

Title: An economic analysis of transjugular intrahepatic portosystemic covered stent shunt for variceal bleeding and refractory ascites in a Spanish setting

Authors: Rafael Bañares^{1,2,3}, Agustín Albillos^{4,5}, Mitesh Nakum⁶, Salvador Gea⁷, Angel Varghese⁸, William Green⁸

Affiliations:

¹ Servicio de Medicina de Aparato Digestivo. Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain.

² Universidad Complutense de Madrid, Madrid, Spain.

³ Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain.

⁴ Departamento de Gastroenterología y Hepatología, Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain.

⁵ Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain.

⁶ W L Gore & Associates Ltd, Newark, United States

⁷ W. L. Gore y Asociados, SL, Barcelona, Spain.

⁸ York Health Economics Consortium Ltd, York, United Kingdom.

Corresponding author

Name: Angel Varghese

Email address: angel.varghese@york.ac.uk

Address: Enterprise House, Innovation Way University of, York YO10 5NQ

Supplementary Material

Cost-effectiveness of transjugular intrahepatic portosystemic covered stent shunt for variceal bleeding and refractory ascites in a Spanish setting

Table of Contents

Title: An economic analysis of transjugular intrahepatic portosystemic covered stent shunt for variceal bleeding and refractory ascites in a Spanish setting	1
A: Treatment Costs	3
<i>TIPSS procedure costs</i>	3
<i>EBL treatment costs (Indication 1 – AVB)</i>	3
<i>LVP treatment cost (indication 2 – refractory ascites)</i>	4
B. Adverse Event Costs	5
<i>Shunt dysfunction</i>	5
<i>Variceal bleeding</i>	5
<i>Ascites</i>	6
<i>Hepatic Encephalopathy (HE)</i>	6
<i>Spontaneous Bacterial Peritonitis (SBP)</i>	7
C: Sensitivity and Scenario Analysis Inputs	8
<i>Scenario analysis – AVB (indication 1)</i>	13
D: Probabilistic Results	14
<i>Indication 1 (AVB)</i>	14
<i>Indication 2 (RA)</i>	14
References	16

A: Treatment Costs

TIPSS procedure costs

The cost breakdown and total cost associated with TIPSS treatment is detailed in Table S1 below.

TIPSS procedure consumables include antibiotics and general anaesthetic. 1g of Ceftriaxone is administered intravenously for surgical prophylaxis. Unit cost per 100 1 gram vials was €286.70 [1]. 100mg of propofol (general anaesthetic) was applied in the model.

According to expert opinion diagnostic procedure costs are applicable for both elective and non-elective cases. Repeat implantations are associated with 2 bed days in hospital, based on expert opinion. Technical failure of initial TIPSS application is associated with additional procedure time of 2 hours for all relevant HCPs involved.

Table S1: TIPSS procedural costs per person

	Units	Total cost	Source (units; costs)
Consumables			
All procedure consumables ^a	1.00	€4,019.44	KOLs; [2]
Diagnostic procedures			
Abdomen CT scan	0.80	€124.00	KOLs; [3]
Doppler ultrasound	1.00	€67.00	
Echocardiogram	0.50	€46.00	
Electrocardiogram	1.00	€150.00	
Healthcare professionals time: pre-procedure (units in hours)			
Hepatologist	0.17	€4.21	KOLs; [4]
Radiologist	0.17	€4.21	
Healthcare professionals time: procedure (units in hours)			
Radiologist	2.00	€50.54	KOLs; [4]
Radiologist trainee	2.00	€23.66	
Radiographer	2.00	€33.84	
Nurse	4.00	€96.92	
Anaesthetist	2.00	€50.54	
Hospital excess bed days			
Elective cases	2.00	€1,176.00	KOLs; [3]
Non-elective cases	5.00	€2,940.00	
Total costs (elective)		€5,851.99	
Total costs (non-elective)		€7,615.99	

^a Consumables include: VIATORR stent, TIPs kit, antibiotics, balloon catheter, X-ray, and propofol.

EBL treatment costs (Indication 1 – AVB)

The cost breakdown and total cost associated with EBL treatment is detailed in Table S2 below.

Everyone undergoing EBL was assumed to receive pharmaceutical treatment with either carvedilol or propranolol. Total cost was based on administering pharmaceuticals for 12 months. People on EBL treatment underwent four outpatient EBL sessions, 2 in the first month and 2 and in the second month, following the initial EBL session at first bleeding. People who did not suffer a further bleeding episode also received subsequent management with additional EBL sessions at 6, 12, and 24 months.

