Health Intervention and Technology Assessment Program

What is the best value for money for preventing carbamazepine-induced severe drug reactions in Thailand?

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Outline

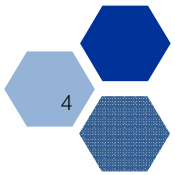
- Background
- Objective
- Methodology
- Result
- Feasibility and budget impact analysis
- Conclusion

Background

- Topic is prioritized by stakeholders under “Research for development of health benefit package under universal coverage scheme”.
- Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe adverse drug reactions and life-threatening. These affect quality of life and health expenditure.
- The association between HLA-B*1502 and SJS/TEN in carbamazepine (CBZ) user.
- HLA-B*1502 screening is not covered in the health benefit package of the Universal Coverage Scheme (UC).

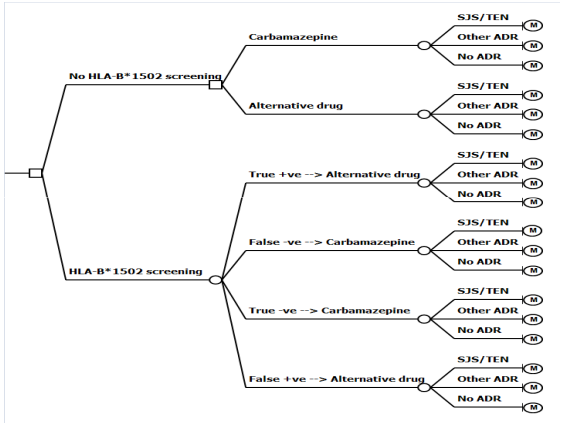
Objective

- To assess the value for money of HLA-B*1502 screening compared to
  - The current practice in which patients received CBZ without the screening
  - Not prescribing CBZ but alternative drugs with higher cost and less likelihood to develop severe reactions



Methodology

- Study design
  - Retrospective descriptive study
  - Cost-utility analysis
  - Model-based economic evaluation
    - Decision tree
    - Markov model
- Target population
  - Epilepsy
  - Neuropathic pain
- Perspective
  - Societal perspective



