analysis to quantify potential cost savings at the population level as opposed to the individual level, making it more informative for business decision makers.
- ▶ We relied on longitudinal, concrete claims data to calculate disease transition probabilities, frequencies, and costs, whereas most existing literature gathers such data points through meta-analysis.

more accurately. The resulting transition tables can be found in [eAppendices C and D](#).

Economic Model Development

The model was built to project medical cost savings driven by the device, relative to the net cost of the device. Two sources of value generation are considered. First, VCTE/CAP tests result in earlier identification of patients with FLD, allowing for proactive intervention to slow down disease progression in these patients. Second, use of the VCTE/CAP test reduces the volume of current diagnosis methods, such as liver biopsy, imaging, and laboratory work (definitions of utilization categories can be found in [eAppendix E](#)). The aggregate effect of VCTE/CAP on utilization and cost is estimated by comparing the current-state diagnosis and treatment (usual care) pathways with future-state pathways (after the introduction of the device). The economic model includes the following parameters:

- The population in the model is held constant over time (ie, the number of new entrants into the health plan is equal to the number of members who left the plan in the prior period either through death or change in coverage).
- For the purpose of trending, we adopt an inflation rate of 2% and medical trend rate of 6%.^{11,12}
- Rental cost of the VCTE/CAP device is \$2800 per month per unit.
- Assuming that device adoption is limited to specialists and that it will ramp up gradually over time, one-third of eligible members are assumed to have access to the test by year 3. If the device is assumed to be deployed at point-of-care settings, we assume final penetration rates will be higher and that half of the total membership will have access by year 3. The number of devices assumed to be installed in each period is based on the penetration rates described above, a member-to-primary care physician ratio of 1500:1, and a member-to-specialist ratio of 3750:1.^{13,14} An implication for smaller payers is that as the plan population gets smaller, the concentration of members

TABLE 1. Prevalence of Diagnosed and Undiagnosed Liver Disease

Disease level	Commercial diagnosed FLD (observed)	Commercial undiagnosed FLD (estimated)	Medicare diagnosed FLD (observed)	Medicare undiagnosed FLD (estimated)
Level 1	1.16%	28.50%	1.18%	28.49%
Level 2	0.07%	5.36%	0.17%	5.26%
Level 3	0.06%	0.45%	0.26%	0.25%
Level 4	0.04%	0.00%	0.22%	0.00%
Level 5	0.01%	0.00%	0.05%	0.00%

FLD, fatty liver disease.

TABLE 2. Utilization Reduction Assumptions by Disease Level

Disease level	Liver biopsy	Laboratory test	Imaging
Level 1: simple fatty liver	90%	20%	90%
Level 2: steatohepatitis/fibrosis	60%	20% increase	10%
Level 3: cirrhosis	10%	5%	5%
Level 4: end-stage liver disease	0%	0%	0%
Level 5: liver cancer	0%	0%	0%

with access to specific physicians may become more diluted. As such, we have modeled various penetration assumptions that scale member access.

Clinical Assumptions

To quantify the downstream benefits of early identification of liver disease, we imputed the prevalence of undiagnosed liver disease at each disease level by subtracting the observed prevalence rates in claims data from the total estimated US prevalence rates reported in Estes et al.⁴ Because this study focuses solely on NAFLD, we scaled up the estimates according to the ratios observed in claims data to reflect the total prevalence of all FLD conditions. The resulting prevalence rates are presented in **Table 1**. Unsurprisingly, the diagnosis prevalence rates are much higher in the Medicare population compared with commercial, and much more so in the more severe disease levels.

Research findings suggest a high correlation between FLD and diabetes.^{2,15} To remain conservative with the impact and savings estimates, we assume that increases in screening of patients who unknowingly carry FLD are limited to the diabetes population. The number of incrementally diagnosed patients with liver disease is then calculated to be the portion of the population who have a liver condition, do not currently have a liver diagnosis, have diabetes, visit their doctor, and have access to a VCTE/CAP device at their doctor’s office. A formulaic representation of the logic is included in **eAppendix F**.

Although identifying more patients who unknowingly carry liver disease is beneficial for early intervention and outcomes

improvement, it likely drives up health care costs in the short term as providers address the condition. Based on clinical expert input, we modeled increases in health care costs when patients with undiagnosed liver disease are made aware of their liver condition by assuming they receive a 1-time imaging test, additional annual office visits, and additional annual laboratory tests.