Table S2: Costs per person for people receiving endoscopic band ligation plus pharmaceuticals

	Dose/units	Total cost	Source (units; costs)
Pharmaceuticals (total costs per month)*			
Carvedilol	25 mg daily	€ 6.56	KOLs; [1]
Propranolol	40 mg daily	€ 1.23	
Endoscopic band ligation			
Outpatient EBL (follow up)	7	€ 4,689.30	KOLs; [5]
Total costs (24-month survival)		€ 4,750.80	

* Proportion using carvedilol = 25%, propranolol = 75%.

LVP treatment cost (indication 2 – refractory ascites)

The cost breakdown and total cost associated with LVP treatment is detailed in Table S3 below.

All consumable costs, excluding human albumin, were informed by expert opinion (based on a consultant in the purchasing department of a public hospital group in Catalonia). Human albumin cost per procedure is based on a total dose of 73.6 g, based on expert opinion. The unit cost for a 50 ml solution containing 10g of albumin was €36.90 [1].

People on TIPSS require 1.1 LVP sessions on average in the first month after TIPSS to drain the accumulation of fluid that occurred prior to implantation. This is based on evidence from Bureau et al. (2017) [6], where, for a sample of 29 people who underwent TIPSS, 32 LVPs were required.

Table S3: Large volume paracentesis plus human albumin costs per procedure per person

	Dose/units	Total cost	Source (units; costs)
Procedure costs			
Sundries	1.00	€ 193.00	[3]
Consumables			
Catheter and pack	1.00	€ 17.55	KOL; KOL
Connector	1.00	€ 0.30	
Drain	1.00	€ 0.75	
2L drainage bag	1.00	€ 0.40	
Human albumin (unit = dose)	73.6 g	€ 271.58	KOLs; [1]
Nurse (units = hours)	2.00	€ 48.46	KOL; [4]
Hospital stay (units = days)			
Day case	1.00	€ 588.00	KOLs; [3]
Total costs		€ 1,120.04	

B. Adverse Event Costs

Shunt dysfunction

A summary of the costs associated with shunt dysfunction is detailed in the table below.

Shunt dysfunction is applicable for both indications 1 and 2 and required re-intervention. In this population, 72.5% of re-interventions required angioplasty according to expert opinion. For the remaining cases, the method of management was to introduce a balloon expandable stent and, in some cases, a second graft stent (i.e. VIATORR or a bare stent). The proportion who required a second graft stent varied by indication (see table below for details).

Table S4: Total cost per shunt dysfunction, by indication

	Unit costs	Percentage receiving procedure	Total costs	Source [costs; %]
Angioplasty	€ 2,758.00	72.5%	€ 1,999.55	[3]; KOLs
TIPSS reintervention		27.5%		
Balloon expandable stent	€ 4,056.04	100%	€ 1,115.41**	[7]*; KOLs
Non-elective TIPSS (Indication 1)	€ 2,812.00	10%	€ 77.33**	GORE: KOLs
Non-elective TIPSS (Indication 2)	€ 2,812.00	100%	€ 773.30**	
Total cost shunt dysfunction – indication 1 (AVB)			€ 3,192.29	
Total cost shunt dysfunction – indication 2 (RA)			€ 3,888.26	

* Annual inflation rates calculated using OECD data on healthcare expenditure per capita in Spain which is reported between 2015-2019 [8]. The annual inflation rate for 2020 is assumed to be equal to the mean inflation rate for 2015-2019.

** Calculated by multiplying it by 27.5% (i.e. 1 – 72.5%).

Variceal bleeding

The table below outlines the cost associated with recurrent variceal bleeding adverse event for indication 1. For indication 2, the cost of treating recurrent bleeding, as estimated for the TIPSS arm (€4,279), was applied for the TIPSS and LVP treatment arms.

Table S5: Variceal bleeding cost per person (indication 1)

	TIPSS		EBL		Source [units; costs]
	Units	Total costs	Units	Total costs	
Endoscopy	1.00	€ 669.90	1.00	€ 669.90	KOL; [5]
Pharmacotherapy					
Terlipressin	0.075	€ 28.99	0.075	€ 28.99	KOL; [1]
Somatostatin	0.700	€ 151.77	0.700	€ 151.77	
Octreotide	0.225	€ 17.80	0.225	€ 17.80	
TIPSS (rescue therapy)	NA	NA	0.5	€ 2,141.68*	Table S1
EBL sessions	NA	NA	0.14	€ 448.30	Table S2
Hospital admission					
Non-elective days	5.10	€ 2,998.80	7.97	€ 4,686.36	[3]

ICU	25.0%	€ 411.25	25.0%	€ 411.25	[3]
TOTAL		€ 4,278.51		€ 8,556.06	

* Unit costs based on TIPSS stent cost, consumables, and procedure costs.