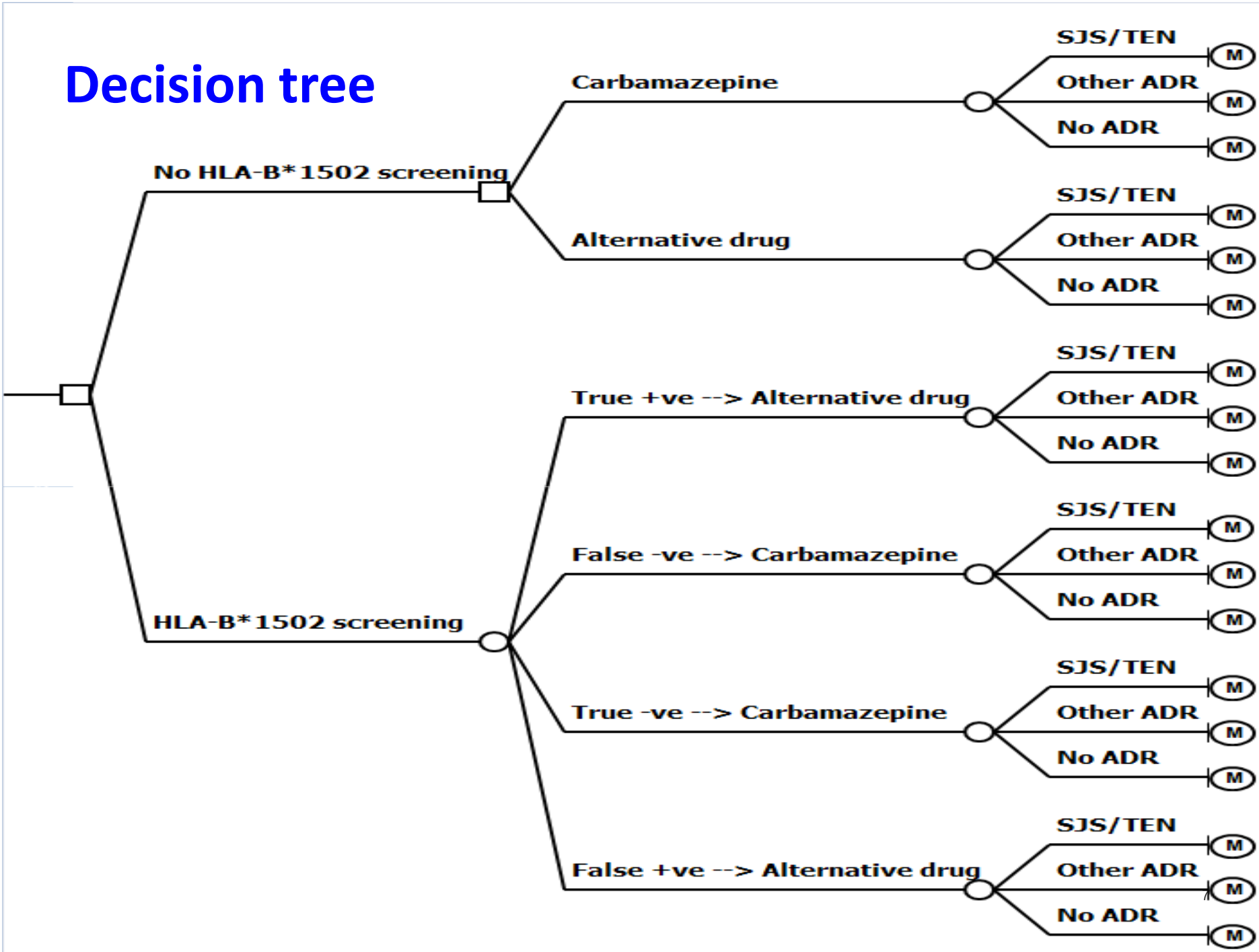
Methodology

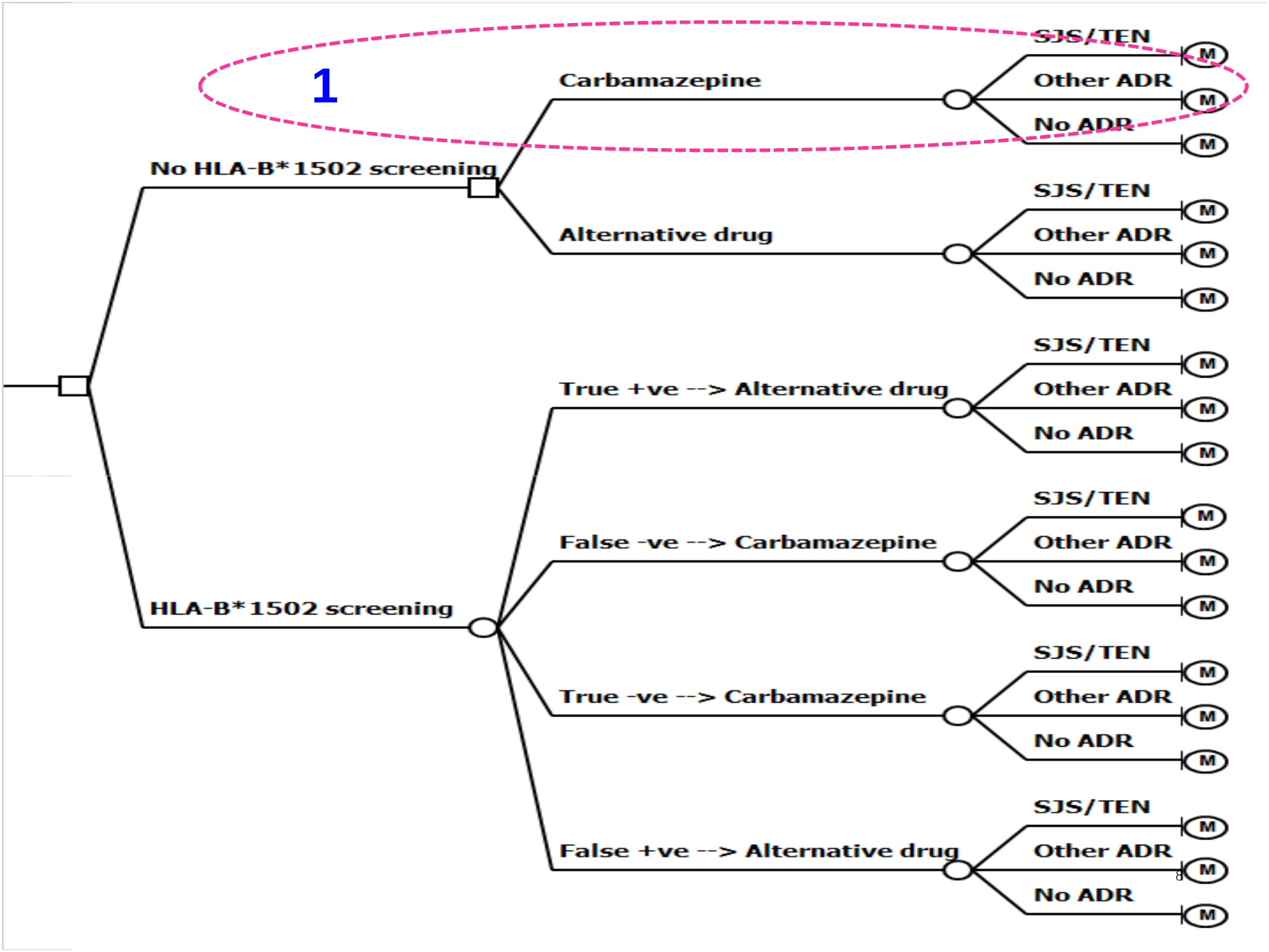
- **Comparator**
  - CBZ without pre-treatment HLA-B*1502 screening (current practice)
- **Interventions**
  - HLA-B*1502 screening before start CBZ
  - Start with alternative drugs