For the earlier stages of FLD, no effective treatment is demonstrated beyond weight loss and lifestyle changes. However, research has suggested that when patients are led to focus on their disease, they are more likely to engage in positive lifestyle changes that encourage recovery even without medical treatment. For example, in a meta-analysis of randomized controlled trials of NASH, around 21% to 33% of patients given placebo demonstrated significant improvements in various measures of liver health.¹⁶ Therefore, we model a 10% to 25% decrease in disease progression and/or increase in regression (smaller change for patients with less severe levels and vice versa) for those who are incrementally diagnosed. In addition, many payers offer chronic condition management (CCM) programs that drive positive lifestyle changes. The model incorporates the impact of CCM programs on the faster regression for patients with newly diagnosed FLD by referencing the impact of weight loss on fatty liver resolution previously studied through research.^{17,18} If a CCM program is available to induce positive lifestyle changes and weight loss, the model calculates an increased likelihood of improving steatosis and/or fibrosis when undiagnosed liver patients are identified and enroll in a CCM program. This increase ranges from 10% to 20% for the commercial population and 5% to 10% for the Medicare population.

The second component through which we quantify the impact of VCTE/CAP relates to its medical substitution effects. Using VCTE/CAP to diagnose liver conditions can replace certain procedures that are traditionally used for testing. The utilization reduction assumptions employed in the model are presented in **Table 2**, and the resulting utilization and cost impact are displayed in **eAppendices G and H**.

Negative VCTE/CAP results for fibrosis generally eliminate the need for liver biopsies and the need to continue prescribing imaging tests after an initial imaging. A large portion of complex laboratory tests may also be avoided. If VCTE/CAP results indicate fibrosis, however, confirmatory testing via biopsy may be prescribed. Alternatively, confirmatory testing can also shift to laboratory tests or imaging, which, given their noninvasiveness, may be preferred by patients.¹⁹ In addition, VCTE/CAP better distinguishes the precirrhotic patients from cirrhotic patients than the traditional Fibrosis-4 (FIB-4) score method and can thus avoid cancer screening for the precirrhotic patients, as well as reduce monitoring from the typical semiannual imaging and lab tests prescribed for patients with cirrhosis to once per year or less.²⁰

Finally, if VCTE/CAP were to be made available at point-of-care settings, we also assume that this results in a 5% reduction in office visits for lower-severity patients (levels 1 and 2) to acknowledge potentially reduced referrals to liver specialists for the initial testing or monitoring of FLD.

TABLE 3. Scenario Results for Medicare Model

Scenario	A	B	C	D	E	F	G	H
Population size	100,000	100,000	100,000	100,000	100,000	100,000	10,000	10,000
Market segment	Medicare	Medicare	Medicare	Medicare	Medicare	Medicare	Medicare	Medicare
Projection time frame (years)	5	3	5	3	5	3	5	3
Penetration expectations	High	Medium	High	Medium	High	Medium	Low	Low
Place of service	Point of care	Point of care	Point of care	Point of care	Specialist	Specialist	Point of care	Point of care
CCM availability	Yes	Yes	No	No	No	No	Yes	Yes
Gross savings	\$20.9 million	\$6.9 million	\$13.5 million	\$3.7 million	\$10.1 million	\$2.3 million	\$1.7 million	\$0.5 million
Net savings	\$15.9 million	\$4.4 million	\$8.5 million	\$1.2 million	\$8.8 million	\$1.7 million	\$1.3 million	\$0.3 million
ROI	315%	174%	169%	49%	654%	249%	307%	160%
Net savings PMPM	\$2.64	\$1.21	\$1.41	\$0.34	\$1.46	\$0.46	\$2.11	\$0.84

CCM, chronic condition management; PMPM, per member per month; ROI, return on investment.

RESULTS

Real-world outcomes vary based on the specific payer scenario. In this subsection, results are reported for representative combinations of input scenarios. The key levers that influence outcomes include projection time frame, market segment, device penetration expectations, device place-of-service setting, and availability of a CCM program. All savings are reported on a cumulative basis over the entire projection time frame. We also report savings on a per-member per-month (PMPM) basis over the entire population (not just those with FLD).