Ascites

The table below details the costs associated with ascites adverse event for indication 1. It was assumed that all ascites episodes are either grade two or three, based on grade 1 ascites being undetectable without an ultrasound. Grade 2 ascites was treated with diuretics with reduced salt intake. Grade three was treated with LVP and diuretics where repeat LVP sessions may be required if unresolved.

Cost of spironolactone is based on fifty 25mg tablets costing €2.50 [1]. Based on expert opinion, 100mg daily dose was applied in the model for 3 months.

Table S6: Ascites adverse event cost per person (indication 1)

	Dose/units	Total costs	Source [units; costs]
Grade 2			
Spironolactone	100 mg daily	€18.26	KOLs; [1]
Grade 3			
Spironolactone	100 mg daily	€18.26	KOLs; [1]
LVP	1.20	€1,300.44*	KOLs
Procedure	1.00	€193.00	KOLs; [3]
Consumables	1.00	€290.58	KOLs; KOLs
Nurse (unit = hours)	0.50	€12.12	KOLs; [4]
Hospital cost (day case)	1.00	€588.00	KOLs; [3]
Total cost per ascites episode (indication 1)		€668.48**	

* Calculated by taking the product of 1.2 units and sum of parameters making up the LVP procedure.

** Based on an equal weighting of 50% for grade 2 and 3 events.

For indication 2, following drainage of the accumulated fluid post TIPSS implantation, patients treated with TIPSS may still suffer a recurrence of refractory ascites that require a session of LVP. One session of LVP was estimated to cost **€1,120** based on 2 hours of nurse time (€48.46), procedure cost, consumables, and hospital day case cost.

Hepatic Encephalopathy (HE)

The table below outlines the cost of treating HE. Two forms of HE was considered in the model: mild and severe. However, according to expert opinion, there was no difference in management between the two in the Spanish setting.

Table S7: Hepatic encephalopathy average event cost per person

	Dose	Percentage receiving procedure	Total costs	Source [%; costs]
Lactulose ^a	80g daily	100%	€69.15	KOLs; [1]
Rifaximin ^b	1,200mg daily	100%	€840.99*	KOLs; [1]
TIPSS re-intervention	NA	5%	€343.40**	KOLs; Table S1
Total cost of HE (mild/severe)			€1,253.54	

^a 100 mg of lactulose for oral use cost €2.84 [1].

^b 12 pack of 200 mg rifaximin tablets cost €9.21 [1].

* Based on administering treatment for 6 months.

** TIPSS re-intervention include consumables, healthcare professionals, 2 bed days (all estimated to be €5,459) & management with balloon stent (estimated to be €1,409).

Spontaneous Bacterial Peritonitis (SBP)

The cost associated with the management of SBP is outlined in the table below. Cost of albumin was estimated based on a 50ml solution containing 10g of albumin costing €36.90 [3]. Cost of ciprofloxacin was estimated based on a 14 pack tablets costing €3.28 [1]. Cost of cefotaxime was estimated based on a 1g vial costing €3.12 [1].

Table S8: Spontaneous Bacterial Peritonitis adverse event cost per person

	Units	Total costs	Source [units; costs]
IV albumin (87.5 mg)	2.00	€645.76	[9]; [1]
Non-elective excess days	3.50	€2,058.00	KOLs; [3]
Antibiotics			
Cefotaxime 5-day course (4 g daily for 5 days)*	0.75	€8.15	[9]; [1]
Ciprofloxacin 7-day course (1 g daily for 7 days)	0.25	€0.59	KOLs; [1]
Total cost of SBP		€2,752.50	

* EASL clinical guidelines SBP (2010) [9]

C: Sensitivity and Scenario Analysis Inputs

Probabilistic sensitivity analysis inputs for indications 1 and 2.

Table S9: PSA parameters for indication 1 (AVB)

