Published in final edited form as:
Clin Gastroenterol Hepatol. 2008 December ; 6(12): 1418–1424. doi:10.1016/j.cgh.2008.08.005.

Cost-Effectiveness of Alternative Surveillance Strategies for Hepatocellular Carcinoma in Patients with Cirrhosis

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Abstract

Background & Aims—The rising incidence of hepatocellular carcinoma (HCC) in the United States has significant health and economic consequences. Ultrasound (US) surveillance is recommended for patients with cirrhosis because of their high risk of HCC and improving treatment outcomes for small tumors. We assessed the costs, clinical benefits, and cost-effectiveness of US surveillance and alternative strategies for HCC in cirrhosis using a computer-based state transition model with parameters derived from available literature.

Methods—Our model compared a policy of no surveillance to six surveillance strategies in cirrhotic patients ages 50 years and older in the United States: 1) annual US; 2) semiannual US; 3) semiannual US with alphafetoprotein; 4) annual computed tomography (CT); 5) semiannual CT; and 6) annual magnetic resonance imaging. The number of screening tests needed to detect one small HCC, cost per treated HCC, lifetime costs, quality-adjusted life expectancy, and incremental cost-effectiveness ratios were calculated.

Results—Semiannual US surveillance for HCC in cirrhosis increased quality-adjusted life expectancy by 8.6 months on average, but extended it nearly 3.5 years in patients with small treated tumors. Semiannual US surveillance had an incremental cost-effectiveness ratio of $30,700 per quality-adjusted life year (QALY) gained, and was more cost-effective than the alternative surveillance strategies using a threshold of $50,000 per QALY gained. The incremental cost-effectiveness ratios for the combined alphafetoprotein/US and annual CT strategies exceeded $50,000/QALY unless the sensitivity and specificity of US fell below 65% and 60%, respectively.

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Conflict of interest: No author has a conflict of interest to disclose.

Conclusion—Semiannual US surveillance for HCC in cirrhotic patients improves clinical outcomes at a reasonable cost.

The incidence of hepatocellular carcinoma (HCC) in the U.S. has doubled over the last two decades, resulting in an estimated 1 billion dollars in direct and indirect health care costs.[1–3] Because the prognosis of advanced HCC is poor, surveillance for the detection of small tumors in high-risk populations has become common practice. The majority of gastroenterologists use semiannual ultrasound and the serum tumor marker alphafetoprotein (AFP) to detect HCC in cirrhotic patients [4], of whom 2–8% develop the tumor annually.[5–7] Studies suggest that surveillance detects tumors at earlier stages and improves survival, but no randomized, controlled trial has been performed in cirrhotics.[8–11] Recent guidelines from the American Association for the Study of Liver Diseases (AASLD) advocate annual or semiannual surveillance with ultrasonography (US) in cirrhosis.[12] Because its sensitivity and specificity are limited, use of AFP is recommended only when ultrasound is unavailable.[12, 13]

The cost-effectiveness of HCC surveillance with US alone in a general population of cirrhotics has not been evaluated in the United States. Surveillance with AFP and US, or with computed tomography (CT), has been demonstrated to be cost-effective in select populations such as liver transplant candidates, Child's class A cirrhotics with long life expectancy, and those with hepatitis B or C cirrhosis.[14–19] Historically, the utility of surveillance has been limited by poor treatment outcomes even in early stage disease and suboptimal screening test characteristics. With improvements in treatment options for small tumors and the diagnostic accuracy of radiologic imaging, routine surveillance for HCC in cirrhosis is more likely to provide measurable clinical benefits.

In recent years local ablative therapies such as radiofrequency ablation (RFA) have permitted patients with advanced liver disease or comorbidities that preclude resection or transplantation to be treated successfully.[20] Liver transplantation is not only a viable treatment for HCC, but changes to the MELD (Model for End-Stage Liver Disease) scoring system, a numerical scale used for liver allocation, now give patients with small tumors priority in the transplant process. For patients meeting the Milan transplant criteria, those with a single HCC less than 5 centimeters or no more than three tumors each smaller than 3 centimeters, long-term survival post-transplant approaches that observed for nonmalignant indications.[21] As survival for limited stage disease improves, the consequences of missing small HCC grow.