Table 3 illustrates the various outcomes scenarios for the Medicare model. Under scenario E, for example, a high device penetration level is modeled for a Medicare payer with 100,000 members deploying devices at specialists, where high device penetration corresponds to gradually ramping up device placement to give one-third of members access at their specialists over 2 years. This scenario produces an estimated 5-year cumulative gross savings of \$10.1 million and a net savings (subtracting device rental) of \$8.8 million. This corresponds to a 5-year 6.5:1 ROI and a net savings of \$1.46 PMPM.

Compared with scenario E, scenario C produces a less robust financial bottom line at \$1.41 net savings PMPM and a 1.7:1 ROI, driven by the disproportionate increase in device rental cost in comparison with the increase in medical savings. However, it is important to note that a point-of-care strategy will more effectively drive positive outcomes in a much broader patient base, while still producing significant savings compared with a specialist-only deployment strategy.

When factoring in the impact that CCM programs may have in terms of inducing positive lifestyle changes and curbing disease progression in those incrementally diagnosed patients with liver disease, we see the strongest financial outlooks of \$15.9 million total net savings or \$2.64 PMPM over 5 years in scenario A. This emphasizes the importance of pairing effective intervention strategies together with the diagnosis and monitoring solutions to drive the best outcomes.

FIGURE. Illustration of Net Savings PMPM for Scenario A



PMPM, per member per month; yr, year.

For small payers (with a population of 10,000) we model more conservative penetration assumptions, and in practice it may be important for payers with diluted member-to-provider distribution to take steps in managing the concentration of membership per device to maintain high ROI, potentially via dedicated testing centers or different processes compared with deploying the devices at provider offices directly. Scenarios G and H produced smaller savings compared with their larger-payer counterparts in scenarios A and B, but the results are still positive and represent significant savings potential.

The Figure displays annual net savings results for scenario A and illustrates the time interplay of the ROI. Because the majority of savings are caused by a decrease in the speed of the progression of the disease, year 1 net savings tend to be negative as the projected

TABLE 4. Scenario Results for Commercial Model

Scenario	I	J	K	L	M	N	O	P
Population size	100,000	100,000	100,000	100,000	100,000	100,000	10,000	10,000
Market segment	Commercial	Commercial	Commercial	Commercial	Commercial	Commercial	Commercial	Commercial
Projection time frame (years)	5	3	5	3	5	3	5	3
Penetration expectations	High	Medium	High	Medium	High	Medium	Low	Low
Place of service	Point of care	Point of care	Point of care	Point of care	Specialist	Specialist	Point of care	Point of care
CCM availability	Yes	Yes	No	No	No	No	Yes	Yes
Gross savings	\$16.5 million	\$6.5 million	\$8.8 million	\$3.0 million	\$6.7 million	\$1.9 million	\$1.4 million	\$0.5 million
Net savings	\$11.4 million	\$4.0 million	\$3.8 million	\$0.5 million	\$5.3 million	\$1.3 million	\$1.0 million	\$0.3 million
ROI	227%	160%	75%	21%	397%	192%	234%	158%
Net savings PMPM	\$1.91	\$1.12	\$0.63	\$0.15	\$0.89	\$0.36	\$1.61	\$0.83

CCM, chronic condition management; PMPM, per member per month; ROI, return on investment.

aggregate cost and increased frequency of FLD testing outweigh the current state of FLD testing costs. Furthermore, the magnitude of net savings tends to increase over time, where there remain residual financial savings from members identified with FLD in earlier years.

Similar scenarios are constructed for the commercial model; results are provided in **Table 4**. The relationships among the various commercial scenarios are consistent with those among the Medicare scenarios described above. Overall, each Medicare scenario produces a stronger financial outcome compared with its commercial counterpart, due to the higher disease prevalence rates in the older population. The commercial scenario outcomes range from \$11.4 million net savings (\$1.91 PMPM, 2.2:1 ROI) over 5 years under scenario I to \$0.3 million net savings (\$0.83 PMPM, 1.6:1 ROI) over 3 years under scenario P.