Parameters	Mean	Standard Error	Distribution	Alpha	Beta
Survival rates					
Survival rate Pharmaceuticals + EBL (12 months)	0.61	0.09	Beta [0,1]	16.72	10.69
Survival rate TIPS (12 months)	0.86	0.13	Beta [0,1]	5.36	0.87
Survival rate Pharmaceuticals + EBL (24 months)	0.61	0.09	Beta [0,1]	16.72	10.69
Survival rate TIPS (24 months)	0.86	0.13	Beta [0,1]	5.36	0.87
TIPs Procedure					
Rate of technical success	0.98	0.01	Beta [0,1]	117.18	2.39
Pre-procedure consultation time	0.17	0.03	Gamma	44.44	0.00
Procedure time (first implant)	2.00	0.30	Gamma	44.44	0.05
Procedure time (addition for tech failure)	2.00	0.30	Gamma	44.44	0.05
Unit Costs Consumables: Balloon Catheter	€ 352.02	€ 52.80	Gamma	44.44	7.92
Unit Costs Consumables: X-ray dye	€ 54.97	€ 8.25	Gamma	44.44	1.24
Unit Costs HCP: Hepatologist	€ 25.27	€ 3.79	Gamma	44.44	0.57
Unit Costs HCP: Radiologist	€ 25.27	€ 3.79	Gamma	44.44	0.57
Unit Costs HCP: Radiologist Trainee	€ 11.83	€ 1.77	Gamma	44.44	0.27
Unit Costs HCP: Radiographer	€ 16.92	€ 2.54	Gamma	44.44	0.38
Unit Costs HCP: Nurse	€ 24.23	€ 3.63	Gamma	44.44	0.55
Unit Costs HCP: Anaesthetist	€ 25.27	€ 3.79	Gamma	44.44	0.57
Unit Costs HCP: Anaesthetist nurse	€ 24.23	€ 3.63	Gamma	44.44	0.55
Unit Cost: Elective Excess Bed Day	€ 588.00	€ 88.20	Gamma	44.44	13.23
Resource Usage: Length of stay (elective)	2.00	0.30	Gamma	44.44	0.05
Unit Cost: Non-Elective Excess Bed Day	€ 588.00	€ 88.20	Gamma	44.44	13.23
Resource Usage: Length of stay (non-elective)	5.00	0.75	Gamma	44.44	0.11
Resource Usage: Length of stay (repeat)	2.00	0.30	Gamma	44.44	0.05
Unit Costs: Abdomen CT Scan	€ 155.00	€ 23.25	Gamma	44.44	3.49
Unit Costs: Doppler ultrasound	€ 67.00	€ 10.05	Gamma	44.44	1.51
Unit Costs: ECHO	€ 92.00	€ 13.80	Gamma	44.44	2.07
Unit Costs: ECG	€ 150.00	€ 22.50	Gamma	44.44	3.38
Resource Usage: ECHO	0.50	0.08	Beta [0,1]	21.72	21.72
Pharmaceuticals + EBL Treatment Costs					
Percentage using Carvedilol	0.25	0.04	Beta [0,1]	33.08	99.25

Unit Costs: Inpatient EBL procedure	€ 3,202.15	€ 480.32	Gamma	£44.44	£72.05
Unit costs: Outpatient EBL procedure	€ 669.90	€ 100.49	Gamma	£44.44	£15.07
Resource Usage: EBL procedures month 1	2.00	0.30	Gamma	44.44	0.05
Follow-Up					
Unit costs: Angiography	€ 305.00	€ 45.75	Gamma	44.44	6.86
Unit costs: Venography	€ 289.00	€ 43.35	Gamma	44.44	6.50
Variceal bleeding					
Rate of bleeding at 12 months (VIATORR)	0.03	0.00	Beta [0,1]	43.08	1392.96
Rate of bleeding at 12 months (EBL)	0.47	0.07	Beta [0,1]	23.09	26.03
Rate of bleeding at 24 months (VIATORR)	0.03	0.00	Beta [0,1]	43.08	1392.96
Rate of bleeding at 24 months (EBL)	0.50	0.08	Beta [0,1]	21.72	21.72
Treatment Strategy (Pharma + EBL): % TIPs	0.50	0.08	Beta [0,1]	21.72	21.72
Treatment Strategy (Pharma + EBL): % EBL	0.14	0.02	Beta [0,1]	38.08	233.93
Terlipressin (%)	0.08	0.01	Beta [0,1]	41.04	506.11
Octreotide (%)	0.23	0.03	Beta [0,1]	34.22	117.87
Resource Usage: Length of hospital stay (VIATORR)	5.10	0.77	Gamma	44.44	0.11
Resource Usage: Length of hospital stay (VIATORR)	7.97	1.20	Gamma	44.44	0.18
Unit costs: Critical care per FCE	€ 1,645.00	€ 246.75	Gamma	44.44	37.01
Resource Usage: % requiring ICU stay (VIATORR)	0.25	0.04	Beta [0,1]	33.08	99.25
Resource Usage: % requiring ICU stay (Pharma+ EBL)	0.25	0.04	Beta [0,1]	33.08	99.25
Reintervention					
Probability of re-intervention following shunt dysfunction	0.07	0.03	Beta [0,1]	6.00	76.00
Percentage re-intervention requiring angioplasty	0.73	0.11	Beta [0,1]	11.50	4.36
Unit costs: Angiography	€ 2,758.00	€ 413.70	Gamma	44.44	62.06
Unit costs: balloon expandable stent	€ 1,408.68	€ 211.30	Gamma	44.44	31.70
Resource Usage: % TIPs reintervention requiring second stent	0.10	0.02	Beta [0,1]	39.90	359.10
Hepatic Encephalopathy					
Probability of HE at 12 months (VIATORR)	0.28	0.04	Beta [0,1]	31.72	81.57
Probability of HE at 12 months (Pharma + EBL)	0.40	0.06	Beta [0,1]	26.27	39.40

