

Cost-Effectiveness of the Baveno VI Criteria Compared With Endoscopy for High-Risk Varices in Patients With Child-Pugh A Cirrhosis



Elena Pizzo,^{1,*} Tuba Saygı n Avşar,^{1,*} Juan G. Abralde s,² Joan Genesca,^{3,4} and Emmanuel A. Tsochatzis⁵

¹Department of Applied Health Research, University College London, London, United Kingdom; ²Division of Gastroenterology, Liver Unit, University of Alberta, Edmonton, Canada; ³Liver Unit, Digestive Diseases Division, Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca, Vall d'Hebron Barcelona Hospital Campus, Universitat Autònoma de Barcelona, Barcelona, Spain; ⁴Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Instituto de Salud Carlos III, Madrid, Spain; and ⁵University College London Institute for Liver and Digestive Health, Royal Free Hospital and University College London, London, United Kingdom

Cost-effectiveness of the Baveno VI criteria compared to endoscopy for high-risk varices in patients with cirrhosis Child A

What is the most cost-effective approach for identifying high risk varices?

Baveno VI criteria: Annual screening and targeted endoscopy for patients with platelet count < 150,000 mm³ and/or LSM > 20 KPa

Endoscopy (EGD): Biannual screening with endoscopy for everyone

Cost-effectiveness analysis



Public healthcare payer perspective

Findings

0.16 additional QALYs are produced
Incremental cost is £326 (\$443.41) in the UK
Baveno VI criteria are cost-effective compared to EGD in the UK, Canada and Spain
Despite the small risk of false negatives, Baveno VI criteria could avoid unnecessary endoscopies, with significant cost savings

Elena Pizzo, Tuba Saygı n Avşar, Juan G. Abralde s, Joan Genesca, Emmanuel A. Tsochatzis
e.tsochatzis@ucl.ac.uk

Clinical Gastroenterology and Hepatology

BACKGROUND & AIMS:

Although upper gastrointestinal endoscopy (EGD) remains the gold standard for detecting varices in cirrhosis, the Baveno VI criteria proposed a combination of transient elastography and platelet count that could rule out high-risk varices, therefore sparing the need for an endoscopy, with significant potential cost savings. We performed a cost-effectiveness analysis of the Baveno VI criteria compared with EGD in the diagnosis of high-risk varices in cirrhosis.

METHODS:

We built an analytical decision model to estimate the cost and benefits of using the Baveno VI criteria compared with EGD in patients with Child-Pugh A cirrhosis. The analysis was performed from the UK National Health Service perspective, over 1, 5, and 20 years. A Markov model was populated with data from published evidence. Outcomes were measured in terms of quality-adjusted life years (QALYs) and avoided deaths. The analyses were repeated for Canada and Spain, using relevant cost inputs.

*Authors share co-first authorship.

Abbreviations used in this paper: cACLD, compensated advanced chronic liver disease; EBL, endoscopic band ligation; EGD, endoscopy; HRV, high-risk varices; ICER, incremental cost-effectiveness ratio; LSM, liver stiffness measurement; NHS, National Health Service; NMB, net monetary benefit; NSBB, nonselective β -blocker; QALY, quality-adjusted life year; WTP, willingness to pay.

Most current article

© 2024 The Author(s). Published by Elsevier Inc. on behalf of the AGA Institute. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1542-3565

<https://doi.org/10.1016/j.cgh.2024.05.012>

RESULTS:

The Baveno VI criteria were cost effective compared with endoscopy in all analyses. For 1000 patients, they produced 0.16 additional QALYs at an incremental cost of £326 (\$443.41) over 5 years, resulting in an incremental cost of £2081 (\$2830) per additional QALY gained. The incremental net monetary benefit of Baveno VI compared with EGD was £2808 (\$3819) over 5 years per patient. Baveno VI criteria also were cost effective in Canada and Spain. Deterministic and probabilistic sensitivity analysis supported these findings.

CONCLUSIONS:

The findings demonstrate that the Baveno VI criteria are cost effective, suggesting that they should be considered for widespread implementation on the basis of safety, appropriateness, and economic grounds.

Keywords: Elastography; Platelets; Economic Evaluation; Decompensation; Portal Hypertension.

Liver cirrhosis is the most common complication of chronic liver diseases and can be classified into 2 distinct prognostic phases: a preliminary asymptomatic phase, termed *compensated cirrhosis*, that can progress to decompensated cirrhosis at a rate of 5% to 7% per year.^{1,2} The term *compensated advanced chronic liver disease* (cACLD) has been proposed to stratify asymptomatic patients based on their risk of developing liver-related events and has introduced the use of noninvasive fibrosis tests into risk stratification.^{3,4} Portal hypertension reflects the structural and functional changes that characterize liver cirrhosis. The development of varices commonly is the first manifestation of clinically significant portal hypertension and is a hallmark in the natural history of cirrhosis.⁵ The diagnosis of varices, especially large varices, defined also as high-risk varices (HRV), has a prognostic importance in patients with cirrhosis. In the past decades, a strong effort was made to assess the risk of varices noninvasively, to establish combined clinical criteria to avoid unnecessary endoscopies on one side, without missing HRV on the other. The Baveno VI Consensus has proposed that in the scenario of a cACLD patient with Child-Pugh A cirrhosis, a platelet count $>150,000/\text{mm}^3$ and a liver stiffness measurement (LSM) <20 kPa, the endoscopy screening safely can be avoided.^{3,6} Moreover, the expanded Baveno VI criteria have been proposed to spare a higher number of endoscopies through an optimized cut-off platelet value ($>110,000/\text{mm}^3$) and LSM value (<25 kPa). The performance of the expanded Baveno VI criteria potentially could avoid double the number of endoscopies compared with the Baveno VI criteria, with a risk of missing HRV in 1.6% of patients within the criteria and 0.6% in the overall cohort of 925 analyzed patients.⁷ Both criteria were validated in large cohorts of patients with compensated cirrhosis of different etiologies.^{8,9}

The cost effectiveness of these criteria has not been assessed to date. We therefore investigated the cost-effectiveness analysis of the Baveno VI criteria compared with endoscopy (EGD) in the diagnosis of high-risk varices in patients with cACLD/Child-Pugh A cirrhosis.

