

# Cost Effectiveness of Splenic Artery Embolization versus Splenectomy after Trauma in the Netherlands

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## ABSTRACT

**Purpose:** To demonstrate that splenic artery embolization (SAE) is more cost-effective than splenectomy from a societal perspective in the Netherlands.

**Materials and Methods:** Patient-level data obtained from the SPLENIQ study were used to populate a health economic model and were supplemented with expert opinion when necessary. Propensity score matching was used to correct for baseline differences in injury severity scores. The health economic model consisted of 3 health states (complications after intervention, SAE failure, and recovery) and a dead state. Model outcomes were incremental quality-adjusted life years (QALYs) and incremental costs of SAE over splenectomy. The Dutch health economic guidelines were followed. The model used a lifetime time horizon. Uncertainty was assessed using probabilistic sensitivity analysis and scenario analyses.

**Results:** Patients undergoing SAE had a higher life expectancy than patients undergoing splenectomy. Incremental QALYs were 3.1 (mostly explained by difference in life expectancy), and incremental costs were €34,135 (explained by costs related to medical consumption and lost productivity in additional life years), leading to an incremental cost-effectiveness ratio of €11,010 per QALY. SAE was considered cost-effective in >95% of iterations using a threshold of €20,000 per QALY.

**Conclusions:** SAE results in more QALYs than splenectomy. Intervention costs for SAE are lower than that for splenectomy, but medical consumption and productivity costs in later years are higher for SAE due to better survival. SAE was found to be cost-effective compared with splenectomy under appropriate Dutch cost-effectiveness thresholds.

## ABBREVIATIONS

HRQOL = health-related quality of life, ICER = incremental cost-effectiveness ratio, ISS = injury severity score, NOM = nonoperative management, PSA = probabilistic sensitivity analysis, QALYs = quality-adjusted life years, SAE = splenic artery embolization

Trauma is the leading cause of death for individuals aged <45 years in the United States (1). The spleen is one of the most frequently affected organs in blunt abdominal trauma (2). Standard of care for spleen injuries varies according to the severity of the injury. At the least severe end of the spectrum, nonoperative management (NOM) is the current standard of care for spleen injuries and is successful in up to 90% cases (3). For most severe trauma and hemodynamically unstable patients, surgical removal of the spleen (splenectomy) is currently the preferred treatment option. Patients who do not fall in these 2 groups undergo splenic artery embolization (SAE) or splenectomy. The American Association for the Surgery of Trauma grading has been used for treatment decisions in splenic trauma. Still,

guidelines for choosing between SAE and splenectomy are often lacking, and the choice of treatment is up to the treatment centers and individual physicians (4).

Only a limited number of studies provide a head-to-head comparison of the effectiveness between splenectomy and SAE. An Italian study (5) showed that splenectomy was associated with an increased risk of complications, but not with mortality, compared with SAE. However, these findings are likely to be affected by baseline differences in injury severity and admission vitals between groups. Studies investigating blunt abdominal trauma have traditionally focused on morbidity and mortality and neglected health-related quality of life (HRQOL) after trauma, albeit most patients survive their trauma. HRQOL is an important

**RESEARCH HIGHLIGHTS**

- Patient-level data were retrieved from a Dutch retrospective and prospective observational study. Patients were propensity-matched using injury severity scores.
- Splenic artery embolization (SAE) resulted in more quality-adjusted life years than splenectomy.
- Intervention costs for SAE were lower than that for splenectomy, but medical consumption and productivity costs in later years were higher for SAE because of better patient survival. Total costs were higher for SAE than for splenectomy.
- SAE was found to be cost-effective compared with splenectomy under conventional cost-effectiveness thresholds.

outcome measure for patients in particular, as the physiologic descriptions of health are not always correlated with how patients experience their health status. In addition, patients might respond differently to the same underlying clinical criteria (6). For policymakers, HRQOL can be used along with survival to calculate quality-adjusted life years (QALYs), a generic measure of health that can be compared across diseases. As a result, QALYs are a preferred measure of effectiveness in cost-effectiveness research (7). Although data on HRQOL after the injury of the spleen specifically are limited, available evidence on trauma injuries in general shows that HRQOL is impaired compared with that of the general population (8,9).

Evidence on costs of SAE and splenectomy is limited. A study (10) in the United States found that health care costs of splenectomy were higher than that of SAE. The long-term costs from follow-up health care utilization were not included in this study. Next to health care costs, traumatic injuries can lead to losses in productivity, as patients might need to stop working permanently or temporarily (11). Associated costs also need to be included when a cost-effectiveness study is conducted from a societal perspective.

