

Background

Pharmacological management of acute stroke consists primarily of intravenous tissue plasminogen activator (IV rt-PA). However, there are some limitations for this treatment. The main is the time-frame for administration of IV rt-PA (4.5 hours of symptom onset of stroke). Mechanical thrombectomy (MT, removal of a clot by use of a surgical device) can be administered up to 8 hours of symptom onset. There are 1st and 2nd generation mechanical thrombectomy devices. Second-generation endovascular stent retrieval devices have shown promising results in clinical trials, both on effectiveness and safety.

Objective

The aim of this economic analysis was to evaluate cost-effectiveness of MT added to BSC when compared to BSC alone in patients with AIS in Poland. The analysis was performed according to PICO formula.

(P)opulation	Patients with acute ischemic stroke in a subgroup of patients: » contraindicated to IV rt-PA » suitable for IV rt-PA
(I)ntervention	MT using a stent retriever added to BSC
(C)omparator	BSC treatment alone
(O)utcomes	LYG, QALY, Cost (PLN)

Model Structure

A cost-utility analysis was performed. The model uses a Markov structure and is split into two distinct phases: an acute phase (from stroke onset to 90 days) and rest-of-life phase (spanning from 91 days to death). There are 7 health states based on the modified Rankin Scale (mRS) scores 0 to 6. In acute phase all treatment effect occurs. In base case during each cycle of rest-of-life phase patient can stay in the same health state as in the end of acute phase, die or experienced a recurrent stroke. In case of recurrent stroke the patient re-entered the model from the start (such patient have a mRS score equal to or greater than their mRS before that recurrent stroke). Half cycle correction was applied.