Materials and Methods

The Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) was followed in this study.¹⁰ A hypothetical cohort of 1000 patients with Child-Pugh A cirrhosis was modeled. In the intervention arm, patients were tested annually using the Baveno VI criteria to decide whether they required an EGD. After a negative test (defined as platelet count $>150,000/\text{mm}^3$ and LSM values <20 kPa), they were assumed to be retested after 1 year; if the test result was a false negative they could experience bleeding and potentially die. Patients with a platelet count $<150,000/\text{mm}^3$ and/or LSM value >20 kPa were underwent endoscopy. Patients with high-risk varices on endoscopy were treated with a nonselective β -blocker (NSBB) or had a band ligation (endoscopic band ligation [EBL]). In the comparator arm, all patients received endoscopy, and patients who did not have high-risk varices were invited to a retest in 2 years, based on the current guidelines.¹¹ During this time, they could experience bleeding and die.

Economic Model

We built an analytical decision model to estimate the cost and benefits of using the noninvasive Baveno VI criteria compared with the standard of care (EGD) in patients with Child-Pugh A compensated cirrhosis, consisting of a decision tree and a Markov state-transition model. A short-run decision analytical model (Figure 1) was created to assess costs and clinical outcomes within 1 year from diagnosis and subsequently was used to distribute a theoretical cohort of patients into a long-run Markov state-transition model, to estimate the expected costs and outcomes over a time horizon of 5 years and 20 years using cycles of 1 year (Figure 2).

Model Inputs

Probabilities on the prevalence of varices, liver disease progression, variceal bleeding, and death and

transition probabilities over time were taken from available evidence and are summarized in [Table 1](#).

We populated the model using data from the most recent published evidence.^{7,12,24,25}

We assessed the costs of the diagnostic interventions (Baveno VI criteria and EGD), the costs to treat varices (NSBBs or EBL), and the costs of treatments associated with false-negative results or adverse events in both options using the unit costs from the National Schedule Reference costs in 2018¹⁶ ([Table 1](#)). All the costs were in 2022 UK£, inflated as necessary. The key outcomes also were reported, in 2022 US\$, using Bank of England conversion rates (1 Great Britain Pounds = 1.36 US\$).¹⁹ The unit costs for Canada and Spain were reported in 2023 Euros and converted into US\$ for comparison, using Bank of England rates (1 Euros = 1.05 US\$).¹⁹

The cost of using the Baveno VI criteria was £67 per patient and the cost of EGD was £411 per patient (range, £400–£421).²¹ The cost of NSBBs for 1 year was estimated at £29.66 (range, £26.69–£32.63) (assuming a treatment with 12.5 mg/d of carvedilol).²² The cost of EBL was estimated at £5525 per person based on the unit cost of £1381 (range, £1064–£1644), assuming 4 sessions were performed in 1 year.¹⁶ The cost of treating variceal bleeding was estimated at £5435 per person, including hospital admission.²¹

Modeling Assumptions

We made some modeling assumptions owing to the absence of data or computational practicalities. It was assumed that patients could experience variceal bleeding once. No patient had hepatocellular carcinoma. No relationship was assumed between bleeding and non-liver-related mortality risk. For model simplicity, we also assumed that a patient would keep taking β -blockers for the rest of their life and would not be tested again unless they experienced bleeding, whereas patients on band ligation would receive band ligation every 2 years and be tested every year. Additionally, in the base-case, it was assumed that no patient would progress to Child-Pugh B state or develop hepatocellular carcinoma.

Outcomes and Analyses

Outcomes were measured in terms of accurate diagnosis, and quality-adjusted life years (QALYs), which combine length of life and quality of life, based on National Institute for Health and Care Excellence recommendations.^{17,23} The analysis was performed adopting the UK National Health Service (NHS) and Personal Social Services perspective. Additionally, the analysis was repeated from the health care payer perspective in Canada and Spain, updating the unit costs included in the model ([Supplementary Table 1](#)).

The time horizon was 5 years, reflecting the disease progression and average life expectancy of the patients

What You Need to Know

Background

The Baveno VI criteria (combination of platelet count and liver stiffness) can be used to spare endoscopies for variceal screening in Child-Pugh A cirrhosis, however, their cost effectiveness has not been established.

Findings

We found that the use of the Baveno VI criteria is cost effective compared with upper gastrointestinal endoscopy, with consistent results across all sensitivity analyses, in 3 different countries.