Cost-effectiveness studies are used to establish the efficiency of health care spending. The outcomes of such studies can be used to determine optimal treatment strategies. In a cost-effectiveness study, both costs and effects of interventions are compared. Since, to our knowledge, there are currently no cost-effectiveness studies comparing SAE with splenectomy, this study aimed to estimate the cost effectiveness of SAE and splenectomy from a societal perspective in the Netherlands.

**MATERIALS AND METHODS**

A detailed description of the materials and methods is shown in **Appendix A** (available online on the article's **Supplemental Material** page at [www.jvir.org](http://www.jvir.org)).

**STUDY DETAILS**

**Study type:** Retrospective, observational, cohort study  
**Level of evidence:** 3 (SIR-C)

**Patient Population**

Patient-level data were derived from the SPLENIQ study, a single-center retrospective and a multicenter prospective observational study investigating the effects of NOM, SAE, and splenectomy in patients who suffered splenic injury after blunt abdominal trauma, with the primary aim of examining patients' quality of life (12). The SPLENIQ study included adult patients with a splenic injury after trauma. The inclusion and exclusion criteria of the SPLENIQ study have been described elsewhere (12). The study has been approved by the Medical Ethical Committee Brabant (METC Brabant, protocol numbers NL54339.028.15 and NL54542.028.016 for the retrospective and prospective studies, respectively). In the prospective study, patients were included in the period between March 2018 and December 2018, with a 1-year follow-up. In the retrospective study, patients in the period between January 2005 and February 2017. The baseline population characteristics are presented in **Table 1**.

As data were derived from an observational study, patients were not randomly allocated to treatment. Instead, physicians used patient characteristics to determine the perceived optimal treatment. To control for differences between patients who underwent SAE and those who underwent splenectomy, in this way reducing selection bias, propensity score matching was performed. For this purpose, the injury severity score (ISS) was used as a covariate in a matching procedure using kernel weighting. With this type of matching, all patients who underwent SAE were included in the analyses and were matched to a weighted composite of patients who underwent splenectomy (patients with a larger difference in propensity score received a lower weight). As such, the sample size was retained, and bias was not increased (13).

**HRQOL and QALYs**

For the cost-effectiveness study, HRQOL was expressed in utilities, on a scale from 0 (dead) to 1 (perfect health). The utility values were derived from the prospective SPLENIQ study. As part of this study, the patients completed the EQ-5D-5L instrument (14). The instrument comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), which can be scored with 5 levels, and a visual analog scale. The EQ-5D-5L was completed at 1 week and at 1, 3, 6, and 12 months after the injury. The Dutch tariff was used to calculate utility values (15). To account for background morbidity, an age decrement was used, implying that HRQOL decreased slightly every year. The utility decrement was derived from data from the Netherlands (16).

**Table 1.** Baseline Patient Characteristics

Patient characteristic	SAE	Splenectomy	Pooled
Age	46.9 (19.7)	40.2 (18.1)	45.6 (19.3)
Male	74.1%	85.7%	76.5%
Injury severity score	26.3 (13.5)	43.6 (17.5)	29.5 (15.6)
Multitrauma	60.0%	57.1%	59.4%
Comorbidities at the time of trauma	50.0%	27.3%	30.7%
Quality of life at the time of trauma	0.376 (0.363)	0.390 (0.236)	0.379 (0.311)

Note—Standard deviation in parentheses.  
SAE = splenic artery embolization.

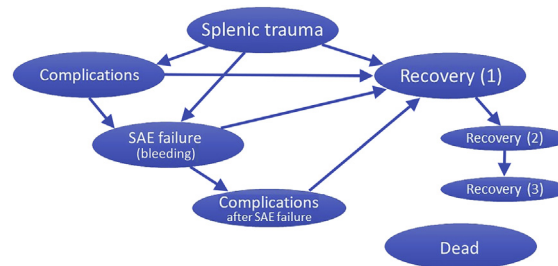
The utility values were combined with survival to calculate QALYs.

## Costs

The procedure-related costs of SAE and splenectomy consisted of 2 components. The first component consisted of costs related to the capital costs of the operating room, salaries of medical personnel employed by the hospital (ie, medical specialists costs were not included), material used in the procedure, and overhead costs. These costs were provided by the financial department of the Elisabeth Tweesteden Ziekenhuis (ETZ; a level 1 trauma center). The second component consisted of costs related to specialists' time. These costs were not included in the ETZ cost estimate, as specialists are generally not employed by the hospital in the Netherlands. Instead, the procedure duration (measured by the financial administration of ETZ) was multiplied by hourly wage rates (ie, €118 per patient-related hour) as reported in the Dutch manual for costing studies (17).