% of HE episodes classified as severe (VIATORR)	0.25	0.07	Beta [0,1]	5	24
% of HE episodes classified as severe (Pharma + EBL)	0.25	0.11	Beta [0,1]	4	12
Resource usage: % of HE requiring repeat TIPs procedure	0.05	0.01	Beta [0,1]	42.17	801.27
Ascites					
Probability of ascites at 12 months (VIATORR)	0.13	0.02	Beta [0,1]	38.54	257.90
Probability of ascites at 12 months (EBL)	0.33	0.05	Beta [0,1]	29.45	59.79
Cost per Ascites episode (LVP procedure costs)	€ 668.48	€ 100.27	Gamma	44.44	15.04
Utilities					
Chronic liver disease Child-Pugh 2	0.67	0.10	Beta [0,1]	14.00	6.89
(Additional) disutility Chronic liver disease Child-Pugh 3	0.11	0.02	Beta [0,1]	39.45	319.15
Disutility active bleeding	0.15	0.02	Beta [0,1]	37.44	205.36
Disutility TIPs (initial implant & shunt dysfunction)	0.15	0.02	Beta [0,1]	37.44	205.36
Disutility mild HE	0.07	0.01	Beta [0,1]	41.26	548.21
(Additional) disutility severe HE	0.06	0.01	Beta [0,1]	41.72	653.58
Disutility ascites	0.13	0.02	Beta [0,1]	38.76	271.35

Table S10: PSA parameters for indication 2 (RA)

Parameters	Mean	Standard Error	Distribution	Alpha	Beta
TIPs Procedure					
Rate of technical success	0.98	0.05	Beta [0,1]	7.02	0.14
Pre-procedure consultation time	0.17	0.04	Gamma	16.00	0.01
Procedure time (first implant)	2.00	0.30	Gamma	44.44	0.05
Procedure time (addition for tech failure)	2.00	0.30	Gamma	44.44	0.05
Unit Costs Consumables: Balloon catheter	€ 352.02	€ 52.80	Gamma	€ 44.44	€ 7.92
Unit Costs Consumables: X-ray dye	€ 54.97	€ 8.25	Gamma	€ 44.44	€ 1.24
Unit Costs Consumables: Propofol	€ 2.58	€ 0.39	Gamma	€ 44.44	€ 0.06
Unit Costs Consumables: Antibiotics	€ 2.87	€ 0.43	Gamma	€ 44.44	€ 0.06
Unit Costs HCP: Hepatologist	€ 25.27	€ 3.79	Gamma	€ 44.44	€ 0.57
Unit Costs HCP: Radiologist	€ 25.27	€ 3.79	Gamma	€ 44.44	€ 0.57
Unit Costs HCP: Radiologist Trainee	€ 11.83	€ 1.77	Gamma	€ 44.44	€ 0.27
Unit Costs HCP: Radiographer	€ 16.92	€ 2.54	Gamma	€ 44.44	€ 0.38
Unit Costs HCP: Nurse	€ 24.23	€ 3.63	Gamma	€ 44.44	€ 0.55
Unit Costs HCP: Anaesthetist	€ 25.27	€ 3.79	Gamma	€ 44.44	€ 0.57