Implications for patient care

This study shows the cost effectiveness of these criteria and makes the argument for a more widespread implementation.

affected by cirrhosis. We also estimated the outcomes over 1 year and 20 years. All costs after the first year were discounted at an annual rate of 3.5%.²³

The cost effectiveness of the Baveno VI criteria compared with EGD was measured in terms of the incremental cost per QALY gained (ICER), and net monetary benefits (NMBs). NMBs were calculated as the mean QALYs per patient accruing to that treatment multiplied by the maximum willingness to pay (WTP) for a QALY (the cost-effectiveness threshold) minus the mean cost per patient for the treatment. The equation is as follows:

$$QALY \text{ gains per person} \times WTP \text{ per QALY} - \text{cost per person}$$

WTP per QALY was £20,000, based on the national guidelines in the United Kingdom.²³ We also conducted a budget impact analysis to see the funding implications of introducing the Baveno VI criteria to the NHS, based on 28,000 people living with compensated cirrhosis in the United Kingdom with an incidence of 35.9 new cases every 100,000 in 2017²⁶ and 7000 new cases every years.

Additionally, scenario analyses were conducted to estimate the impact of changes in the cost-effectiveness outcomes, changing the probability of HRV and using the expanded Baveno VI criteria for the diagnosis of high-risk varices as described in the [Supplementary Table 1](#).⁷

Sensitivity Analyses

We performed several sensitivity analyses to explore the uncertainties around our estimates. In the univariate sensitivity analyses we varied the model inputs, one at a time within the ranges listed in [Supplementary Table 2](#) to understand which model inputs have significant impacts on the cost-effectiveness estimates. The prevalence of HRV was paid specific attention, exploring how the

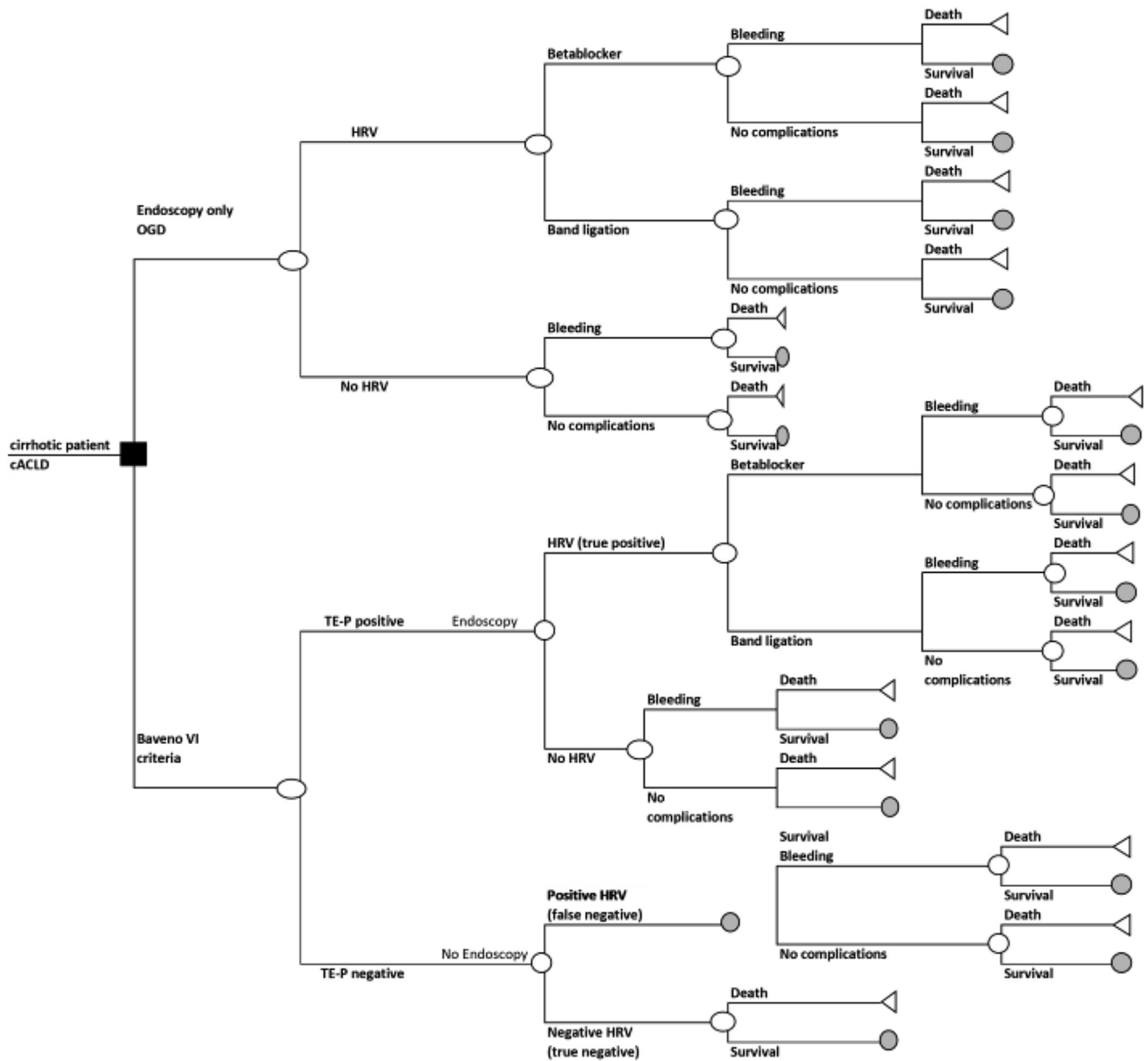


Figure 1. Decision tree. A decision tree was used to calculate test outcomes and costs within the first year, and to distribute patients to initial health states in the Markov state transition model for the long-term simulation. cACLD, compensated advanced chronic liver disease; HRV, high-risk varices; EGD, esophagogastroduodenoscopy; TE-P, transient elastography - platelet count (Baveno VI criteria).

model findings change when it increased substantially up to 50%. Further sensitivity analyses were performed to estimate cost effectiveness when people who tested negative are screened every 2 years in both the Baveno VI and EGD arms and when 50% of people in the EGD arm underwent Fibroscan (Echosens, Hong Kong) before endoscopy as part of their routine clinical care. Additionally, the impact of incorporating the probability of transition to the Child-Pugh B state into the model also was estimated.