Initial hospitalization following injury was measured as part of the SPLENIQ study. The follow-up health care consumption was measured using the iMTA Medical Consumption Questionnaire (18). The iMTA Medical Consumption Questionnaire was measured at 1, 3, 6, and 12 months after the injury. Resource use was valued using Dutch reference prices, derived from the Dutch manual for costing studies (17). The medication prices were obtained from medicijnkosten.nl, a website hosted by the Dutch National Healthcare Institute.

Since the study had a societal perspective, productivity costs were also included in the model. The productivity losses were measured using the iMTA Productivity Cost Questionnaire (19). The iMTA Productivity Cost Questionnaire was measured at 1, 3, 6, and 12 months after the injury as part of the SPLENIQ study. As per the Dutch health economic guidelines, the friction cost method was used in the calculation of production costs, meaning that productivity costs from long-term absenteeism are limited to the friction period of 14 weeks. The valuation of the production losses was based on the Dutch costing manual. Costs of informal care were not included in the analyses due to the lack of data on informal care consumption. All costs have been expressed in 2019 euros.



**Figure 1.** Schematic structure of cost-effectiveness model. SAE = splenic artery embolization.

## Model Analysis

A Markov model was used to analyze the cost effectiveness of SAE versus splenectomy in the Netherlands. The model used a lifetime time horizon. Furthermore, a societal perspective was adopted to adhere to the Dutch guidelines (20). The outcome of the model, the incremental cost-effectiveness ratio (ICER), is presented as incremental cost per QALY gained.

## Model Structure

The Markov model consisted of 3 main health states (complications after intervention, SAE failure, and recovery) and a dead state. The patients who underwent splenectomy could not enter the SAE failure state. After SAE failure, the patients were assumed to undergo another intervention, either splenectomy or SAE. Transitions to the dead state were possible from all stages. **Figure 1** provides a schematic overview of the cost-effectiveness model.

## Transition Probabilities

Transition probabilities were derived from the retrospective and prospective SPLENIQ study. General population mortality in the Netherlands, derived from Statistics Netherlands (21), was used as the transition probability of dying in the recovery state.

## Sensitivity and Scenario Analyses

In the univariate sensitivity analyses, the impact of parameter uncertainty of individual parameters on the ICER was tested.

A probabilistic sensitivity analysis (PSA) was performed to assess the combined parameter uncertainty in the model. A total of 1,000 simulations were drawn. The results of the PSA were presented in a cost-effectiveness plane and an acceptability curve. In the Netherlands, the appropriate cost-effectiveness threshold is based on disease severity. Disease severity was calculated using the iMTA Disease Burden Calculator (22).

In scenario analyses, the structural uncertainty of the model is assessed. In 1 scenario analysis, the effect of productivity costs was assessed by only including medical costs. In addition, shorter time horizons were tested (1 and

**Table 2.** Total Costs and Effects and Incremental Costs and Effects of SAE and Splenectomy (Discounted and Lifetime Horizon)

Outcome	SAE	Splenectomy	Incremental
QALYs	20.333	17.233	3.100
Total costs	€233,755	€199,620	€34,135
Intervention costs	€942	€1,874	-€932
Medical consumption costs	€149,167	€127,469	€21,699
Productivity costs	€83,645	€70,277	€13,368
ICER			€11,010/ QALY

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; SAE = splenic artery embolization.

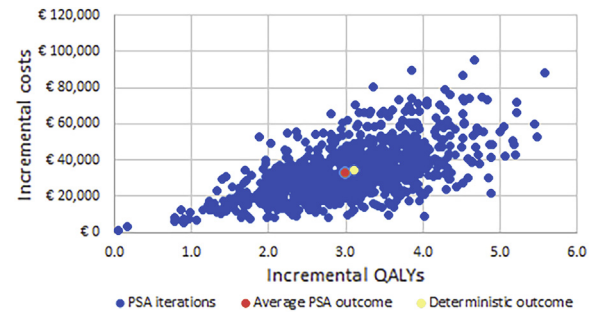
10 years, base case lifetime), and a larger prior for Dirichlet distributions was used (1.0, base case 0.5). In other scenario analyses, transition probabilities were determined differently. First, transition probabilities were determined using a 1:1 propensity matching procedure, as opposed to kernel weighting in the base case analysis. Finally, transition probabilities were derived from the international literature (4,22).