In addition to more promising treatment outcomes, technological advances have also expanded the range of available screening modalities for HCC. While US is recommended for surveillance, CT or magnetic resonance imaging (MRI) may be more sensitive in detecting small HCC.[22, 23] Triple-phase CT, in which portal venous phase, arterial phase and noncontrast imaging highlight different tumor characteristics, is more sensitive than US and is used increasingly frequently for surveillance by some clinicians.[4] The relative performance and costs of these tests in the context of a surveillance program have not been formally evaluated.

With the imminent peak in chronic hepatitis C cirrhosis and the rising incidence of nonalcoholic fatty liver disease, the burden of HCC is expected to grow in the coming years.[2] In light of potentially more effective, yet expensive, diagnostic tests and treatments, we used the best available data to estimate the benefits, costs and cost-effectiveness of US alone compared to alternative surveillance strategies for HCC in cirrhosis.

METHODS

Analytic Overview

We developed a computer-based Markov model (TreeAge Pro software 2005) to simulate disease progression, surveillance, diagnosis, and treatment of HCC in a cohort of patients with compensated cirrhosis. In comparison to no surveillance, we assessed 1) annual US; 2) semiannual US; 3) semiannual US with AFP; 4) annual CT; 5) semiannual CT; and 6) annual MRI surveillance. Model outcomes included the number of screening tests needed to diagnose one small HCC, cost per treated HCC, lifetime costs, quality-adjusted life expectancy, and incremental cost-effectiveness ratios (2004 U.S. $ per quality-adjusted life year gained). We adopted a health system perspective and followed the recommendations of the Panel on Cost-Effectiveness in Health and Medicine.[24] One-way and two-way sensitivity analyses were performed to identify individual parameters with the greatest influence on our results.

Model

A cohort of 50 year-old individuals representative of patients with compensated cirrhosis in the U.S. enter the state transition model and move through a series of health states designed to reflect important stages in the natural history of cirrhosis, tumor progression and treatment (Figure 1).

Surveillance Algorithms and Treatment

To estimate the effect of surveillance, the model distinguishes between detected and undetected HCC. Depending on the accuracy and timing of surveillance, HCC might be detected early via surveillance or remain undetected until an advanced stage. Compensated and decompensated cirrhotics were eligible for surveillance with any of the six strategies. Tumor stage at diagnosis depended on the tumor growth rate and likelihood of detection at any surveillance interval. Patients with compensated cirrhosis in whom “small HCC” was detected (defined as tumors meeting the Milan criteria) were eligible for liver transplantation, resection or local ablative therapies; while decompensated cirrhotics were treated with transplant or local ablation only. Patients with advanced tumors received only palliative care.

A number of assumptions were made in the base case including (1) a positive surveillance US was evaluated with a dynamic imaging study, either triple-phase CT or MRI, as recommended by AASLD guidelines; (2) serum AFP was considered positive above a 20 ng/mL cut-off, and was evaluated with a dynamic imaging study even when the corresponding US was negative; (3) all suspicious lesions found on imaging were biopsied, and biopsy was assumed to be perfect, without mortality risk; (4) no additional imaging was

performed prior to biopsy in the CT or MRI strategies; and (5) patients with false-positive screening tests returned to their previous surveillance test and schedule once biopsy confirmed their true disease status.

Data

Table 1 summarizes selected model parameters used in the model. A base-case value and plausible range was established for each model input based on published literature and expert assumptions. When several estimates were available, we prioritized estimates from larger, well-controlled, prospective studies in Western populations.

Natural history and progression of cirrhosis—Based on large epidemiologic studies, the average life expectancy of compensated cirrhosis is between 10 and 13 years.[25–28] Between 5–7% of compensated cirrhotics progress to decompensated disease each year, developing ascites, variceal bleeding or encephalopathy.[28] The median life expectancy of decompensated disease is 2 years.[28–30] Because 20% of the annual excess mortality from compensated and decompensated cirrhosis is attributable to HCC, we adjusted the mortality rates accordingly to avoid double-counting HCC deaths.[25–30] With this adjustment, predicted life expectancy for compensated cirrhosis in the model approximated that reported in the literature.