We also undertook a probabilistic sensitivity analysis to determine the impact of the uncertainty surrounding the model input parameters.²³ Distributions were assigned to each parameter value and a random value from the corresponding distribution was selected. As

recommended in the literature, Dirichlet and beta distributions, which were used for the probabilities and the health utilities and gamma distributions, were used for the cost inputs.²⁶

The probabilistic sensitivity analysis generated an estimate of the mean cost and mean QALYs, along with the 95% CI. Monte Carlo simulation was repeated until model convergence was achieved with 10,000 iterations, and the results for each simulation were recorded. The proportion of times the intervention was cost effective was calculated for a range of values of the WTP for a QALY. The results are summarized using cost-effectiveness acceptability curves. The mean cost, QALYs, and NMB for each treatment were calculated from the 10,000 simulations.

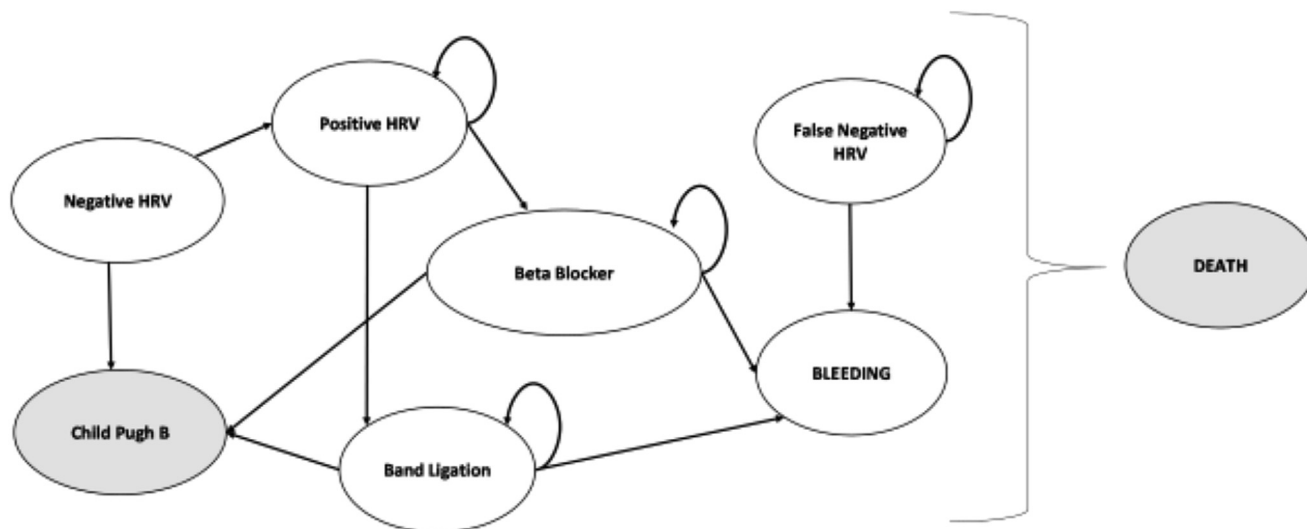


Figure 2. Markov model illustration. A Markov model was used to simulate the costs and outcomes over 5 years and the patient’s lifetime. The state transition model simulated disease history as annual transitions between different health status. We assumed Child-Pugh B and death were absorbing states because after this the diagnostic intervention was no longer needed. The Child-Pugh B state was considered only in the 1-way sensitivity analysis. HRV, high-risk varices.

Table 1. Input Parameters

Input parameter	Baseline	95% CI	Distribution	Reference
Probabilities				
Probability of HRV	0.10	0.05–0.20	Dirichlet	Augustin, 2017 ⁷
Meeting Baveno VI criteria	0.29	0.20–0.43	Dirichlet	Estimates based on the prevalence of HRV, sensitivity and specificity values
Sensitivity	0.97	0.95–0.98	Dirichlet	Stafylidou 2019 ¹²
Specificity	0.32	0.26–0.39	Dirichlet	Stafylidou 2019 ¹²
PPV	0.14	0.25–0.28	Dirichlet	Estimates based on the prevalence of HRV, sensitivity and specificity values
NPV	0.99	0.95–0.98	Dirichlet	D’Amico 2017 ¹³
Transition from stage A to B (per year – sensitivity analysis)				
Probability of β -blocker treatment	0.8	0–1	Dirichlet	Per NICE guidelines ¹¹
Probability of band ligation treatment	0.2	0–1	Dirichlet	Per NICE guidelines ¹¹
Bleeding after missed HRV	0.10		Dirichlet	D’Amico 2017 ¹³
Bleeding after β -blocker	0.068	0–1	Dirichlet	Gluud 2012 ¹⁴
Bleeding after band ligation	0.043	0–1	Dirichlet	Gluud 2012 ¹⁴
Death after bleeding	0.022	0.3–4.7	Dirichlet	Conejo 2018 ¹⁵
Death owing to other reasons	0.143	0–1	Dirichlet	Imperiale 2007 ¹⁶
Discount factor	0.035	0–1	Dirichlet	NICE 2013 ¹⁷
Utilities				
Compensated cirrhosis, band ligation	0.53	0.46–0.81	Beta	Mahady 2012 ¹⁸
Compensated cirrhosis, β -blockers	0.55	0.46–0.81	Beta	Mahady 2012 ¹⁸
Bleeding episode	0.400	0.14–0.66	Beta	Wells 2004 ¹⁹
Negative for HRV	0.62	0.46–0.81	Beta	Mahady 2012 ¹⁸
People with HRV not treated	0.60	0.46–0.81	Beta	
Child–Pugh B	0.51	0.46–0.81	Beta	Younossi 1999 ²⁰
Costs, 2021/2022 prices				
Elastography	£67.81	£47.46–£88.15	Gamma	NSRC 2019 ^{a21}
Platelets	£3.13	£2.19–£4.07	Gamma	NSRC 2019 ^{a21}
Endoscopy	£411.00	£400–£421	Gamma	NSRC 2022 ²²
β -blocker, 1 year	£29.66	£26.69–£32.63	Gamma	BNF 2022 ²³
Band ligation, 4 sessions	£5524	£4440–£6860	Gamma	NSRC 2019 ^{a21}
Variceal bleeding, admission	£5435	£2012– £6827	Gamma	NSRC 2022 ²²