## RESULTS

The average population age in the model was 46 years, and 76.5% of the patients were men. The patients who received SAE had a remaining life expectancy of 31.5 years, whereas propensity-matched patients who received splenectomy had a remaining life expectancy of 26.6 years (patients who received SAE lived on average 4.8 years longer than patients who received splenectomy, undiscounted values). The differences between treatments were concentrated in the first months after trauma; almost all survivors fully recovered after a period of 3 months in both groups. Discounted incremental QALYs of SAE compared with splenectomy were 3.1. QALY differences were mostly driven by differences in survival. The differences in health outcomes were only observed in the first cycles of the model, after which almost all survivors were in the recovery state, from which only background mortality resulted in transitions to the dead state (**Fig E1**, available online at [www.jvir.org](http://www.jvir.org)).

Although intervention costs of splenectomy were higher than those of SAE, total costs were higher for SAE than for splenectomy. This was due to costs in additional life years in the SAE cohort. The incremental costs of medical consumption were €21,699, and incremental productivity costs were €13,368. The total incremental costs were €34,135. The incremental costs per QALY gained were €11,010. **Table 2** provides the outcomes for both SAE and splenectomy.

**Figure 2** shows the outcomes of the PSA. All iterations were in the northeast quadrant. The deterministic outcome and average PSA outcome (€11,020 per QALY) were similar. Based on the disease burden, the cost-



**Figure 2.** Cost-effectiveness plane (discounted values and lifetime horizon). PSA = probabilistic sensitivity analysis; QALY = quality-adjusted life year.

effectiveness threshold was €20,000 per QALY in all 1,000 PSA iterations. The severity-adjusted probability of being cost-effective was 97.4%.

The cost-effectiveness acceptability curve is shown in **Figure 3**. At a willingness to pay of €10,000 per QALY, 43.9% of iterations were cost-effective. At a willingness to pay of €18,000 per QALY, 95.0% of iterations were cost-effective.

**Figure 4** provides the results of the 1-way sensitivity analyses in a tornado diagram. The most influential parameters were the health state costs for the long-term recovery state (ie, recovery 3), since these were used over a long time in the model.

**Table 3** provides the outcomes of the scenario analyses. Zero discounting increased both incremental costs and incremental QALYs. Due to differential discounting of costs and effects in the base case, the undiscounted ICER was higher than in the base case. Excluding the productivity costs reduced the incremental costs of SAE, leading to a lower ICER than the base case. Shorter time horizons (ie, 1 and 5 years) resulted in lower incremental costs and QALYs than the base case, since long-term costs and effects were ignored in the analyses. Using alternative sources for determining transition probabilities did not result in major differences in the ICER.

## DISCUSSION

This study investigates the cost effectiveness of SAE and splenectomy in the Netherlands. SAE was more effective than splenectomy, particularly due to better survival in the first period after trauma, after which almost all patients recovered. HRQOL for recovered patients was comparable to the Dutch general population estimates. QALY losses were mostly related to life years lost in the first period after trauma. Better survival did result in higher costs due to resource consumption for a longer time.

In the absence of other cost-effectiveness studies comparing SAE with splenectomy, the findings of the current study cannot be compared with those of previous studies. However, some comparisons between SAE and splenectomy with a focus on costs and effects have been

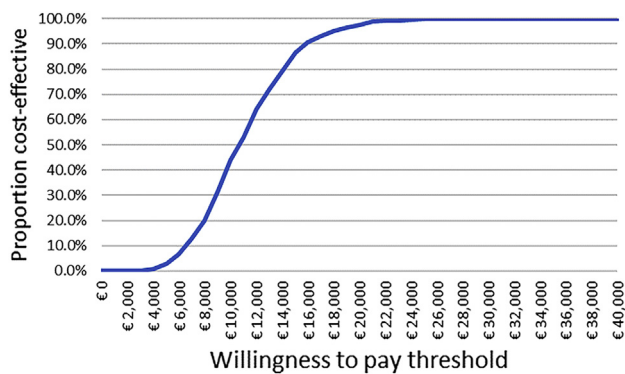


Figure 3. Cost-effectiveness acceptability curve.

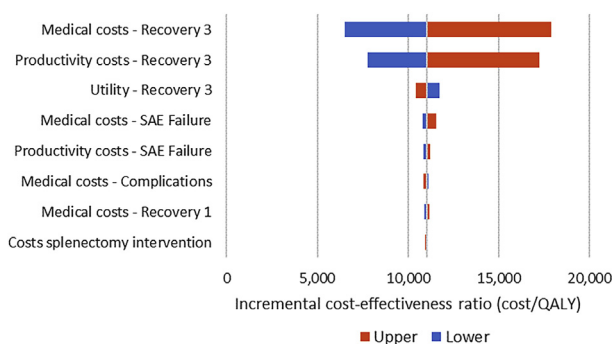


Figure 4. Tornado diagram 1-way sensitivity analyses. QALY = quality-adjusted life year, SAE = splenic artery embolization.