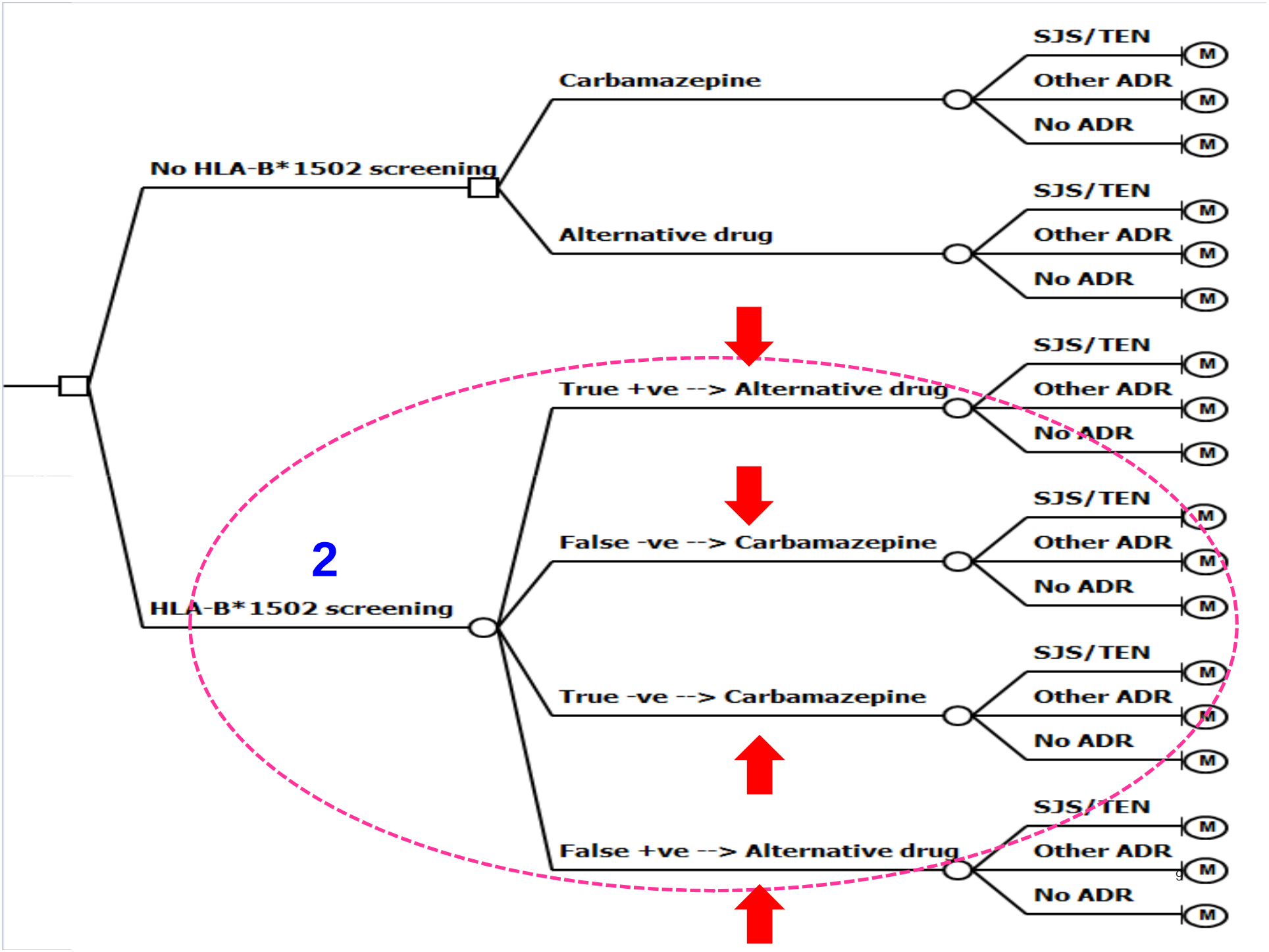
Alternative drugs

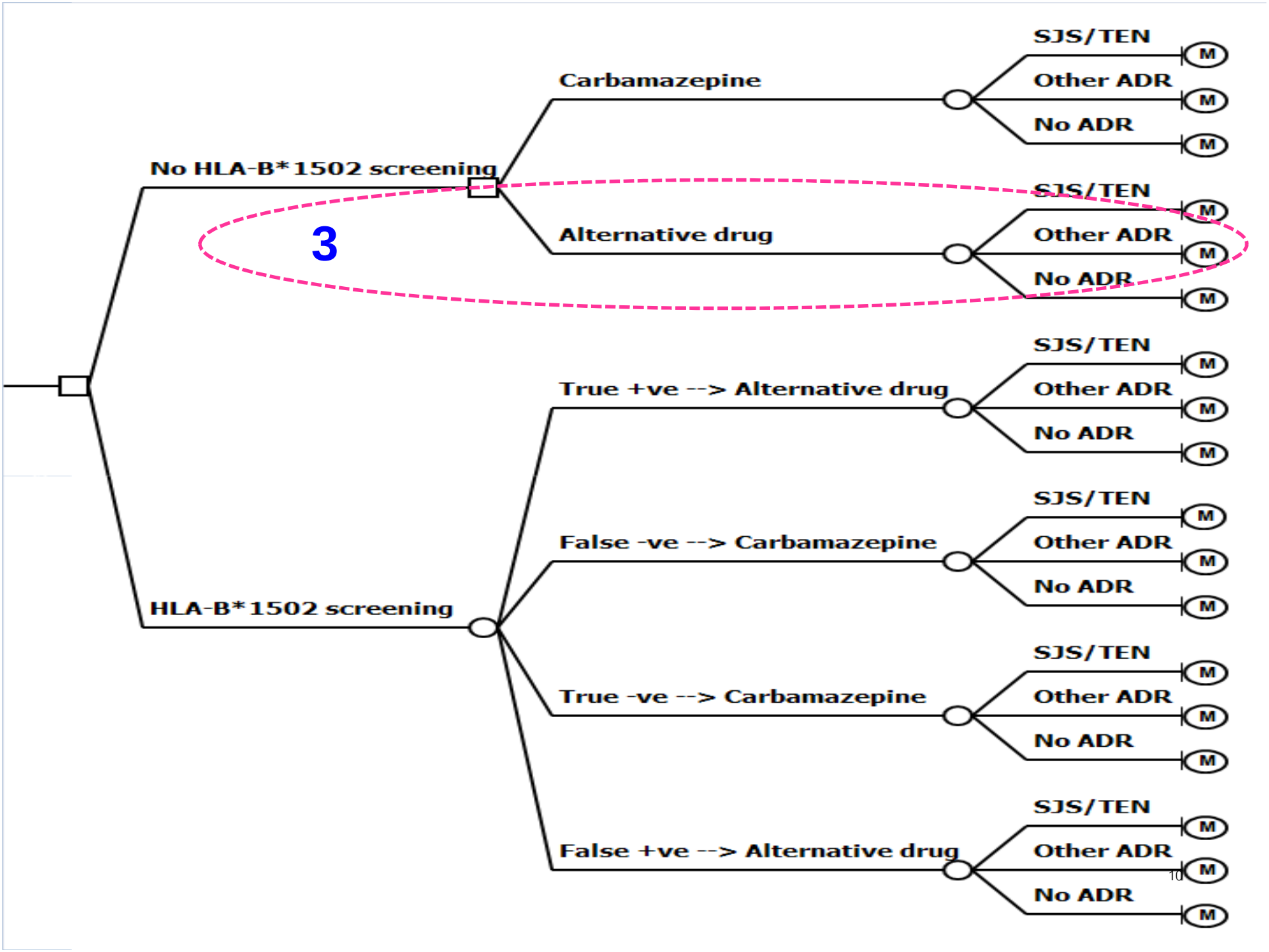
- **epilepsy**: valproic acid 500 mg (1.5g/d)
- **neuropathic pain**: gabapentin 300 mg (1.2g/d)