BNF, British National Formulary; HRV, high-risk varices; NA, not available; NICE, National Institute for Health and Care Excellence; NPV, negative predictive value; NSRC, national schedule of reference costs; PPV, positive predictive value; HRV, high risk varices.

^aInflated to 2021/2022 prices using National Health Service inflation indices.

Results

Using base-case values, the Baveno VI criteria were estimated to produce more health benefits (0.0001 QALYs) at a lower cost (-£44.06; \$59.92) in the first year (Table 2). Thus, Baveno VI was found dominant over EGD in this analysis. Baveno VI was cost effective in the long term because it produced 1.84 QALYs over 5 years and 2.91 QALYs over 20 years, compared with 1.68 and 2.69 QALYs gained with EGD, respectively. Baveno VI was associated with a cost of £1734 (\$2358) over 5 years and £3134 (\$4262) over 20 years, while the cost of surveillance with EGD was estimated as £1408 (\$1915) over 5 years and £2716 (\$3286) over 20 years (Table 2). Thus, the incremental cost (ICER) per QALY was £2081 (\$3819) in the first 5 years and £3172 (\$5178) in 20 years, indicating that the Baveno VI option was highly cost effective compared with OGD at a WTP of £20,000 per QALY.

The budget impact analysis showed that the cost of EGD would be £3,341,148 (\$4,541,961) in the first year, based on 7000 new cases every year, assuming all new cases of cirrhosis are screened for varices. If the same people were screened with the Baveno VI criteria, the cost would have been £3,032,724 (\$4,124,505), with a savings of £308,424 (\$419,457) for the NHS in the first year alone.

The scenario analyses showed that using the Baveno VI criteria was cost effective when the prevalence of HRV was 0.20 and 0.05, with ICER per QALY estimates of £1828 (\$2486) and £2293 (\$3119), respectively (Supplementary Table 3). The expanded Baveno VI criteria also were cost effective with an ICER of £639 (\$869) per QALY in the 5-year estimates.

The cost-effectiveness findings for Canada and Spain were comparable with the UK estimates. Baveno VI was found to be dominant over EGD in Canada in the analysis with a 1-year time horizon. ICER per QALY estimates were €3535 (\$3712) over 5 years and €4610 (\$4841) over 20 years (Supplementary Table 4). Thus, the Baveno VI criteria is a cost-effective option in Canada. Similarly, in Spain, Baveno VI was dominant over EGD in 1 year. ICERs were estimated as €1966 (\$2064) over 5 years and as €2225 (\$2336) over 20 years per QALY (Supplementary Table 5).

Sensitivity Analyses

The results of the 1-way sensitivity analysis showed that the Baveno VI criteria would remain cost effective when the key parameters were varied (Figure 3 and Supplementary Table 6). The parameters with the greatest impacts on the outcomes were the sensitivity and specificity of the Baveno VI criteria and the impact on health utilities of untreated varices that require treatment. Varying the prevalence of HRV up to 50% did not change the findings because ICER per QALY

estimates remained very low for both the Baveno VI and expanded Baveno criteria (Supplementary Table 7).

When people who tested negative were screened every 2 years in both the Baveno VI and EGD arms instead of annual screening in the Baveno arm, the cost difference between Baveno VI and EGD was reduced from £326.04 to £29.22, and the incremental QALY gains per patient were reduced from 0.1567 to 0.0462 over 5 years (Supplementary Table 8). The ICER per QALY was reduced from £2080 to £633. In another analysis, it was assumed that 10% of the EGD patients would undergo Fibroscan in addition to endoscopy, and this reduced the ICER per QALY to £1680 (Supplementary Table 9). Similarly, when a small proportion of patients (0.05) transitioned to Child-Pugh B every year, the ICER per QALY was reduced from £2080 to £1639 because the cost difference per patient was reduced from £326 to £277 while incremental QALY gained per patient increased from 0.1567 to 0.1691 over 5 years (Supplementary Table 10).