DISCUSSION

The importance of early identification of liver disease is often overlooked, and the clinical pathways to stage liver disease have not been incorporated into the mainstream practice flows of primary care physicians. Most health plans have experience managing the high cost of treating HCV. Diagnosis and management of HCV can be performed through blood tests alone, but there is considerable variability in diagnostic workup for FLD, involving many testing modalities. High diagnostic variability combined with the lack of a clear diagnostic pathway expose health plans to unnecessary and preventable excessive costs across a large segment of their patient populations. Moreover, current testing patterns have left a vast majority of FLD cases currently undiagnosed and progressing at worrisome rates. By identifying disease early, when it is more easily mitigated, health deterioration and associated preventable future costs can be proactively managed or avoided. This economic model demonstrates that deploying VCTE/CAP devices to screen for and monitor liver stiffness and liver fat in members with diabetes can yield net savings to the payer, directly affecting bottom-line performance. Although short-term costs increase due to implementation of the testing devices and the identification and

management of additional patients with active liver disease, the incremental cost is outweighed by the downstream savings from the avoidance of, or delay of progression to, advanced liver disease. The reductions in unnecessary referrals, biopsies, and imaging further increase cost savings.

The model also demonstrates that cost savings are increased when expanding access to a broader patient base. High penetration of the VCTE/CAP device in primary care, combined with more intensive behavioral engagement through CCM programs, yield the highest returns in both Medicare and commercial settings.

Although our model regards only the population with diabetes as being at high risk for FLD, it is important to note that many other indicators are also relevant to FLD, including obesity, metabolic syndrome, and cardiovascular disease. Applying the device beyond the diabetes population is likely to expand the clinical benefits to more patients who unknowingly have FLD. At the same time, marginal identification rates may decrease as service utilization climbs when more low-risk patients are included. This competing impact between savings and cost leaves opportunities for future analyses on this subject.

Specific to NAFLD, the VCTE/CAP technique can more accurately assess NAFLD over time than can blood test scores, such as the FIB-4 and NAFLD fibrosis scores, that rely on biomarkers found in blood.² These blood test scores cannot determine the severity of NAFLD in one-third of the population, for whom a quantitative test, such as VCTE/CAP, is required. As health plans and clinical societies continue to emphasize the management of liver health, it is important to focus on implementing tests that are accurate and precise—yet easy to use—in the management of high-prevalence diseases.

Limitations

This analysis relies on a set of assumptions that are informed by clinical experts and the literature. We performed due diligence in verifying the reasonability of all assumptions but acknowledge the possibility for certain assumptions to deviate from reality. Our results should not be viewed as an exact prediction of real-life outcomes, but rather should be used to inform directionality

and relative magnitudes by decision makers. For example, the actual prescribing patterns of physicians, once they are equipped with the VCTE/CAP device, may significantly vary depending on administration guidance, reimbursement structure, local clinical practice, and other factors. If physicians do not follow the screening guidelines for patients who are at risk of having FLD, for example, they would not realize the benefits of incrementally identifying a significant portion of patients with FLD who are currently unaware of their disease.

In addition, although granular clinical differences may exist between AFLD and NAFLD, the model relied on the assumption that AFLD and NAFLD generally follow similar diagnostic pathways and responses to lifestyle interventions. We deem this an appropriate assumption because VCTE/CAP applies equally to both types of FLD by detecting liver stiffness and fat, and the main treatment intervention recommended for FLD is healthy lifestyle changes and weight loss.

Finally, the pharmaceutical industry is aggressively developing treatments for this silent pandemic.^{21,22} The effect of such potential drug launches is not included in this model because of uncertainties around these launches.

CONCLUSIONS

Through modeling care pathways and expenditure, we demonstrated that deploying VCTE/CAP devices to screen for and monitor liver stiffness and liver fat for members with diabetes is economically beneficial to the payer. The short-term incremental costs of device implementation and managing additional patients are outweighed by the downstream savings from avoidance or delay of advanced liver disease. ■

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eAppendix A. ICD 10 Diagnosis Codes for Patient Identification