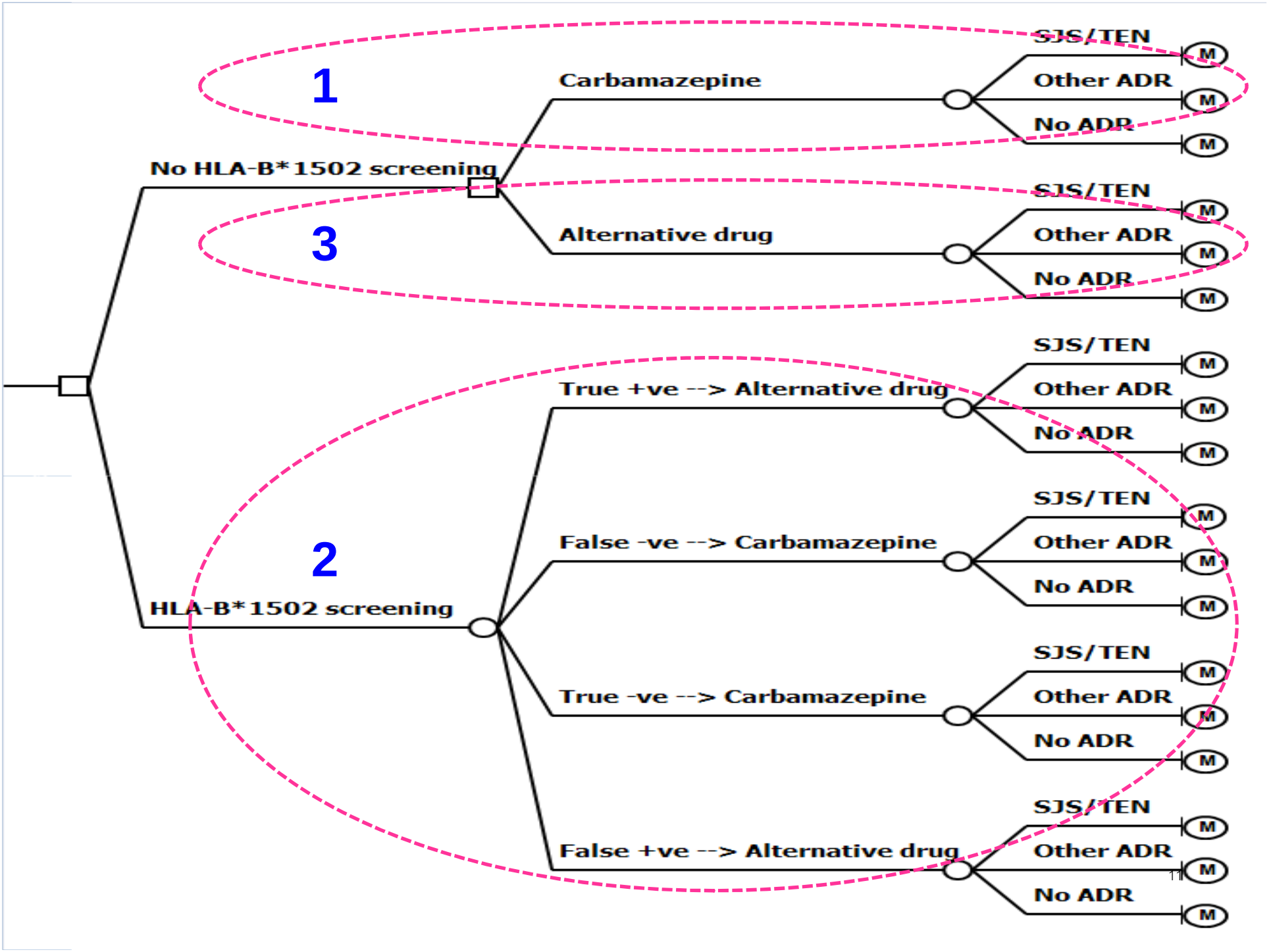
Decision tree




1
No HLA-B*1502 screening
Carbamazepine
Alternative drug
HLA-B*1502 screening
True +ve --> Alternative drug
False -ve --> Carbamazepine
True -ve --> Carbamazepine
False +ve --> Alternative drug
SJS/TEN
Other ADR
No ADR
M