The probabilistic sensitivity analysis showed that the Baveno VI criteria produced more QALYs (0.14; 95% CI, 0.11–0.17) at a higher cost (£259; 95% CI £65–£449) over 5 years, with an ICER of £1888 per additional QALY gained (Supplementary Table 11). Uncertainty around the estimates are shown in Figure 4. The Baveno VI criteria were cost effective compared with EGD in all 10,000 iterations and were dominant over EGD in 2%.

The cost-effectiveness acceptability curve shows that the Baveno VI criteria had 100% probability of being cost effective at a WTP of £6000 per QALY (Supplementary Figure 1).

Discussion

In this study, we have shown that the use of the noninvasive Baveno VI criteria are cost effective compared with the use of EGD for screening for high-risk varices in patients with Child-Pugh A cirrhosis both at 1 year and in the longer-term evaluations. The Baveno VI criteria produced an additional 0.16 QALYs per patient at an incremental cost of £326, resulting in an ICER of £2081 per QALY over 5 years. This is substantially lower than the standard thresholds used by the National Institute for Health and Care Excellence (£20,000–30,000 per QALY) and by most health care services in high-income countries. Importantly, the Baveno VI remained cost effective in all the sensitivity analyses. This study assessed the cost effectiveness of these criteria and makes the argument for more widespread implementation. Importantly, we showed that the criteria were cost effective in 3 different countries/health care systems.

The Baveno VI criteria have a very high specificity, thus minimizing the proportion of patients with false-negative results. Even if HRV are missed, retesting happens within 12 months, thus reducing the probability of variceal bleeding. The use of noninvasive techniques results in

Table 2. Deterministic Model Outcomes

1-year outcomes	Endoscopy	Baveno VI	Incremental
Deaths, n	143	143	0.0021
LYs per patient	0.856881	0.8569	0.0000
QALYs per patient	0.52	0.52	0.0001
Cost per patient	£477.31 \$649.14	£433.25 \$589.22	-£44.06 -\$59.92
Net monetary benefit	£10,020.06 \$13,627.28	£10,066.50 \$13,690.44	£46.44 \$63.16
ICER per QALY			Dominant
5-year outcomes			
Deaths, n	539	538	-0.6267
LYs per patient	3.0396	3.0415	0.0018
QALYs per patient	1.6839	1.8406	0.1567
Cost per patient	£1407.82 \$1914.63	£1733.85 \$2358.04	£326.04 \$443.41
Net monetary benefit	£32,269.85 \$43,886.99	£35,077.82 \$47,705.83	£2807.97 \$3818.84
ICER per QALY			£2080.63 \$2829.66
20-year outcomes			
Deaths, n	956	955	-0.9579
LYs per patient	4.85	4.86	0.0108
QALYs per patient	2.69	2.91	0.2262
Cost per patient	£2416.24 \$3286.09	£3133.86 \$4262.05	£717.62 \$975.96
Net monetary benefit	£51,319.91 \$69,795.08	£55,126.99 \$74,972.70	£3807.08 \$5177.62
ICER per QALY			£3172.02 \$4313.94

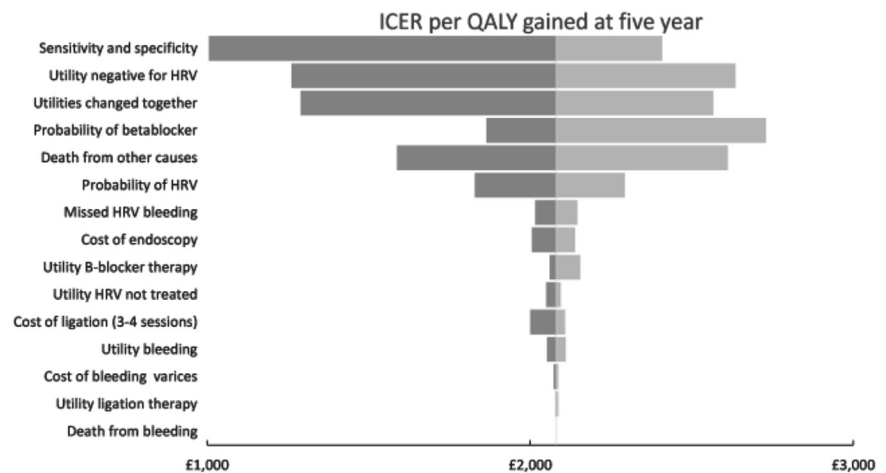
ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year.

significant efficiency improvement for health care services and redirection of freed capacity to reducing endoscopy waiting lists. This became even more apparent during the coronavirus disease-2019 pandemic, when access to EGD became restricted because it was classed an aerosol-generating procedure that could increase viral transmission. It also reduces anxiety for patients and the discomfort of an invasive procedure. It should be

mentioned, however, that sparing endoscopies could result in missing the incidental detection of esophageal and gastric cancers, particularly in patients with higher risk, such as those who misuse alcohol.

In recent years, the focus slowly has been shifting in patients with cirrhosis and portal hypertension from prevention of variceal bleeding to prevention of decompensation. Based on results from the β blockers to

Figure 3. Tornado diagram of the deterministic sensitivity analysis. This figure shows how ICER per QALY estimates changed when parameters changed discretely. The parameters are presented in order of the largest to smallest impact on the final results (eg, varying the sensitivity and specificity parameter has the highest impact on the ICER, while changing the probability of death from bleeding has little impact on the ICER). HRV, high-risk varices; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.