Incidence and natural history of HCC—The annual incidence of HCC is approximately 5%, with a range of 2–8% in cohort studies of cirrhotics undergoing surveillance.[5–8, 10, 31–33] Median survival for patients with small or advanced HCC is two years or six months, respectively.[34–39] Tumor growth was assumed to be linear, with a doubling time between 117 and 195 days.[37, 40, 41] Based on this doubling time, approximately 40% of tumors progress from limited to advanced stage each year. Because systemic chemotherapy and other treatments for advanced disease have not significantly improved survival [42, 43], advanced cancer was not treated in the model.

Surveillance test characteristics—The sensitivity of US for HCC surveillance ranges from 40–81% and its specificity from 80–100%.[44–49] The sensitivity of triple-phase CT is higher at 85–90%, but its specificity similar at 80–96%.[22, 44, 45, 48–52] Serum AFP is far less sensitive (40–65%) and specific (63–94%) at the 20 ng/mL cut-off.[53–57] The sensitivity and specificity of MRI approach 90%.[49, 58, 59] Test characteristics were assumed to be invariant across the spectrum of liver disease. Because test characteristics vary widely in the literature, preference was given to studies using a screening framework, a pathologic gold standard and those reporting per-patient rather than per-lesion sensitivity and specificity. Similarly, because CT and MRI studies tend to use the exacting gold standard of liver explant and include missed subcentimeter lesions in the sensitivity calculation, these lesions were excluded from the analysis when possible to permit comparability to US studies.

Risks and prognosis of HCC treatment—For compensated cirrhotics with HCC meeting Milan criteria, treatment options with curative intent include transplantation, resection or local ablative therapy. Decompensated cirrhotics with HCC are candidates for transplant or local therapy only.[60] RFA was evaluated as the sole local therapy because its

efficacy is similar to chemoembolization and ethanol injection[61], and it is widely available in the U.S. The perioperative mortality of liver transplant, resection and RFA are 4.3%[62], 3.9%[63], and 0.3%[64], respectively. Following successful transplantation for small HCC, five-year survival approaches 70%.[21, 62, 63, 65, 66] Five-year survival after resection is less than 50%, due to tumor recurrence.[63, 67–70] Five-year survival with RFA ranges from 31–46% depending on the underlying liver disease.[20, 71–74] Overall survival, rather than recurrence-free survival, was used for prognosis. We assumed that recurrent HCC was not treated and that HCC was treated with a single modality only, not sequential therapy such as RFA followed by transplant.

We consulted four expert hepatologists to estimate the proportion of small HCC eligible for each of the curative therapies, since published data on this parameter are sparse. By conservative estimates, approximately 70% of compensated and 30% of decompensated cirrhotics with small HCC are treatment-eligible, with the remainder excluded due to poor tumor location, advanced liver disease, advanced age or comorbid illness. Based on a Medicare population with HCC, in which treatment rates are lower than in our model's younger cohort, we assumed that the proportion of treatment-eligible compensated cirrhotics undergoing resection, local ablation and transplant was 40%, 40%, and 20%, respectively.[75] We assumed that 40% of treatment-eligible decompensated cirrhotics were transplant-eligible. We varied these estimates widely in sensitivity analyses.

Costs and quality of life—Direct medical costs were derived from 2004 Medicare CPT reimbursement, the 2003 Nationwide Inpatient Sample, and published literature.[15, 76, 77] The annual costs of cirrhosis disease management included office visits, blood work, and occasional complications of decompensated disease, but not orthotopic liver transplantation or surveillance for HCC or esophageal varices. Literature-based estimates were used for the quality of life weights.[76–78] We did not consider temporary reduction in quality of life due to surveillance or treatment since these are small compared to the underlying disease.

RESULTS

Life Expectancy and HCC Outcomes

For compensated cirrhotics ages 50 and older, the average per-person quality-adjusted life expectancy (QALE) is 7.3 years in the absence of surveillance. The undiscounted gain in QALE was 6.8 months with annual US. Increasing the US frequency to twice yearly provides an additional 1.8 months of QALE. Incremental gains from the other strategies were smaller; for example, adding serum AFP improves the effectiveness of semiannual US surveillance by only 0.6 months (Table 2). Although semiannual US increases QALE by 8.6 months on average, it extends it nearly 3.5 years in patients with diagnosed and treated small HCC.