Scenario	Incremental costs	Incremental QALYs	ICER (QALY)
Base case	€34,135	3.100	€11,010
No discounting costs and effects	€64,374	4.058	€15,863
Exclude productivity costs	€20,767	3.100	€6,698
Time horizon, 1 year	€690	0.109	€6,358
Time horizon, 5 years	€8,855	0.488	€18,150
Time horizon, 10 years	€15,388	1.038	€14,823
PSM, 1:1 matching	€3,251	0.298	€10,908
Transition probability literature	€21,091	2.024	€10,418

ICER = incremental cost-effectiveness ratio; PSM = propensity score matching; QALY = quality-adjusted life year.

published. The study by Bruce et al (9) found that intervention costs of SAE are lower than that of splenectomy. Although intervention costs of SAE were lower than those of splenectomy in the current study as well, the absolute intervention costs deviate from the U.S. costs. The costs and cost-effectiveness estimates are often difficult to compare between countries because of international differences in a variety of factors, including patient characteristics, health care financing, (intervention) costs, quality of life values, and study perspective (23). The current

cost-effectiveness study was conducted in the Dutch setting, according to the Dutch health economic guidelines. The suitability of model settings and parameter values should, therefore, be validated before using the outcomes in other countries.

The study by Aiolfi et al (4) compared the outcomes of SAE and splenectomy. Overall, the findings were similar to those observed in the SPLENIQ study and used in the current analyses. It should be noted that the patient groups in the study by Aiolfi et al (4) were significantly different with respect to injury severity and vital signs, and no matching was applied. The SPLENIQ input data were, therefore, preferred over the data from the study by Aiolfi et al (4). In a scenario analysis, transition probabilities were derived from the study by Aiolfi et al (4). The outcomes of that scenario analysis did not differ much from the base case analysis, since transition probabilities, particularly with regard to survival, were not very different.

No randomized controlled trials comparing SAE and splenectomy are available to inform the cost-effectiveness model. Instead, data were derived from the observational SPLENIQ study. In general, observational studies are disposed to selection bias. To mimic the characteristics of a clinical trial, propensity score matching was applied to compare SAE with splenectomy. Although this method balances the patients according to the variables included in the matching procedure, unknown and unobserved differences between patient groups that affect the choice of treatment are not corrected for. In the current study, 1 single variable (ie, ISS) was included in the matching procedure, and other potential confounders were not corrected for. As such, propensity score matching will not reach the level of randomized studies. The matching methodology of kernel weighting versus 1:1 matching did affect the ICER.

The Markov model assumes homogeneity of patients in any specific health state. Although propensity score matching was used to control for baseline differences in ISS, other characteristics have not been controlled for.

Transition probabilities, utility values, and cost estimates were derived from the SPLENIQ study. Although SPLENIQ was a multicenter study, the number of observations in the study were rather limited. The number of observations was further reduced because of the matching procedure necessary for making appropriate comparisons. The uncertainty around point estimates was reflected in the PSA. Still, the vast majority of iterations (ie, 97.4%) were cost-effective at an appropriate threshold of €20,000 per QALY.

The procedure-related costs were calculated using cost estimates from ETZ, which was similar to a benchmark cost price for top clinical care hospitals in the Netherlands. The procedure-related cost might be different for academic hospitals. However, the impact on the results is likely to be minimal, since procedure-related costs only represent a small proportion of total costs for both SAE and splenectomy arms in the cost-effectiveness study.

Furthermore, procedure time is likely to be similar in academic hospitals, which reduces potential differences in cost estimates.

A substantial portion of patients with splenic injuries receive NOM. Since NOM was outside the scope of this study, it was not included as a treatment option in the cost-effectiveness model. Including NOM in the model would necessitate information on transition probabilities. However, patients receiving NOM are likely to have a different prognosis than patients who receive SAE or splenectomy. Patients, thus, have to be matched before NOM could be included in the cost-effectiveness analysis. A recent study (24) on the cost effectiveness of SAE versus NOM in the United States showed that SAE was more expensive and resulted in less QALYs. Future studies have to explore how these results translate to other countries.

In conclusion, SAE results in more QALYs than splenectomy. The intervention costs for SAE are lower than for splenectomy, but the medical consumption and productivity costs in later years are higher for SAE due to better survival. SAE was found to be cost-effective compared with splenectomy.

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None of the authors have identified a conflict of interest.