ICD 10	ICD 10 Description	Disease Level	Disease Level Description		
K760	Fatty (change of) liver, not elsewhere classified	1	Simple Fatty Liver		
K7689	Other specified diseases of liver				
K769	Liver disease, unspecified				
K709	Alcoholic liver disease, unspecified				
K700	Alcoholic fatty liver				
K710	Toxic liver disease with cholestasis				
K718	Toxic liver disease with other disorders of liver				
K719	Toxic liver disease, unspecified				
K77	Liver disorders in diseases classified elsewhere				
K7581	Nonalcoholic steatohepatitis (NASH)	2	Steatohepatitis / Fibrosis		
K740	Hepatic fibrosis				
K7589	Other specified inflammatory liver diseases				
K759	Inflammatory liver disease, unspecified				
K742	Hepatic fibrosis with hepatic sclerosis				
K7010	Alcoholic hepatitis without ascites				
K7011	Alcoholic hepatitis with ascites				
K702	Alcoholic fibrosis and sclerosis of liver				
K713	Toxic liver disease with chronic persistent hepatitis				
K714	Toxic liver disease with chronic lobular hepatitis				
K7150	Toxic liver disease with chronic active hepatitis without ascites				
K7151	Toxic liver disease with chronic active hepatitis with ascites				
K716	Toxic liver disease with hepatitis, not elsewhere classified				
K730	Chronic persistent hepatitis, not elsewhere classified				
K731	Chronic lobular hepatitis, not elsewhere classified				
K732	Chronic active hepatitis, not elsewhere classified				
K738	Other chronic hepatitis, not elsewhere classified				
K739	Chronic hepatitis, unspecified				
K752	Nonspecific reactive hepatitis				
K754	Autoimmune hepatitis				
K7460	Unspecified cirrhosis of liver			3	Cirrhosis
K7469	Other cirrhosis of liver				
K741	Hepatic sclerosis				
K7030	Alcoholic cirrhosis of liver without ascites				
K7031	Alcoholic cirrhosis of liver with ascites				
K7040	Alcoholic hepatic failure without coma				
K7041	Alcoholic hepatic failure with coma				
K717	Toxic liver disease with fibrosis and cirrhosis of liver				

K7110	Toxic liver disease with hepatic necrosis, without coma		
K743	Primary biliary cirrhosis		
K744	Secondary biliary cirrhosis		
K745	Biliary cirrhosis, unspecified		
I8500	Esophageal varices without bleeding	4	End Stage Liver Disease
I8501	Esophageal varices with bleeding		
I8510	Secondary esophageal varices without bleeding		
I8511	Secondary esophageal varices with bleeding		
K7111	Toxic liver disease with hepatic necrosis, with coma		
K7201	Acute and subacute hepatic failure with coma		
K7210	Chronic hepatic failure without coma		
K7211	Chronic hepatic failure with coma		
K7290	Hepatic failure, unspecified without coma		
K7291	Hepatic failure, unspecified with coma		
K766	Portal hypertension		
K767	Hepatorenal syndrome		
K7681	Hepatopulmonary syndrome		
C220	Liver cell carcinoma		
C228	Malignant neoplasm of liver, primary, unspecified as to type		
C229	Malignant neoplasm of liver, not specified as primary or secondary		

eAppendix B. Excluded Conditions

Patients with diagnosis codes that correspond to the following CMS-HCCs are excluded from the analysis. However, diagnosis codes related to liver cancers were removed from HCCs 8 and 9 (i.e. having liver cancer diagnosis codes did not exclude members from the analysis).

HCC	HCC Description
8	Metastatic Cancer and Acute Leukemia*
9	Lung and Other Severe Cancers*
46	Severe Hematological Disorders
70	Quadriplegia
71	Paraplegia
73	Amyotrophic Lateral Sclerosis and Other Motor Neuron Disease
74	Cerebral Palsy
80	Coma, Brain Compression/Anoxic Damage
82	Respirator Dependence/Tracheostomy Status
106	Atherosclerosis of the Extremities with Ulceration or Gangrene
134	Dialysis Status
136	Chronic Kidney Disease, Stage 5
157	Pressure Ulcer of Skin with Necrosis Through to Muscle, Tendon, or Bone
158	Pressure Ulcer of Skin with Full Thickness Skin Loss
162	Severe Skin Burn or Condition
166	Severe Head Injury
167	Major Head Injury

*having liver cancer diagnosis codes did not exclude members from the analysis.