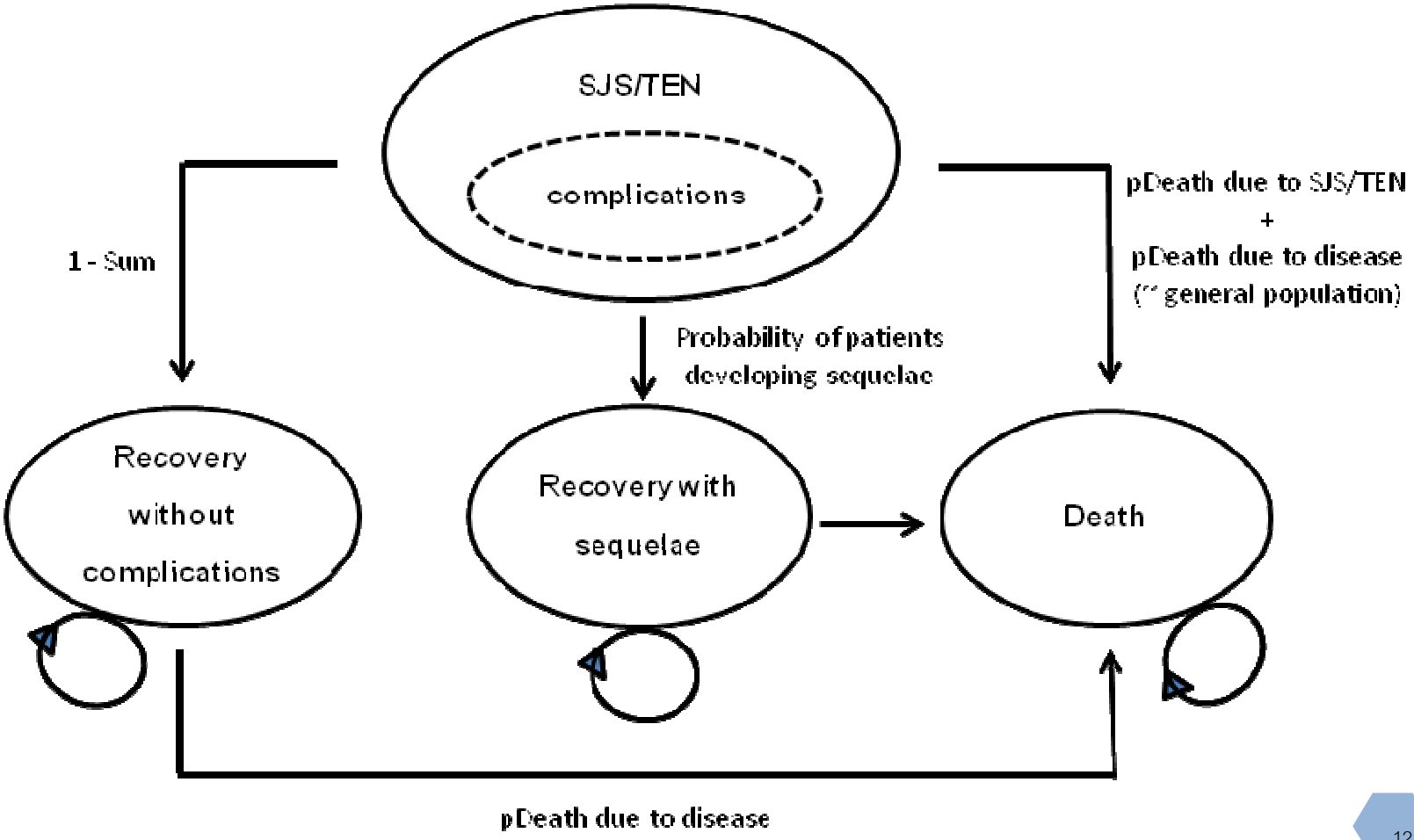

No HLA-B*1502 screening
Carbamazepine
Alternative drug
SJS/TEN
Other ADR
No ADR
M
HLA-B*1502 screening
2
True +ve --> Alternative drug
False -ve --> Carbamazepine
True -ve --> Carbamazepine
False +ve --> Alternative drug


No HLA-B*1502 screening
Carbamazepine
SJS/TEN
Other ADR
No ADR
Alternative drug
SJS/TEN
Other ADR
No ADR
3
HLA-B*1502 screening
True +ve --> Alternative drug
SJS/TEN
Other ADR
No ADR
False -ve --> Carbamazepine
SJS/TEN
Other ADR
No ADR
True -ve --> Carbamazepine
SJS/TEN
Other ADR
No ADR
False +ve --> Alternative drug
SJS/TEN
Other ADR
No ADR


1
2
3
No HLA-B*1502 screening
HLA-B*1502 screening
Carbamazepine
Alternative drug
True +ve --> Alternative drug
False -ve --> Carbamazepine
True -ve --> Carbamazepine
False +ve --> Alternative drug
SJS/TEN
Other ADR
No ADR
M