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## APPENDIX A

### Patient Population

Patient-level data were derived from the SPLENIQ study, a single-center retrospective and a multicenter prospective observational study investigating the effects of nonoperative management, splenic artery embolization (SAE), and splenectomy in patients who suffered splenic injury after blunt abdominal trauma, with the primary aim of examining patients' quality of life (1). The SPLENIQ study included adult patients with a splenic injury after trauma. The inclusion and exclusion criteria of the SPLENIQ study have been described elsewhere (1). The study has been approved by the Medical Ethical Committee Brabant (METC Brabant, protocol numbers NL54339.028.15 and NL54542.028.016 for the retrospective and prospective studies, respectively). In the prospective study, patients were included in the period between March 2018 and December 2018, with a 1-year follow-up. In the retrospective study, patients were included in the period between January 2005 and February 2017 were included. The baseline population characteristics are presented in [Table 1](#).

As data were derived from an observational study, patients were not randomly allocated to treatment. Instead, physicians used patient characteristics to determine the perceived optimal treatment. To control for differences between patients who underwent SAE and those who underwent splenectomy, in this way reducing selection bias, propensity score matching was performed. For this purpose, the injury severity score was used as a covariate in a matching procedure using kernel weighting. With this type of matching, all patients who underwent SAE were included in the analyses and were matched to a weighted composite of patients who underwent splenectomy (patients with a larger difference in propensity score received a lower weight). As such, the sample size was retained, and bias was not increased (2).

### Health-Related Quality of Life and Quality-Adjusted Life Years

For the cost-effectiveness study, health-related quality of life (HRQOL) was expressed in utilities, on a scale from 0 (dead) to 1 (perfect health). The utility values were derived from the prospective SPLENIQ study. As part of this study, the patients completed the EQ-5D-5L instrument (3). The instrument comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), which can be scored with 5 levels, and a visual analog scale. The EQ-5D-5L was completed at 1 week and at 1, 3, 6, and 12 months after the injury. The Dutch tariff was used to calculate utility values (4). To account for background morbidity, an age decrement was used, implying that HRQOL decreased slightly every year. The utility decrement was derived from data from the Netherlands (5).

The utility values were combined with survival to calculate quality-adjusted life years.

### Costs

The procedure-related costs of SAE and splenectomy consisted of 2 components. The first component consisted of costs related to the capital costs of the operating room, salaries of medical personnel employed by the hospital (ie, medical specialists costs were not included), material used in the procedure, and overhead costs. These costs were provided by the financial department of the Elisabeth Tweesteden Ziekenhuis (ETZ; a level 1 trauma center). The second component consisted of costs related to specialists' time. These costs were not included in the ETZ cost estimate, as specialists are generally not employed by the hospital in the Netherlands. Instead, the procedure duration (measured by the financial administration of ETZ) was multiplied by hourly wage rates (ie, €118 per patient-related hour) as reported in the Dutch manual for costing studies (6).

Initial hospitalization following injury was measured as part of the SPLENIQ study. The follow-up health care consumption was measured using the iMTA Medical Consumption Questionnaire (7). The iMTA Medical Consumption Questionnaire was measured at 1, 3, 6, and 12 months after the injury. Resource use was valued using Dutch reference prices, derived from the Dutch manual for costing studies (6). The medication prices were obtained from [medicijnkosten.nl](#), a website hosted by the Dutch National Healthcare Institute.

Since the study had a societal perspective, productivity costs were also included in the model. The productivity losses were measured using the iMTA Productivity Cost Questionnaire (8). The iMTA Productivity Cost Questionnaire was measured at 1, 3, 6, and 12 months after the injury as part of the SPLENIQ study. As per the Dutch health economic guidelines, the friction cost method was used in the calculation of production costs, meaning that productivity costs from long-term absenteeism are limited to the friction period of 14 weeks. The valuation of the production losses was based on the Dutch costing manual. Costs of informal care were not included in the analyses due to the lack of data on informal care consumption. All costs have been expressed in 2019 euros.

### Model Analysis

A Markov model was used to analyze the cost effectiveness of SAE versus splenectomy in the Netherlands. The model used a lifetime time horizon. The cycle length was 1 month to account for rapid transitions between health states following the intervention. The annual discount rates were 4% for costs and 1.5% for effects, as per the Dutch health economic guidelines (9). Furthermore, a societal perspective was adopted to adhere to the Dutch guidelines. The outcome of the model, the incremental cost-effectiveness ratio, is presented as incremental cost per quality-adjusted life year gained. The model was developed in Microsoft Excel 2013 (Microsoft, Redmond, Washington).