eAppendix E. Utilization Category Definitions

Category	Definition
Imaging	Abdominal ultrasound, Computed tomography, Magnetic resonance imaging, Elastography (CPT codes: 76700, 74150, 74181, 0346T, 74160, 74170, 74174, 74175, 74176, 74177, 74182, 74183, 74185, 76705)
Liver Biopsy	CPT codes: 47000, 47001
Lab Tests	Basic metabolic panel, General health panel, Electrolyte panel, Comprehensive metabolic panel, Hepatic function panel, Hepatitis panel, Lipid panel, Renal function panel, Acute hepatitis panel, Albumin, Apolipoprotein, Bilirubin total, Bilirubin direct, Assay bilirubin, Cholesterol total, Creatinine, Creatinine clearance test, Glucose blood test, Glucose tolerance test, Glycosylated hemoglobin test, HDL/LDL, Assay alkaline phosphate, AST, ALT, Assay triglycerides, Bleeding time test, Hemocrit, Hemoglobin, Automated hemogram, Manual platelet count, Automated leukocyte count, Automated platelet count, Coagulation time, Prothrombin test, Partial thromboplastin time (CPT codes: 80048, 80047, 80050, 80051, 80053, 80058, 80059, 80061, 80069, 80074, 82040, 82172, 82247, 82248, 82250, 82465, 82565, 82575, 82947, 82977, 83036, 83718, 84075, 84450, 84460, 84478, 85002, 85013, 85018, 85021, 85032, 85048, 85049, 85345, 85610, 85730, G0096, G0098, 80076, 85023, 85024, 85025, 85027, 85347, 85611, 85732, 85348, 82950, 83037, 84078, 85014, 82962, 84080)
Office Visits	Place of service code=11 (office) and CPT codes: 99201-99205, 99211-99215, 99241-99245
Hospitalizations	Place of service code=21 and revenue codes: 010x - 016x, 020x-021x
ER Visits	CPT codes: 99281-99285, 99288 or revenue codes: 0450-0452, 0456, 0459, 0981

eAppendix F. Formulaic Representation of Incremental Liver Patient Identification Volume

$$N_{new,t} = (N_{total,t} - N_{dx,t}) \times P_{diabetes} \times P_{fatty\ liver | diabetes} \times Visit \times Access_t$$

Where:

$N_{new,t}$ is the number of incrementally diagnosed liver patients in period t ;

$N_{total,t}$ is the number of total members in the population in period t ;

$N_{dx,t}$ is the number of liver patients who already have a diagnosis in period t ;

$P_{diabetes}$ is the prevalence rate of diabetes among the population;

$P_{fatty\ liver | diabetes}$ is the prevalence of fatty liver disease among the diabetes cohort (in other words, the conditional probability of having fatty liver disease given that a member has diabetes);

$Visit$ is the average percentage of diabetes members visiting the doctor in a period;

and $Access_t$ is the percentage of members with access to a VCTE device in period t .

eAppendix G. Disease Level Utilization and Cost Reductions according to Substitution Assumptions, by Utilization Categories, Commercial

Application of Utilization Substitution Assumptions - Commercial

Level 1 Simple fatty liver

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(9.9)	(776)	(1,260)
PMPM	(\$1.1)	(\$6)	(\$99)

Level 2 Steatohepatitis and fibrosis

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(71)	912.0	(77.7)
PMPM	-\$9	\$6	(\$5)

Level 3 Cirrhosis

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(6)	(217)	(48)
PMPM	-\$1	(\$1)	(\$3)

eAppendix H. Disease Level Utilization and Cost Reductions according to Substitution Assumptions, by Utilization Categories, Medicare

Application of Utilization Substitution Assumptions - Medicare

Level 1 Simple fatty liver

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(17)	(1,202)	(2,032)
Cost per Visit	0	\$0	\$0
PMPM	(2)	(\$46)	(\$77)

Level 2 Steatohepatitis and fibrosis

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(70)	1,296.5	(121.0)
Cost per Visit	0	\$0	\$0
PMPM	-\$5	\$102	(\$2)

Level 3 Cirrhosis

Reductions in:	Liver Biopsy	Lab Test	Imaging
Utilization Per 1,000 Per Year	(5)	(284)	(62)
Cost per Visit	\$0	\$0	\$0
PMPM	\$0	(\$9)	(\$2)