Parameters	Mean	Standard Error	Distribution	Alpha	Beta
Unit Costs HCP: Anaesthetist nurse	€ 24.23	€ 3.63	Gamma	€ 44.44	€ 0.55
Unit Cost: Elective Excess Bed Day	€ 588.00	€ 88.20	Gamma	€ 44.44	€ 13.23
Resource Usage: Length of stay (elective)	2.00	0.30	Gamma	44.44	0.05
Unit Cost: Non-Elective Excess Bed Day	€ 588.00	€ 88.20	Gamma	€ 44.44	€ 13.23
Resource Usage: Length of stay (non-elective)	5.00	0.75	Gamma	44.44	0.11
Resource Usage: Length of stay (repeat)	2.00	0.30	Gamma	44.44	0.05
Unit Costs: Abdomen CT Scan	€ 155.00	€ 23.25	Gamma	€ 44.44	€ 3.49
Unit Costs: Doppler ultrasound	€ 67.00	€ 10.05	Gamma	€ 44.44	€ 1.51
Unit Costs: ECHO	€ 92.00	€ 13.80	Gamma	€ 44.44	€ 2.07
Unit Costs: ECG	€ 150.00	€ 22.50	Gamma	€ 44.44	€ 3.38
LVP Costs					
LVP frequency	2.17	0.33	Gamma	44.44	0.05
Unit Costs: Procedure cost/sundries	€ 193.00	€ 28.95	Gamma	€ 44.44	€ 4.34
Unit Costs: Catheter and pack	€ 17.55	€ 2.63	Gamma	€ 44.44	€ 0.39
Unit Costs: Connector	€ 0.30	€ 0.05	Gamma	€ 44.44	€ 0.01
Unit Costs: Drain	€ 0.75	€ 0.11	Gamma	€ 44.44	€ 0.02
Unit Costs: 2L Drainage bag	€ 0.40	€ 0.06	Gamma	€ 44.44	€ 0.01
Unit Costs: Human Albumin	€ 271.58	€ 40.74	Gamma	€ 44.44	€ 6.11
Nurse consultation time	2.00	0.30	Gamma	44.44	0.05
% Elective cases [if hospital patients]	0.66	0.10	Beta [0,1]	14.45	7.44
Unit Costs: Elective inpatient	€ 588.00	€ 88.20	Gamma	44.44	13.23
Unit Costs: Non elective inpatient	€ 588.00	€ 88.20	Gamma	44.44	13.23
Resource Usage: Length of stay (elective & non-elective)	2.80	0.42	Gamma	44.44	0.06
Mean LVP session per TIPs patient	1.10	0.03	Gamma	1526.96	0.00
Follow-Up					
Unit costs: Angiography	€ 305.00	€ 45.75	Gamma	€ 44.44	€ 6.86
Unit costs: Venography	€ 289.00	€ 43.35	Gamma	€ 44.44	€ 6.50
Ascites					
Probability of recurrent ascites: 25 months	0.51	0.04	Beta [0,1]	98.00	94.00
Recurrent Bleeding					
Rate of bleeding at 12 months (VIATORR)	0.0440	0.02	Beta [0,1]	3.78	82.13
Rate of bleeding at 12 months (LVP)	0.18	0.05	Beta [0,1]	12.62	56.73
Total cost per bleeding episode	€ 3,914.61	€ 587.19	Gamma	€ 44.44	€ 88.08

Parameters	Mean	Standard Error	Distribution	Alpha	Beta
Probability of reintervention following shunt dysfunction	0.03	0.03	Beta [0,1]	1.00	28.00
% reintervention requiring angioplasty	0.73	0.11	Beta [0,1]	11.50	4.36
Unit costs: Angioplasty	€ 2,758.00	€ 413.70	Gamma	€ 44.44	€ 62.06
Unit costs: balloon expandable stent	€ 1,408.68	€ 211.30	Gamma	€ 44.44	€ 31.70
Probability of reintervention following shunt dysfunction	0.03	0.03	Beta [0,1]	1.00	28.00
Hepatic Encephalopathy					
Probability of HE at 12-months (VIATORR)	0.35	0.09	Beta [0,1]	10.00	19.00
Probability of HE at 12 months (LVP)	0.33	0.08	Beta [0,1]	11.00	22.00
% of HE episodes classified as severe (VIATORR)	0.40	0.15	Beta [0,1]	4.00	6.00
% of HE episodes classified as severe (LVP)	0.64	0.14	Beta [0,1]	7.00	4.00
Unit costs: Lactulose	€ 69.15	€ 10.37	Gamma	€ 44.44	€ 1.56
Unit costs: Rifaximin	€ 840.99	€ 126.15	Gamma	€ 44.44	€ 18.92
Resource usage: % of HE requiring repeat TIPs procedure	0.05	0.01	Beta [0,1]	42.17	801.27
SBP					
Probability of SBP at 12 months (LVP)	0.06	0.04	Beta [0,1]	2.00	31.00
Resource usage: Mean LOS per SBP episode	3.50	0.53	Gamma	44.44	0.08
Unit Costs: Consultant (medical oncology)	€ 146.00	€ 21.90	Gamma	€ 44.44	€ 3.29
Unit Costs: IV albumin	€ 322.88	€ 48.43	Gamma	€ 44.44	€ 7.26
Unit Costs Ciprofloxacin	€ 2.34	€ 0.35	Gamma	€ 44.44	€ 0.05
Unit Costs Cefotaxime	€ 64.20	€ 9.63	Gamma	€ 44.44	€ 1.44
Utilities					
Chronic liver disease Child-Pugh 2	0.65	0.10	Beta [0,1]	14.91	8.03
Disutilities					
Ascites	0.13	0.02	Beta [0,1]	38.76	271.35
TIPs procedure (initial implant, shunt dysfunction)	0.15	0.02	Beta [0,1]	37.44	205.36
Active bleeding	0.15	0.02	Beta [0,1]	37.44	205.36
Hepatic Encephalopathy (mild)	0.07	0.01	Beta [0,1]	41.26	548.21
Hepatic Encephalopathy (severe)	0.13	0.02	Beta [0,1]	38.54	257.90
Spontaneous bacteria peritonitis	0.12	0.02	Beta [0,1]	38.99	285.93

Scenario analysis – AVB (indication 1)

Scenario analysis inputs for indication 1 informed by the Nicoară-Farcău et al. (2021) [10] meta-analysis.