Lifetime Costs and Cost-Effectiveness Analysis

The average discounted lifetime cost in the absence of surveillance for 50 year-old cirrhotic patients is $26,200. Discounted lifetime per-person cost increased by $8,000 with annual US and by $19,700 with MRI. (Table 2) The incremental cost-effectiveness ratio for annual US

was $21,200 per quality-adjusted life year (QALY) gained. In comparison, semiannual US provided nearly two months of additional quality-adjusted life expectancy for $30,700 per QALY. Adding serum AFP yielded smaller gains in QALE and had an incremental cost-effectiveness ratio of $73,500 per QALY. Semiannual CT, the most effective strategy, had an incremental cost-effectiveness ratio exceeding $300,000 per QALY gained. Annual MRI was more costly and less effective than both of these strategies.

Clinical Impact and Resource Use of Semiannual Surveillance

The clinical impact and resource use of semiannual US surveillance in a model cohort of 10,000 cirrhotics age 50 and over are reported in Table 3. Over a thirty-year period, more than 180,000 surveillance ultrasounds would be performed. Semiannual US surveillance would detect an estimated 3,000 small tumors in the population. Therefore, approximately 60 surveillance ultrasounds are required to detect one small HCC. The average costs per detected and treated small HCC were $117,200 and $179,900, respectively.

Sensitivity Analysis

Sensitivity analyses were performed on all model parameters to identify variables with the greatest influence on (1) the cost-effectiveness of HCC surveillance overall and (2) the performance of semiannual US compared to the alternative strategies. The cost-effectiveness of surveillance in general was most sensitive to alternative assumptions about the population age at the onset of surveillance, the mortality of HCC and the rate of progression. The cost of surveillance exceeds $50,000 per QALY gained if the annual incidence of HCC is less than 0.8%, fewer than 14% of tumors progress from limited to advanced stage each year, patient age is greater than 83 years, or if the likelihood of incidental diagnosis of HCC in patients not undergoing surveillance exceeds 60%. On the other hand, surveillance remains cost-effective even when compliance is imperfect or when non-diagnostic or false negative biopsies occur.

The effect of varying selected parameters on the incremental cost-effectiveness of semiannual US surveillance is demonstrated in Figure 2. If the annual incidence of HCC falls below 2.2%, annual US is preferred to semiannual US based on a $50,000/QALY threshold. When US sensitivity is lower than 65% or the specificity of AFP exceeds 95%, combined AFP/US surveillance is preferred. Annual CT becomes the preferred strategy when US specificity is less than 60%. The incremental cost-effectiveness ratios of semiannual CT and annual MRI consistently exceed $100,000 per QALY.

In 2-way sensitivity analysis, we simultaneously varied the test characteristics of US, CT and MRI. When US sensitivity is poor (0.5), combined AFP/US surveillance is preferred for all tested sensitivities of CT and MRI. Otherwise, semiannual US surveillance is cost-effective in all conditions tested.

DISCUSSION

Our analysis demonstrates that surveillance for HCC in patients with cirrhosis provides substantial life-expectancy gains. Semiannual US surveillance extends per-person QALE by 8.6 months on average compared to no surveillance, a benefit that compares favorably to

screening programs for colon or breast cancer.[79–81] The QALE gain for cirrhotics with detected and treated small HCC exceeds three years. The utility of surveillance in cirrhosis is unsurprising because the incidence of HCC is high in this population; the tumor is asymptomatic in its early phases and unlikely to be detected without surveillance; and treatments are effective for early HCC, while the prognosis for advanced disease is poor. With continued improvement in the life expectancy of cirrhosis and the treatment modalities for HCC, the benefit of surveillance is likely to increase.

While there is no consensus on a cost-effectiveness threshold below which an intervention would be considered unequivocally cost-effective, the value of $50,000 per QALY gained is often cited as a reasonable benchmark for the United States. [24] At this threshold, semiannual US ($30,700 per QALY) is attractive. While one could argue that society has been willing to pay up to $100,000 per QALY gained for certain health interventions, which would imply that combined AFP/US surveillance confers reasonable value for the money ($73,500 per QALY), CT and MRI surveillance would not be regarded as cost-effective under widely varying assumptions.