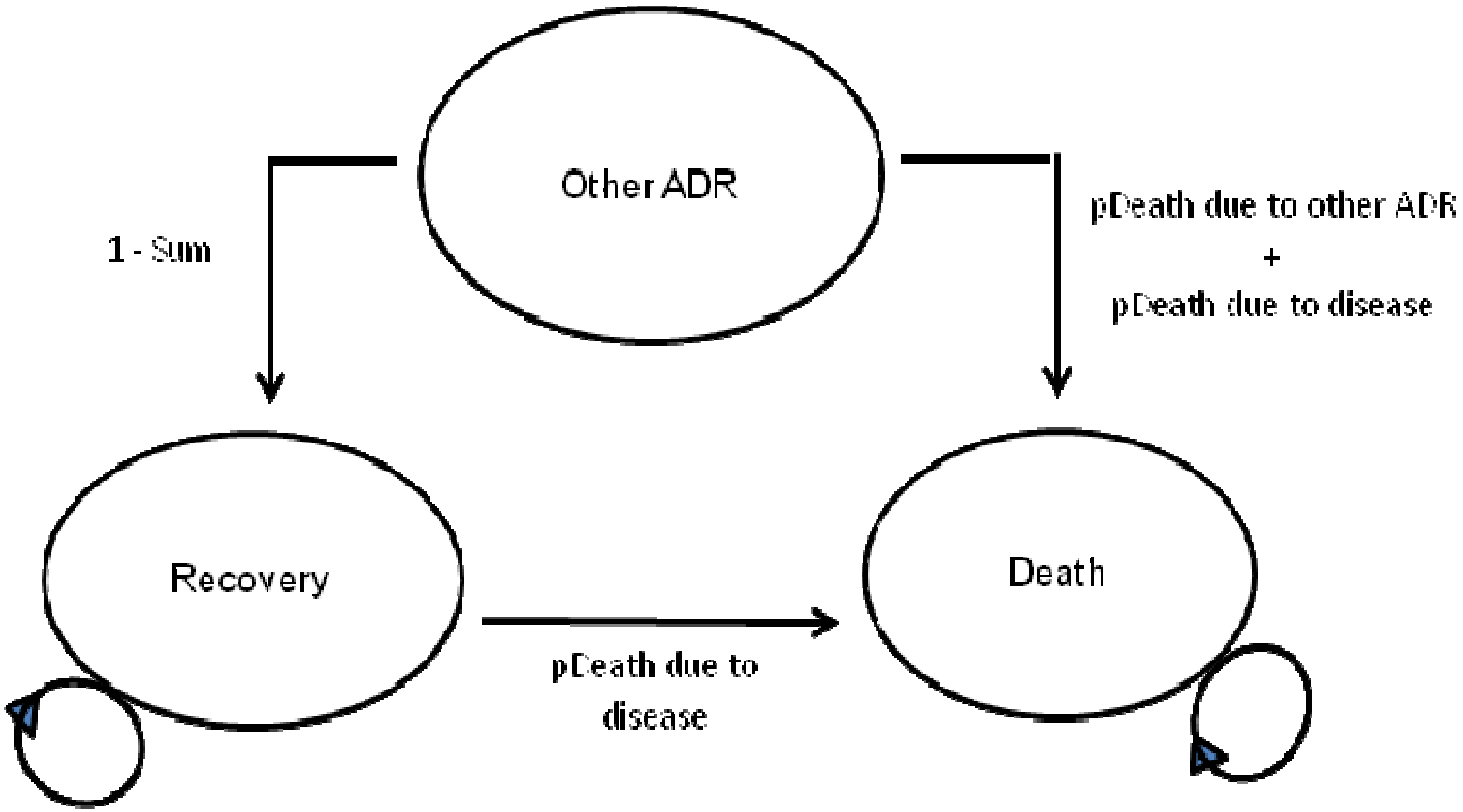
Markov model

SJS/TEN



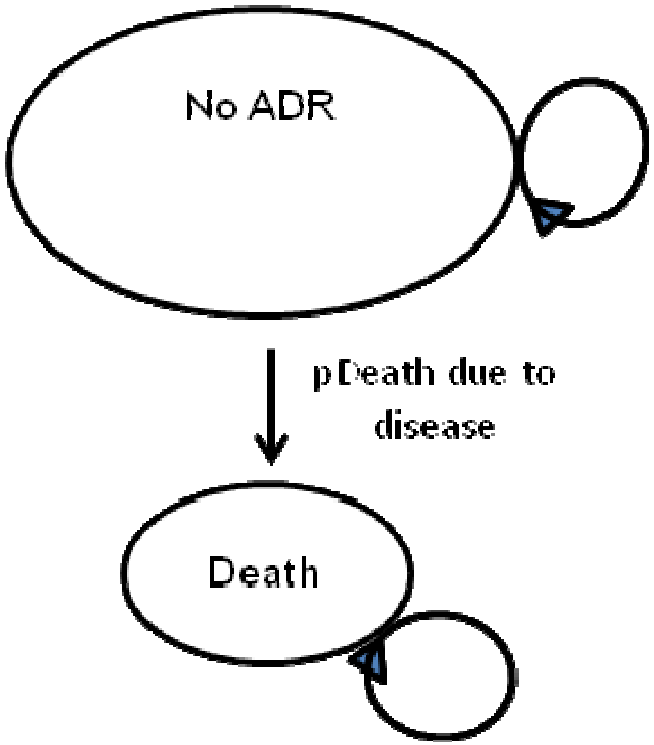
Markov model

Other ADR



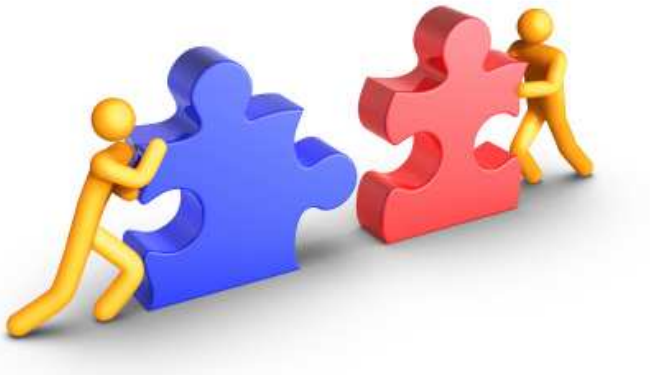
Markov model

No ADR



Methodology

- Time horizon
  - Life-time
  - Treatment period
    - epilepsy: 4 years
    - neuropathic pain: 2 years
- Discount rate
  - 3% (cost and outcome)
- Data collection
  - Case - control
  - Cost - outcome



Data collection: cost

Cost		Source	Perspective	
Category	Subcategory		Provider	Societal
Direct medical	Treatment/ Health care -Drug -Non drug -Procedure	Review chart DMSIC Costing menu	Cost	Cost
Direct non medical	Travel Food House Facilities Personal care	Interview patient	-	Charge
	Time loss	Interview patient	-	Productivity cost

Data collection: outcome

1

- Collect **health preference** by using EQ-5D-TH questionnaire

2

- Calculate **utility score**
  - 0 = death, 1 = full health

3

- Calculate **Quality adjusted life years** (QALYs)
- QALYs = Utility score * Life Years