Figure 1. Acute phase model structure

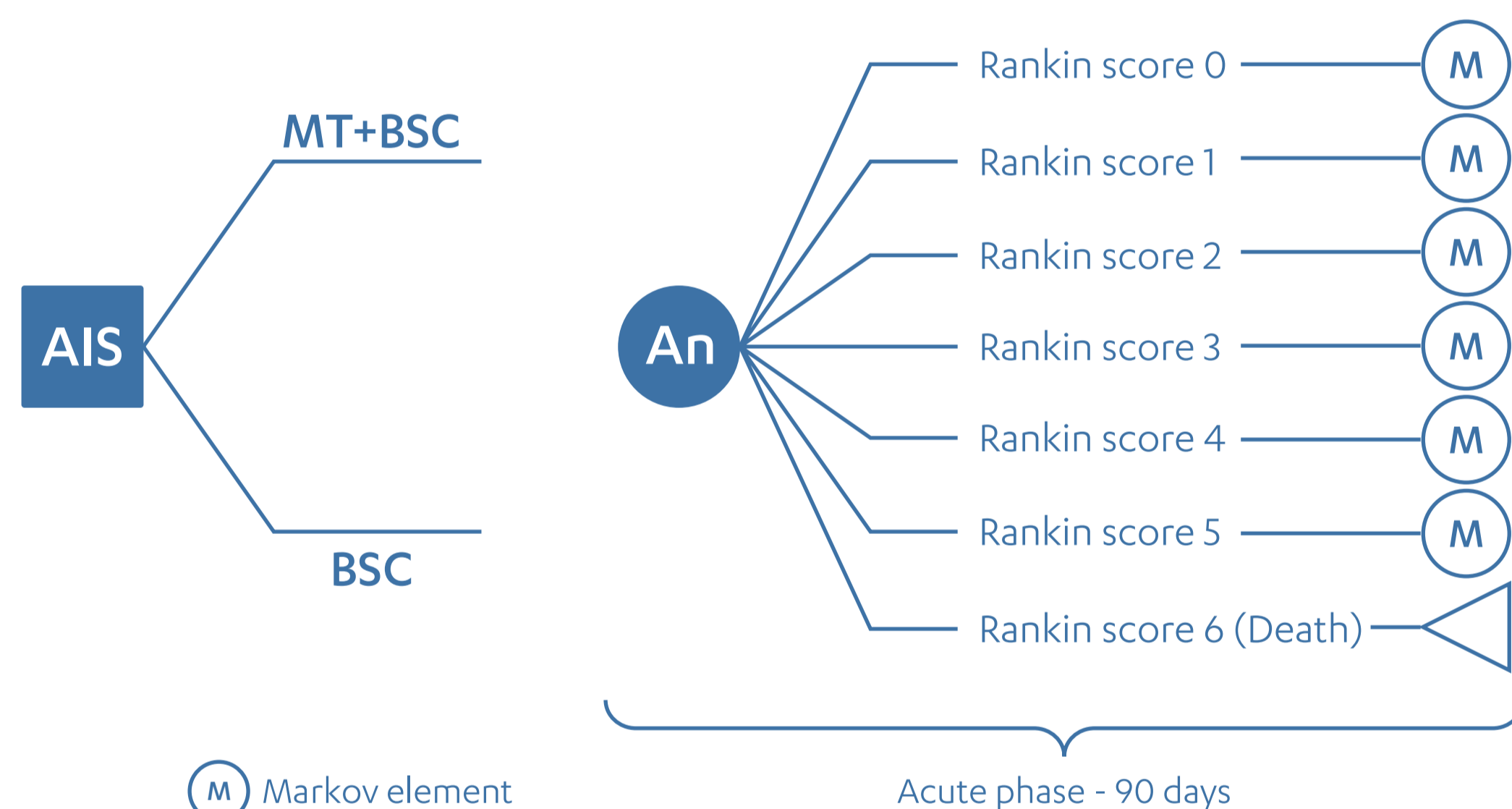
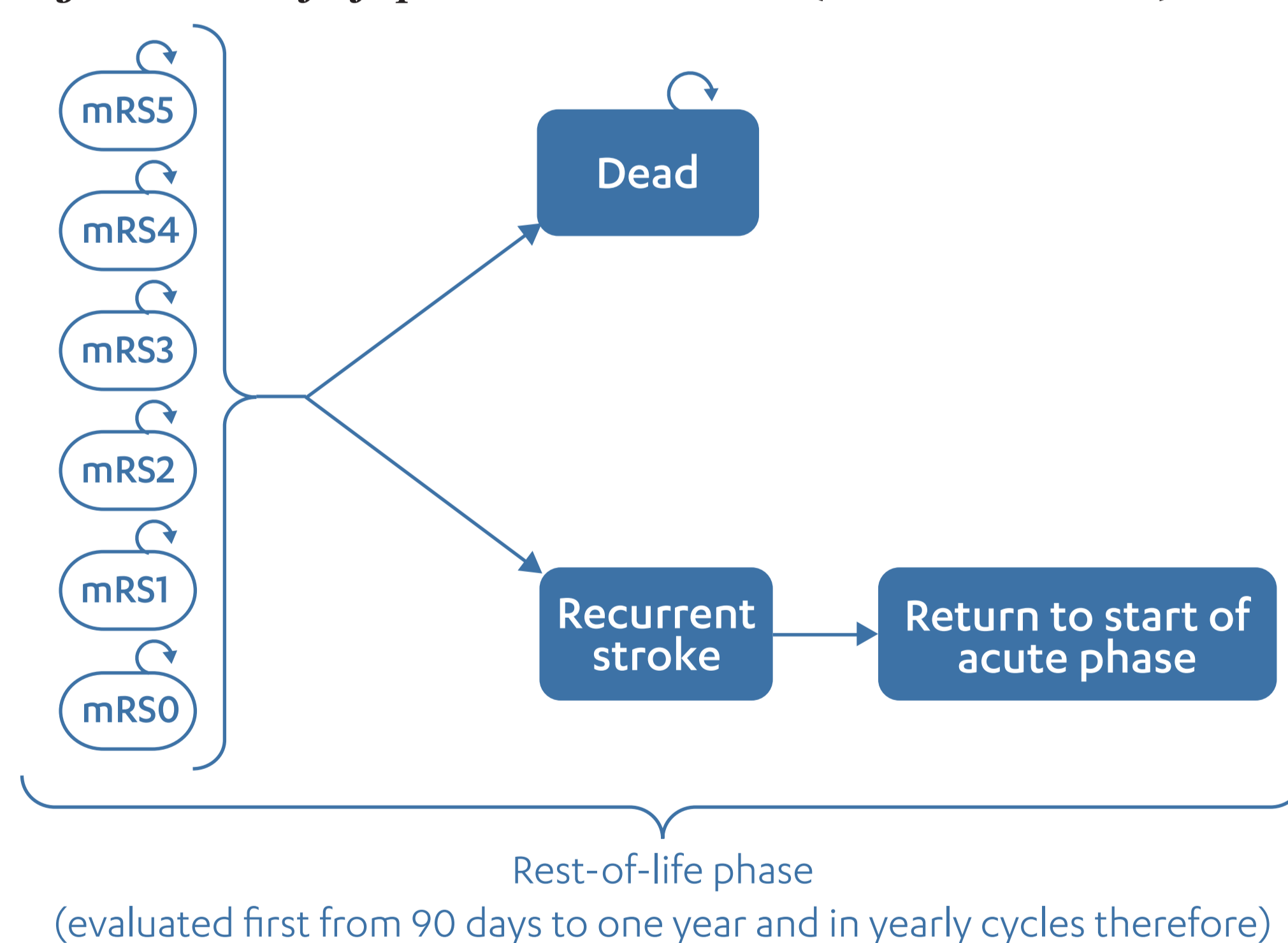