We found that only when US sensitivity and specificity fall below 65% and 60% respectively, do the AFP/US or annual CT strategies become preferred at the $50,000/QALY benchmark. Based on the results of published studies, test characteristics are unlikely to fall into this range. However, in specific circumstances in which US sensitivity or specificity might be poor, such as in patients with ascites, individual decision-making should prevail. As single tests, CT and MRI are each more sensitive than US for detecting early HCC; however, when performed annually these tests are less effective than semiannual US. The rapid doubling time of HCC favors a semiannual surveillance schedule. When compared to semiannual US, semiannual CT or MRI provides a small incremental benefit at a much higher cost. US surveillance also improves as the characteristics of CT and MRI improve because the latter are used as confirmatory tests for a positive US. Our analysis did not consider the risks of radiation or contrast with CT or the additional time needed for MRI, factors that may further favor US surveillance in practice. We also did not consider strategies combining AFP with CT or MRI. Although combining frequent AFP measurements with annual CT or MRI may be more effective, this is unlikely given the limited sensitivity and specificity of AFP compared to advanced imaging.

The addition of AFP to US increases detection of HCC somewhat, but is more costly because falsely positive AFP elevations prompt additional imaging studies. This cost rises further if AFP levels lower than the 20 ng/mL cut-off were to trigger further testing. Despite using favorable test characteristics for AFP, the cost of the combined strategy exceeds $50,000 per QALY. Newer serum tumor markers such as AFP-L3 were not included in the analysis because they are not yet validated for use in screening.[82] If their test characteristics prove to be significantly better than standard AFP, then the combined strategy may become more favorable.

Our results are reasonably consistent with prior cost-effectiveness analyses of HCC surveillance, although no study has evaluated surveillance with US alone in a general population of cirrhotics in the United States. Sarasin and colleagues evaluated semiannual

AFP/US surveillance in compensated cirrhotics.[15] Their model considered surgical resection as the sole treatment modality. Under a best-case scenario, average life expectancy gain from surveillance in this study was 9 months. The cost-effectiveness of surveillance ranged from $26,000 to $284,000 per life year gained, depending on patient age, the incidence of HCC, and prognosis following surgery. Three other studies of surveillance in hepatitis C cirrhosis reported similar cost-effectiveness estimates but did not consider the use of US alone for surveillance.[16–18] A recent study of HCC surveillance in the United Kingdom comparing periodic surveillance with combined AFP/US to strategies using AFP or US alone in alcoholic, HBV-related and HCV-related cirrhosis found that semiannual AFP/US surveillance was most effective but exceeded the typical willingness-to-pay threshold in the U.K. (£30,000/QALY).[19] In this population, a novel “AFP triage” strategy, in which elevated AFP (>20 ng/ml) triggered a diagnostic US, captured much of the clinical benefit of surveillance at a reasonable cost. We did not consider this strategy because an elevated AFP is typically evaluated with CT or MRI in the United States. However, our results suggest that US alone would be a similarly efficient strategy in the United States.

This analysis has several limitations. Because the performance of imaging tests under specific conditions is not described in published studies, we assumed that test characteristics are independent of patient characteristics and tumor size. The preferred strategy may differ if a test consistently performs poorly in certain subgroups, such as in patients with obesity. Similarly, because of methodological differences in published imaging studies, the sensitivities and specificities of US, CT, and MRI utilized in this study may refer to tumors of different sizes. Whereas MRI studies typically incorporate missed subcentimeter lesions into the sensitivity calculations, no lesion this small is detected by US in any study. However, our findings did not differ when each test was assigned perfect test characteristics in sensitivity analyses. Our model was limited by the lack of published data on certain parameters, such as the proportion of small HCCs treated with curative intent, but surveillance remained cost-effective even when these parameters were varied widely in sensitivity analyses. The actual costs of surveillance may be underestimated if clinical practice deviates significantly from our model assumptions.