Table S11: Scenario analysis clinical inputs – indication 1 (AVB)

	Indication 1: AVB		
	TIPSS	EBL	Source
Survival at 12 months	0.790	0.620	Nicoară-Farcău et al. (2021) [10]
Survival at 24 months	0.790 ^a	0.620 ^a	
Recurrent VB at 12 months	0.090	0.300	
Recurrent VB at 24 months	0.090 ^b	0.300 ^b	
Ascites at 12 months	0.116	0.356	
HE at 12 months	0.350	0.260	
% HE severe	0.250	0.250	Lv et al. (2019) [11]

^a12-month survival is assumed to equal to 24-month survival

^b12-month bleeding rates is assumed to equal to 24-month bleeding rates.

D: Probabilistic Results

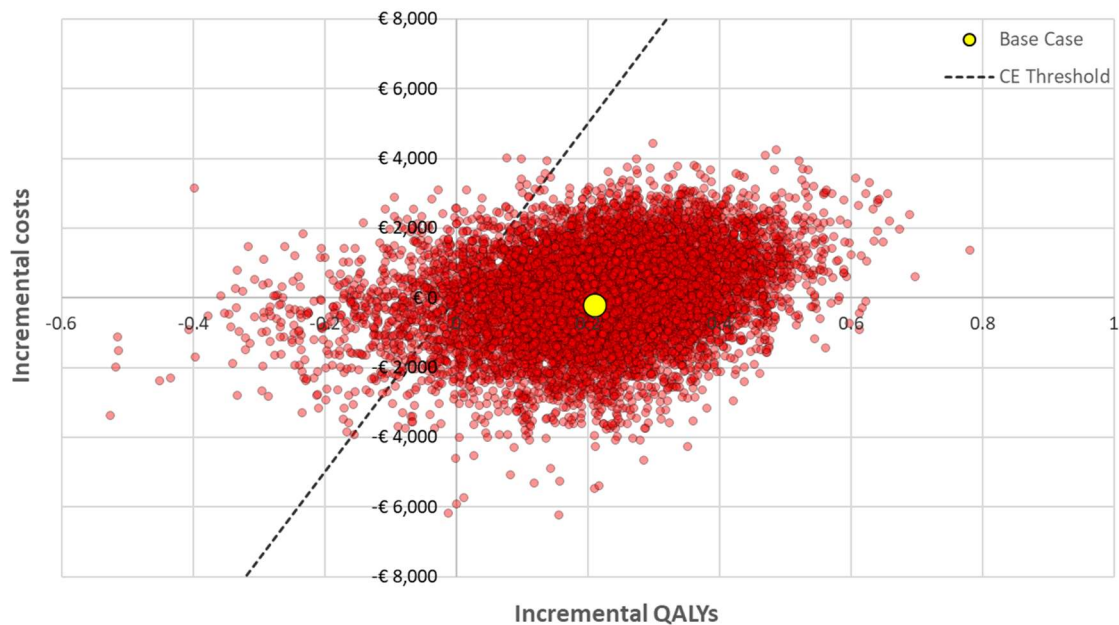
Indication 1 (AVB)

Table S12: PSA results per person – AVB

	TIPSS	EBL	Incremental
Total costs	€ 8,914.00	€ 8,847.00	€ 66.00
Total QALYs	1.04	0.82	0.21
Probabilistic ICER			€ 309.00
Probability TIPSS is cost saving			47%
Probability TIPSS is cost-effective at a threshold of €25,000 per QALY			93%

Abbreviations: QALYs – quality adjusted life year; ICER – incremental cost-effectiveness ratio; TIPSS – transjugular intrahepatic portosystemic stent shunt