Figure 2. Rest-of-life phase model structure (base case scenario)



In sensitivity analysis, a rehabilitation scenario was tested and there is a possibility for improvement or deterioration by one health state since 91 days to one year after stroke (e.g. from mRS5 to mRS4).

Input Data & Assumptions

- Data on effectiveness were taken from a meta-analysis of 5 RCTs clinical trials [1]. In base case scenario mRS distribution was assumed to be the same in both patients subgroups.
- Based on data from RCTs [2-6] probability of symptomatic intracranial hemorrhage (SICH) for MT+BSC or BSC alone was estimated. Additionally adverse events related to MT were imputed.
- Patients baseline characteristic (age: 66 yrs.) was adopted based on patients characteristic in one stroke center [7].
- Health state utilities were taken from Polish study [8].

- Probability of death in rest-of-life phase was adjusted to reflect the higher rates observed in stroke survivors by using risk ratios [9].
- Probability of recurrent stroke was estimated separately for first (4.91%) and subsequent cycles of rest-of-life phase (2.01%) [10]. Recurrent stroke is treated as first ever stroke.
- In base case analysis (rest-of-life phase) there is no possibility for improvement/ worsening (except death) of health state.
- Cost were calculated from public payer (NHF - National Health Fund) or from NHF+patient perspective. Cost of MT+BSC was estimated in accordance with clinical expert opinion (except device cost). It was assumed that 20% of patients need 2 devices per stroke episode. Cost of BSC alone was calculated based on stats for Diagnostic Related Groups in 2014, [11]. Cost of adverse events and health states were estimated based on Polish cost study [12] and in accordance with pricing for procedures in NFZ catalogues. Drug prices were taken from drug reimbursement list.
- Time horizon was assumed to be a lifetime.
- Acceptability threshold in this analysis was 125 955 PLN.
- Cost and QALYs were discounted with 5.0% and 3.5% discount rates.
- One-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) were performed to test robustness of base case results.

Table 1. Data on effectiveness used in base case scenario

Inter-vention	Time point	mRS						
		0	1	2	3	4	5	6
MT+BSC	7 th day	9.40%	12.90%	10.16%	15.56%	14.66%	29.03%	8.30%
	90 th day	9.95%	16.90%	19.12%	16.90%	15.64%	6.16%	15.32%
BSC	7 th day	3.15%	5.62%	5.54%	10.43%	28.78%	35.92%	10.56%
	90 th day	4.96%	7.91%	13.64%	16.43%	24.65%	13.49%	18.91%

Table 2. Values for parameters related to health states in base case scenario

Parameter	mRS							
	0	1	2	3	4	5	6	
Health state utilities	0.884	0.828	0.705	0.597	0.271	-0.027	-	
Relative risk of dying	1.00	1.00	1.12	1.66	1.92	2.57	-	
Cost parameters								
Cost in acute phase [PLN]	NHF	164	1,500	1,500	4,475	4,475	3,664	1,315
	NHF+patient	197	1,533	1,533	4,510	4,510	3,674	1,330
Annual cost in rest-of-life phase [PLN]	NHF	676	676	676	877	877	951	-
	NHF+patient	759	759	759	965	965	974	-