The risk of HCC varies among the different etiologies of cirrhosis, although the precise risk for some etiologies is not well defined. Surveillance of cirrhotic populations with a relatively low risk of HCC, such as patients with primary biliary cirrhosis, appears justified by our finding that surveillance remains cost-effective even with an annual incidence of cancer as low as 0.8%. However, if the estimated incidence of HCC in these populations is less than 2.2%, annual US surveillance rather than semiannual may be preferable. Because our natural history parameters derive from Western populations with mixed etiologies of cirrhosis and our cost data is solely U.S. based, the cost-effectiveness estimates may differ in specific cirrhotic populations and in other countries.

The results of our study predict that surveillance for early HCC will improve clinical outcomes. Our findings support recent AASLD guidelines recommending surveillance with US alone. While the preferred strategy may vary in specific situations, we found that semiannual US is both effective and cost-effective for routine surveillance for HCC in cirrhosis.

Acknowledgments

Financial support: K24DK078772 and T32DK007191

Abbreviations

HCC	hepatocellular carcinoma
US	ultrasound
CT	computed tomography
QALY	quality-adjusted life year
AFP	alphafetoprotein
MELD	Model for End-Stage Liver Disease
MRI	magnetic resonance imaging
QALE	quality-adjusted life expectancy
ICER	incremental cost-effectiveness ratio

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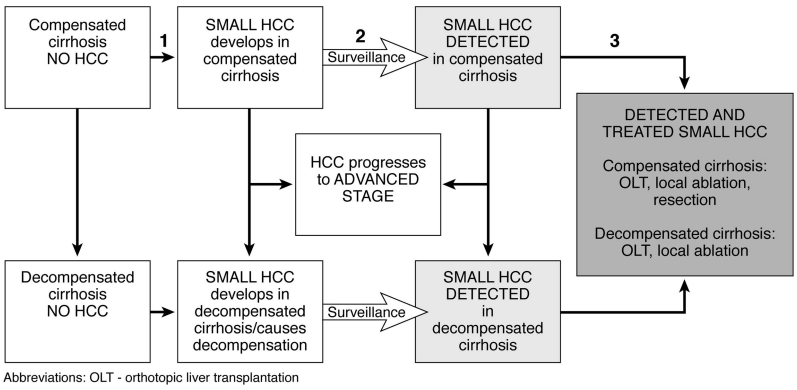

Figure 1.

Simplified schematic of Markov health states. In each cycle, individuals may remain in the same health state, transition to the following state, or die from liver disease or unrelated causes. For example, transition 1 reflects cancer incidence; transition 2 is determined by the sensitivity of the surveillance modality; and transition 3 is the proportion of treatment-eligible tumors. Best available data were used to determine transitions. The grey boxes represent the possible benefit of surveillance: detection and treatment of small HCC.

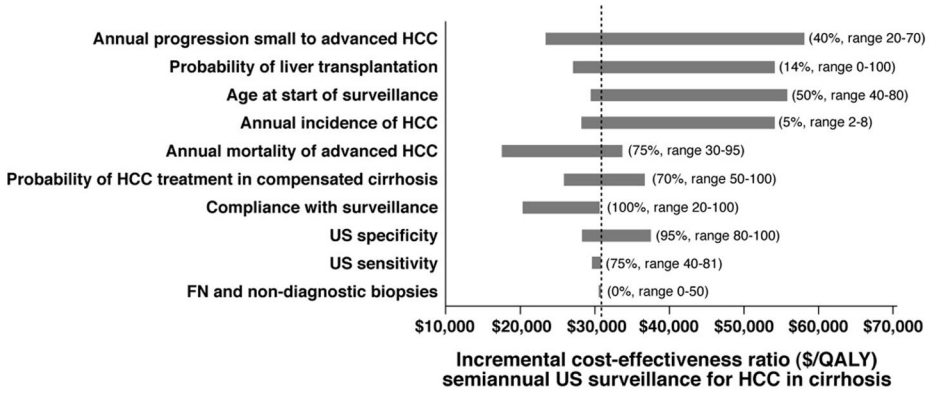

Figure 2.