## Model Structure

The Markov model consisted of 3 main health states (complications after intervention, SAE failure, and recovery) and a dead state. Whether the cause of death was related to spleen injury or not was not distinguished, since values for costs and quality of life of the dead state are the same (ie, no costs and quality of life equal to 0), regardless of the cause of death. SAE failure was defined as bleeding of the spleen after intervention. The patients who underwent splenectomy could not enter the SAE failure state. After SAE failure, the patients were assumed to undergo another intervention, either splenectomy or SAE. The recovery state consisted of 2 tunnel states and a final state to account for differences in costs and HRQOL regarding the time spent in this state. Transitions to the dead state were possible from all stages. **Figure 1** shows a schematic overview of the cost-effectiveness model.

## Transition Probabilities

Transition probabilities were derived from the retrospective and prospective SPLENIQ study. General population mortality in the Netherlands, derived from Statistics Netherlands (10), was used as the transition probability of dying in the recovery state.

**Table E1** provides the base case input values (transition probabilities, utility values, and cost estimates) for the cost-effectiveness model (5).

## Sensitivity and Scenario Analyses

In the univariate sensitivity analyses, the impact of parameter uncertainty of individual parameters on the incremental cost-effectiveness ratio was tested. For this purpose, limits of the 95% confidence intervals for utilities (beta distribution) and costs (gamma distribution) as observed in the SPLENIQ data were used as lower and upper limits.

A probabilistic sensitivity analysis (PSA) was performed to assess the combined parameter uncertainty in the model. For this purpose, the Dirichlet distribution was used for transition probabilities, a beta distribution was used for utilities, and a gamma distribution was used for cost estimates. A total of 1,000 simulations were drawn. The results of the PSA were presented in a cost-effectiveness plane and an acceptability curve. In the Netherlands, the appropriate cost-effectiveness threshold is based on disease severity. Disease severity was calculated using the iMTA Disease Burden Calculator, using patients' age, gender, and quality-adjusted life expectancy estimates obtained from the PSA. Uncertainty in the disease severity estimates was used to inform the severity-adjusted probability of being cost-effective (11).

In scenario analyses, the structural uncertainty of the model is assessed. In 1 scenario analysis, the effect of productivity costs was assessed by only including medical

costs. In addition, shorter time horizons were tested (1 and 10 years, base case lifetime), and a larger prior was used for Dirichlet distributions (1.0, base case 0.5). In other scenario analyses, transition probabilities were determined differently. First, transition probabilities were determined using 1:1 propensity matching procedure, as opposed to kernel weighting in the base case analysis. Finally, transition probabilities were derived from the international literature: transition probabilities for transitioning to adverse events and dead states after the initial intervention were derived from the study by Aiolfi et al (12), supplemented with transition probabilities for SAE failure after SAE from the study by Scarborough et al (13). The transition probabilities must sum to 1. Since transitions to adverse events, SAE failure, and dead states after initial intervention were derived from the literature, transition probabilities for the remaining recovery after intervention health state could be determined by calculus. The mortality rates for the complication health state were determined on the basis of international literature, combined with the prevalence of specific types of adverse events as observed in Aiolfi et al (12).