Figure S1 Cost-effectiveness plane for AVB analysis



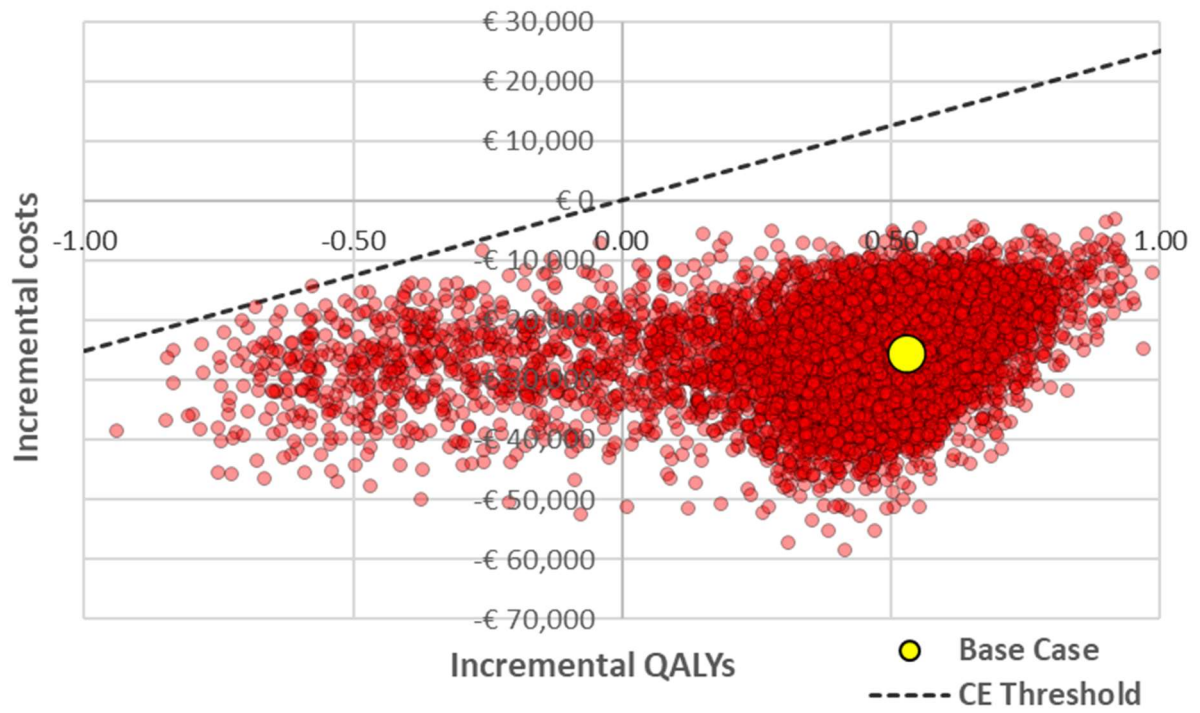
Indication 2 (RA)

Table S13: PSA results per person – RA

	TIPSS	LVP	Incremental
Total costs	€ 9,800.00	€ 35,130.00	-€ 25,330.00
Total QALYs	1.03	0.60	0.42
Probabilistic ICER			Dominant
Probability TIPSS is cost saving			100%
Probability TIPSS is cost-effective at a threshold of €25,000 per QALY			100%

Abbreviations: QALYs – quality adjusted life year; ICER – incremental cost-effectiveness ratio; TIPSS – transjugular intrahepatic portosystemic stent shunt

Figure S2 Cost-effectiveness plane for refractory ascites analysis



References

1. Agencia Española de Medicamentos y Productos Sanitarios. 2021. Available from: <https://www.aemps.gob.es/?lang=ca>.
2. GORE. GORE 2021. Available from: Data on file.
3. Tarifas para la facturación de servicios sanitarios y docentes de Osakidetza para el año 2018. 2018.
4. Catalan Institute of Health (ICS). Remuneration book. In; 2020.
5. Condiciones económicas aplicables a la prestación de determinados servicios de asistencia sanitaria a través de medios ajenos, en el ámbito de gestión del Sescam. 2017.
6. Bureau C, Thabut D, Oberti F, Dharancy S, Carbonell N, Bouvier A, *et al*. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. *Gastroenterology*. 2017;152(1):157-63.
7. Gisbert R, Brosa M. Spanish healthcare costs and cost-effectiveness ratios database: eSalud [Internet]. Barcelona: Oblikue Consulting; 2018. Available from: <http://www.oblikue.com/bddcostes/>.
8. OECD. Health Spending 2021. Available from: <https://data.oecd.org/healthres/health-spending.htm>.
9. European Association for the Study of the L. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol*. 2010;53(3):397-417.
10. Nicoară-Farcău O, Han G, Rudler M, Angrisani D, Monescillo A, Torres F, *et al*. Effects of early placement of transjugular portosystemic shunts in patients with high-risk acute variceal bleeding: a meta-analysis of individual patient data. *Gastroenterology*. 2021;160(1):193-205. e10.
11. Lv Y, Yang Z, Liu L, Li K, He C, Wang Z, *et al*. Early TIPS with covered stents versus standard treatment for acute variceal bleeding in patients with advanced cirrhosis: a randomised controlled trial. *The Lancet Gastroenterology & Hepatology*. 2019;4(8):587-98.