Sensitivity analysis. The effect of varying selected model variables on the ICER of semiannual US surveillance. The values in parentheses are the baseline values for each variable and the plausible range tested in sensitivity analyses. The dashed line indicates the ICER in the base case. The bars show the variability of the ICER caused by changes in the indicated variable, all other variables held constant.

Table 1

Model Variables: Baseline Values and Ranges Used in Sensitivity Analyses

Natural history and treatment-related prognosis		
Compensated cirrhosis-related prognosis[19]		
10-year survival	60%	36%–80%
Adjusted annual excess mortality	0.04	0.016–0.08
Decompensated cirrhosis-related prognosis[19–21]		
2-year survival	50%	47%–63%
Adjusted annual excess mortality	0.28	0.18–0.30
Annual transition of compensated to decompensated cirrhosis[19]	5%	3%–8%
Annual incidence of HCC[4–6,23]	5%	2%–6%
Annual transition from small to large HCC[25, 28]	40%	20%–70%
Annual mortality from large untreated HCC[49, 50]	75%	35%–95%
Liver transplant prognosis[16, 41, 42]		
Perioperative mortality	4.3%	2.3%–6.3%
5-year survival	70%	65%–80%
Hepatic resection prognosis[41,43–45]		
Perioperative mortality	3.9%	3.7%–4.5%
5-year survival	44%	38%–51%
Local ablative therapy (radiofrequency ablation) prognosis[15, 46]		
Perioperative mortality	0.3%	0%–1.8%
5-year survival in compensated cirrhosis	46%	32%–68%
5-year survival in decompensated cirrhosis	31%	27%–40%
Surveillance test characteristics, *%*		
AFP sensitivity[37, 38]	60	40–65
AFP specificity	87	63–94
US sensitivity[29–33]	75	40–81
US specificity	95	80–100
Triple-phase CT scan sensitivity[17,29,30,33–36]	85	50–94
Triple-phase CT scan specificity	90	80–96
MRI sensitivity[33, 39, 40]	88	54–90
MRI specificity	87	82–88
Costs, *US$* (Medicare, National Impatient Sample)[10, 52, 53]		
AFP	$31	20–40
US	185	120–300
Abdominal CT scan	640	390–900
Abdominal MRI	1400	900–1700
Imaging-guided liver biopsy	614	300–1400
Follow-up evaluation for false-positive tests	1200	600–2400

Orthotopic liver transplant	145,000	50,000–200,000
Annual cost after liver transplant	12,000	8000–20,000
Hepatic resection	35,000	15,000–70,000
Outpatient percutaneous radiofrequency ablation	3000	2500–10,000
Annual cost for compensated cirrhosis	1000	200–2000
Annual cost for decompensated cirrhosis	15,000	5000–30,000
Annual cost of advanced HCC	35,000	15,000–70,000
Quality-of-life weights[52–54]		
Compensated cirrhosis	0.8	0.6–1.0
Decompensated cirrhosis	0.65	0.5–0.8
Advanced HCC	0.25	0.1–0.4

Table 2

Costs, QALE, and ICERs for Alternative HCC Surveillance Strategies

Surveillance strategy	QALE, *y* (undiscounted)	QALE, *y* (discounted)	Costs, *US$* (discounted)	ICER
No surveillance	7.28	5.97	26,170	
Annual US	7.84	6.35	34,161	21,200
Annual CT scan	7.94	6.41	39,087	*a*
Annual MRI	7.95	6.42	45,830	*a*
Semiannual US	7.99	6.45	37,272	30,700
Semiannual AFP/US	8.04	6.48	39,552	73,500
Semiannual CT scan	8.06	6.50	45,185	331,800

[a] Annual CT and MRI are dominated by semiannual ultrasound, which is both a more effective and less costly strategy.

Table 3

Clinical Impact and Resource Use of Semiannual Ultrasound Surveillance in a Cohort of 10,000 Cirrhotic Patients Over 30 Years

Outcomes	Value
Number of surveillance tests completed	184,354
Number of small HCC detected	3179
Number of US needed to detect one small HCC	58
Cost per small HCC detected (*US$*)	117,247
Cost per small HCC detected and treated (*US$*)	179,865
QALE gained per treated small HCC (*Y*)	3.45