Health state cost mRS6 in acute phase is assigned for those who die

Table 3. Values for cost parameters related to treatment

Parameter	Value	
Device	30,500 PLN (without 8% tax)	
Cost of MT+BSC	Diagnosis, hospital stay	9,000 PLN
	Procedure	3,000 PLN
	IV rt-PA (if patient is available)	3,000 PLN
Cost of BSC alone	Contraindicated to IV rt-PA	6,955 PLN
	Suitable for IV rt-PA	13,281 PLN
Cost of adverse events	SICH	5,074 PLN
	Related to MT	1,721 PLN (per patient)

Probability of SICH is 4.57% for MT + BSC and 4.29% for BSC alone

Results

MT added to BSC is more effective than BSC alone. As in base case scenario data on patient's characteristic and effectiveness are equal for both analyzed subgroups of patients, results on effectiveness are the same for both subgroups. Estimated difference in QALY is statistically significant. Significance was not tested for LYG's difference.

Table 4. Results of clinical evaluation in terms of LYG and QALY

Category	MT+BSC	BSC	Difference
LYG	12.03	10.61	1.42
QALY	5.29	3.64	1.65

Adding MT to BSC is more expensive than BSC alone. Estimated differences in total costs were statistically significant. However, estimated incremental cost-utility ratios (ICUR) is 4 times less than acceptability threshold.

Table 5. Economic results – patients contraindicated to IV rt-PA

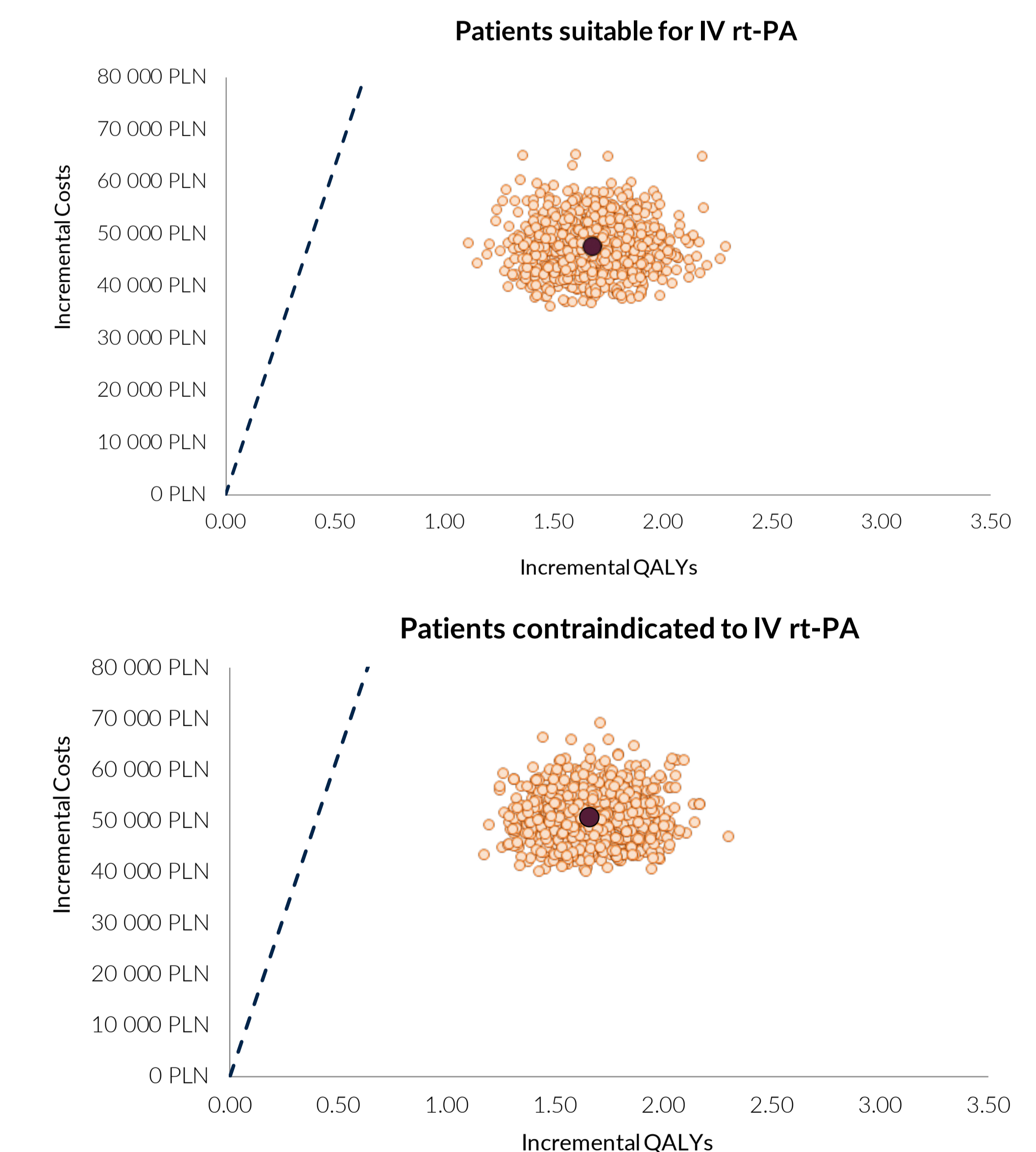
Cost category	MT+BSC	BSC	Difference
NHF perspective			
Intervention	49,074 PLN	6,623 PLN	42,451 PLN
Adverse events	1,860 PLN	208 PLN	1,653 PLN
Health state	8,421 PLN	8,648 PLN	-227 PLN
Recurrent stroke	8,217 PLN	1,411 PLN	6,807 PLN
Total cost	67,573 PLN	16,889 PLN	50,684 PLN
ICUR	-	-	30,713 PLN
NHF+patient perspective			
Intervention & adverse events	as in NHF perspective		
Health state	9,063 PLN	9,195 PLN	-132 PLN
Recurrent stroke	8,222 PLN	1,414 PLN	6,808 PLN
Total cost	68,220 PLN	17,440 PLN	50,780 PLN
ICUR	-	-	30,771 PLN