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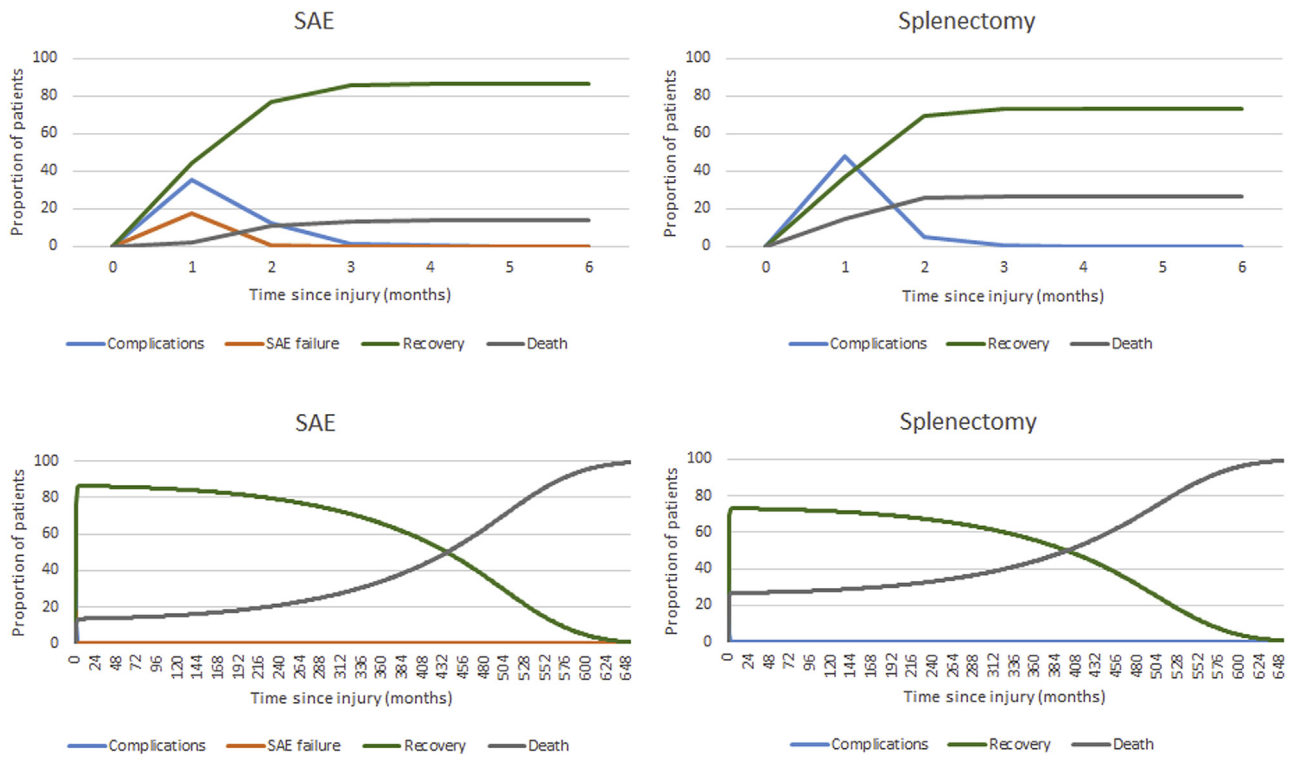


Figure E1. Markov traces. SAE = splenic artery embolization.

**Table E1.** Input Value Cost-Effectiveness Model

Parameter	Base case value	Standard error	Source
Transition probabilities, SAE			
SAE to adverse events	35.6%		SPLENIQ retrospective and prospective study
SAE to SAE failure	17.8%		SPLENIQ retrospective and prospective study
SAE to recovery	44.4%		SPLENIQ retrospective and prospective study
SAE to dead state	2.2%		SPLENIQ retrospective and prospective study
Adverse events to adverse events	10.0%		Assumption
Adverse events to recovery	72.1%		Calculus
Adverse events to dead state	17.9%		Literature on adverse events
SAE failure to adverse events	47.6%		Assumption
SAE failure to SAE failure	0.5%		Expert opinion
SAE failure to recovery	37.7%		Calculus
SAE failure to dead state	14.1%		Calculus
Proportion of patients receiving SAE after SAE failure	3.0%		SPLENIQ retrospective and prospective study
Transition probabilities, splenectomy			
Splenectomy to adverse events	48.2%		SPLENIQ retrospective and prospective study
Splenectomy to recovery	37.3%		SPLENIQ retrospective and prospective study
Splenectomy to dead state	14.5%		SPLENIQ retrospective and prospective study
Adverse events to adverse events	10.0%		Assumption
Adverse events to recovery	67.2%		Calculus
Adverse events to dead state	22.8%		Literature on adverse events
Utility values			
Adverse events	0.551	0.085	SPLENIQ prospective study
SAE failure	0.638	0.171	SPLENIQ prospective study
Recovery cycle 1	0.702	0.056	SPLENIQ prospective study
Recovery cycle 2	0.809	0.034	SPLENIQ prospective study
Recovery cycle 3 onward	0.852	0.026	SPLENIQ prospective study
Age decrement utilities	0.002	0.000	Heijink et al (5)
Intervention costs			
SAE	€614	59	Financial administration
Splenectomy	€1,874	115	Financial administration
Health care costs			
Adverse events	€13,480	5,122	SPLENIQ prospective study
SAE failure	€3,736	3,596	SPLENIQ prospective study
Recovery cycle 1	€4,960	1,657	SPLENIQ prospective study
Recovery cycle 2	€642	236	SPLENIQ prospective study
Recovery cycle 3 onward	€701	307	SPLENIQ prospective study
Productivity costs			
Adverse events	€1,628	700	SPLENIQ prospective study
SAE failure	€5,330	1,742	SPLENIQ prospective study
Recovery cycle 1	€2,865	612	SPLENIQ prospective study
Recovery cycle 2	€953	434	SPLENIQ prospective study
Recovery cycle 3 onward	€402	260	SPLENIQ prospective study

SAE = splenic artery embolization.