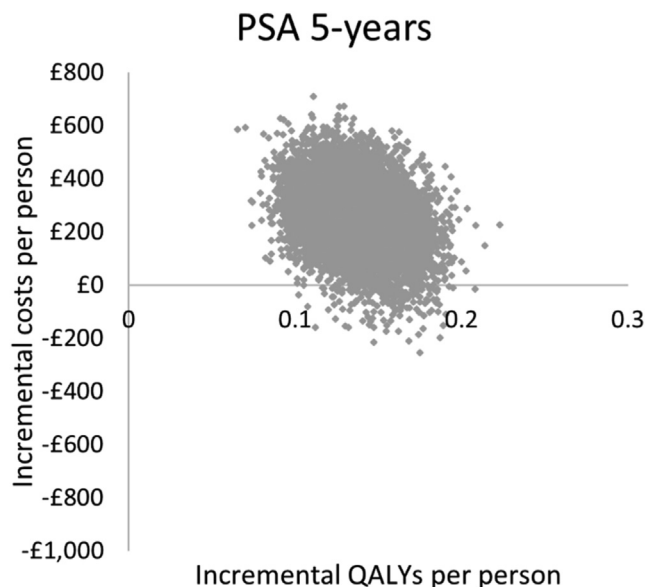


Figure 4. Probabilistic sensitivity analysis (PSA) scatterplot. The figure demonstrates 10,000 simulated iterations of the incremental cost per quality-adjusted life year (QALY) gained of TE-P in the diagnosis of varices. The results show that the higher proportion of results are in the quadrant where an increment in costs is associated with a QALY gain and most of the results are under the £20,000/QALY threshold line, therefore there is a high probability that the TE-P is acceptable. TE-P, transient elastography - platelet count (Baveno VI criteria).

prevent decompensation of cirrhosis in patients with clinically significant portal hypertension randomized trial,²⁷ a more liberal use of NSBBs has been proposed to include all patients with clinically significant portal hypertension rather than patients with high-risk varices.⁴ Larger ongoing trials will determine if this is a valid strategy.²⁸ Even if noninvasive criteria are used to diagnose clinically significant portal hypertension, a significant number of patients will have indeterminate results and still might require screening endoscopies.²⁹ Therefore, the use of the Baveno VI criteria will continue to be relevant in a significant proportion of patients with cACLD. Depending on the expected prevalence of high-risk varices, which in turn depends on the method used for diagnosing cACLD (noninvasive testing vs cross-sectional imaging or biopsy), the use of the expanded Baveno criteria still was cost effective and can be used to decrease further the number of endoscopies performed. Finally, the annual performance of elastography as part of the Baveno VI criteria can add significant prognostic information in patients with cACLD based on the magnitude of annual liver stiffness change.

This study assessed the cost utility of the Baveno VI criteria compared with EGD. We have taken into account the entire diagnostic and treatment pathway of cACLD and provided extensive sensitivity analyses; all of these have shown unequivocally the superiority of the Baveno VI criteria in all scenarios.

The study had some limitations. The first limit was that the costs in the analysis were based on the NHS

reference costs and not assessed using a microcosting approach, but it would have been extremely complex to analyze the costs in such detail. We did not take into account the risk of death during the EGD because this is very rare and not likely to affect the results, but incorporating that would increase the cost effectiveness of the Baveno VI criteria further. The model assumed no patient would develop intolerance to β -blockers and would require ligation. However, because the risk of intolerance was the same in both the no-Baveno and the Baveno arms, this would not change the model outputs. We also did not factor in the small failure rate of Fibroscan, particularly in obese patients. Additionally, this study was undertaken from the sole perspective of the public health care payer and did not include the costs for patients, families, or caregivers to undergo the diagnostic tests and the resulting procedures. When these costs also are considered, it is likely that the Baveno VI criteria would produce more favorable cost-effectiveness outcomes.

Another consideration was the limited data on health utilities among people with cirrhosis. We used the best available evidence based on clinical expertise. The sensitivity analyses showed that utilities had a substantial impact on the ICER per QALY estimates. However, the cost-effectiveness findings remained unchanged. Thus, the impact of this on the study's policy recommendation is negligible.

The economic model was designed based on current UK guidelines and UK-based cost data and most of the clinical parameters were obtained from UK-based studies. Some modeling assumptions may not hold in all clinical scenarios, which could influence the generalizability of results. The model assumption should be validated in other clinical settings. However, our analyses for Canada and Spain indicated that the findings are most likely applicable to most high-income countries and economies, given that clinical practice is similar. The model can be used to evaluate the cost effectiveness of Baveno VI criteria in similar settings after reparameterization.

In conclusion, this study has shown that the use of the Baveno VI criteria is a highly cost-effective option for screening of high-risk varices in patients with Child-Pugh A cirrhosis.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at <https://doi.org/10.1016/j.cgh.2024.05.012>.

References

1. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006;44:217-231.

2. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. *Lancet* 2014;383:1749–1761.
3. de Franchis R. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015; 63:743–752.
4. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - renewing consensus in portal hypertension. *J Hepatol* 2022; 76:959–974.
5. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. *N Engl J Med* 2010;362:823–832.
6. Maurice JB, Brodtkin E, Arnold F, et al. Validation of the Baveno VI criteria to identify low risk cirrhotic patients not requiring endoscopic surveillance for varices. *J Hepatol* 2016; 65:899–905.
7. Augustin S, Pons M, Maurice JB, et al. Expanding the Baveno VI criteria for the screening of varices in patients with compensated advanced chronic liver disease. *Hepatology* 2017;66:1980–1988.
8. Roccarina D, Rosselli M, Genesca J, et al. Elastography methods for the non-invasive assessment of portal hypertension. *Expert Rev Gastroenterol Hepatol* 2018;12:155–164.
9. Bai W, Abraldes JG. Noninvasive assessment oesophageal varices: impact of the Baveno VI criteria. *Curr Opin Gastroenterol* 2022;38:206–215.
10. Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *Int J Technol Assess Health Care* 2022;38:e13.
11. NICE. Cirrhosis in over 16s: assessment and management. 2016. Available at: <https://www.nice.org.uk/guidance/ng50>. Accessed June 17, 2024.
12. Stafylidou M, Paschos P, Katsoula A, et al. Performance of Baveno VI and expanded Baveno VI criteria for excluding high-risk varices in patients with chronic liver diseases: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2019; 17:1744–1755. e11.
13. D'Amico G, Morabito A, D'Amico M, et al. Clinical states of cirrhosis and competing risks. *J Hepatol* 2018;68:563–576.
14. Gluud LL, Krag A. Banding ligation versus beta-blockers for primary prevention in oesophageal varices in adults. *Cochrane Database Syst Rev* 2012;CD004544.
15. Conejo I, Guardascione MA, Tandon P, et al. Multicenter external validation of risk stratification criteria for patients with variceal bleeding. *Clin Gastroenterol Hepatol* 2018;16:132–139.
16. NSRC. National Schedule of Reference Costs year: 2017-18. In: All NHS trusts and NHS foundation trusts HD; 2019.
17. Drummond MF, Sculpher MJ, Claxton K, et al. *Methods for the economic evaluation of health care programmes*. Oxford University Press, 2015.
18. Mahady SE, Wong G, Craig JC, et al. Pioglitazone and vitamin E for nonalcoholic steatohepatitis: a cost utility analysis. *Hepatology* 2012;56:2172–2179.
19. Bank of England. Daily spot exchange rates; 2024.
20. Younossi ZM, Guyatt G, Kiwi M, et al. Development of a disease specific questionnaire to measure health related quality of life in patients with chronic liver disease. *Gut* 1999;45:295–300.
21. NSRC. National Schedule of Reference Costs year: 2020-21. In: Data ANtAft-H. 2022. Available at: <https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/>. Accessed June 17, 2024.
22. British National Formulary. BNF 76; September 2018-March 2019. 2019.
23. NICE. Guide to the methods of technology appraisal 2013. Available at: <https://www.nice.org.uk/process/pmg9>. Accessed June 17, 2024.
24. Imperiale TF, Klein RW, Chalasani N. Cost-effectiveness analysis of variceal ligation vs. beta-blockers for primary prevention of variceal bleeding. *Hepatology* 2007;45:870–878.
25. Wells C, Murrill W, Arguedas M. Comparison of health-related quality of life preferences between physicians and cirrhotic patients: implications for cost-utility analyses in chronic liver disease. *Dig Dis Sci* 2004;49:453.
26. Baio G, Dawid AP. Probabilistic sensitivity analysis in health economics. *Stat Methods Med Res* 2015;24:615–634.
27. Villanueva C, Albillos A, Genesca J, et al. β blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2019;393:1597–1608.
28. McPhail MJW, Patel VC, Carter B. Carvedilol in patients with compensated cirrhosis: the ongoing benefits of definitive randomised trials over meta-analysis in patients with small varices. *J Hepatol* 2023;79:e21–e23.
29. Pons M, Augustin S, Scheiner B, et al. Noninvasive diagnosis of portal hypertension in patients with compensated advanced chronic liver disease. *Am J Gastroenterol* 2021;116:723–732.

Correspondence

Address correspondence to: Elena Pizzo, PhD, Department of Applied Health Research, University College London, London, United Kingdom. e-mail: e.pizzo@ucl.ac.uk; or Emmanuel A. Tsochatzis, PhD, University College London Institute for Liver and Digestive Health, Royal Free Hospital and University College London, London, United Kingdom. e-mail: e.tsochatzis@ucl.ac.uk.

Acknowledgments

Elena Pizzo and Tuba Saygın Avşar were supported by the National Institute for Health and Care Research Applied Research Collaboration North Thames. Joan Genesca was supported in part by the Instituto de Salud Carlos III and cofunded by the European Union (ERDF/ESF, “Investing in your future”).

Author Contributions

Elena Pizzo, Tuba Saygın Avşar, and Emmanuel Tsochatzis made substantial contributions to conception and design, acquisition and curation of data, methodology, and analysis and interpretation of data; drafting, writing the article, and revising it critically for important intellectual content; and final approval of the version to be published. Juan Abraldes and Joan Genesca made substantial contributions to conception and design, acquisition of data, validation and interpretation of data; and final approval of the version to be published.

Conflicts of interest

These authors disclose the following: Joan Genesca has received consulting fees from Boehringer Ingelheim, speaking fees from Echosens, and travel expenses from Gilead and AbbVie; Juan G. Abraldes has received consulting fees from Boehringer Ingelheim, AstraZeneca, Novo Nordisk, 89Gilead, Salix.bio, Advanz, and Boston Pharmaceuticals, and holds research grants from Cook, Gilead, and Salix; and Emmanuel A. Tsochatzis has received consulting fees from Boehringer Ingelheim, Siemens, and NovoNordisk, and speaking fees from Echosens, NovoNordisk, and AbbVie. The remaining authors disclose no conflicts.

Funding

No funding received for this study.