Intervention cost is a sum of cost related to: diagnosis, hospital stay, treatment procedure, device for MT. Health state cost is a sum of cost related to: patient's rehabilitation (acute phase only), ambulatory care and pharmacotherapy (acute and rest-of-life phase) and additional hospitalization (rest-of-life phase only)

Table 6. Economic results – patients suitable to IV rt-PA

Cost category	MT+BSC	BSC	Difference
NHF perspective			
Intervention	51,931 PLN	12,648 PLN	39,283 PLN
Adverse events	1,860 PLN	208 PLN	1,653 PLN
Health state	8,421 PLN	8,648 PLN	-227 PLN
Recurrent stroke	8,666 PLN	2,233 PLN	6,433 PLN
Total cost	70,879 PLN	23,737 PLN	47,142 PLN
ICUR	-	-	28,566 PLN
NHF+patient perspective			
Intervention & adverse events	as in NHF perspective		
Health state	9,063 PLN	9,195 PLN	-132 PLN
Recurrent stroke	8,670 PLN	2,236 PLN	6,434 PLN
Total cost	71,525 PLN	24,287 PLN	47,238 PLN
ICUR	-	-	28,625 PLN

The results of probabilistic sensitivity analysis have shown that probability of being cost-effectiveness for MT + BSC is 100%. In each of OWSA scenarios ICUR value was below acceptability threshold.



Results from NHF perspective are presented. When NHF+patient perspective is taken results are convergent

Conclusions

Treatment of AIS episodes with MT, using a stent retriever, added to BSC is more effective than BSC alone. This implies in a prolongation of expected life-years and significant gain in QALY. Adding MT to BSC is more expensive than BSC alone but as ICUR values are below acceptability threshold such treatment is cost-effective in Polish settings.

References

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AIS	Acute ischemic stroke	IV rt-PA	Intravenous tissue plasminogen activator	MT	Mechanical thrombectomy
BSC	Best standard care	LYG	Life Years Gained	NHF	National Health Fund
ICUR	Incremental cost-utility ratio	mRS	Modified Rankin Scale	OWSA	One-way sensitivity analyses
PSA	Probabilistic sensitivity analysis	QALY	Quality-Adjusted Life Years	SICH	Symptomatic intracranial hemorrhage