Incremental cost-effectiveness ratio (ICER)

$$\text{ICER} = \frac{\text{Cost of tx A- cost of tx B}}{\text{QALY A} - \text{QALY B}}$$

A: new intervention

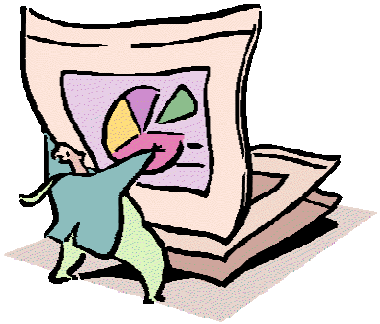
B: existing intervention

CEA threshold in Thailand

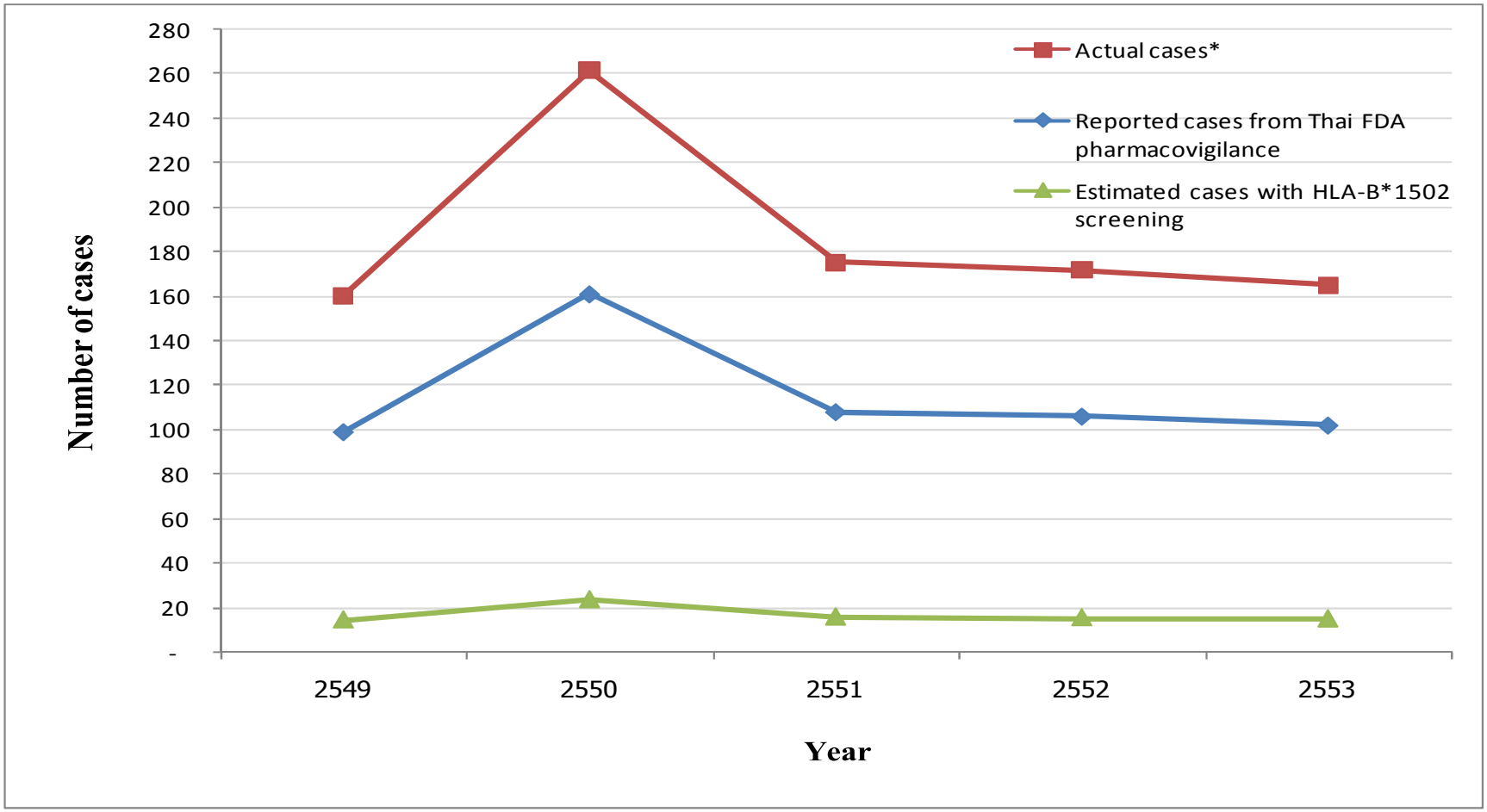
- < 1 GDP ➡ very cost – effective
- 1 -3 GDP ➡ maybe cost – effective
- > 3 GDP ➡ maybe not cost – effective

Result

- Estimating number of SJS/TEN averted
- Incremental cost-effectiveness ratio (ICER)
- Probabilistic sensitivity
- One-way sensitivity



Estimating number of SJS/TEN averted



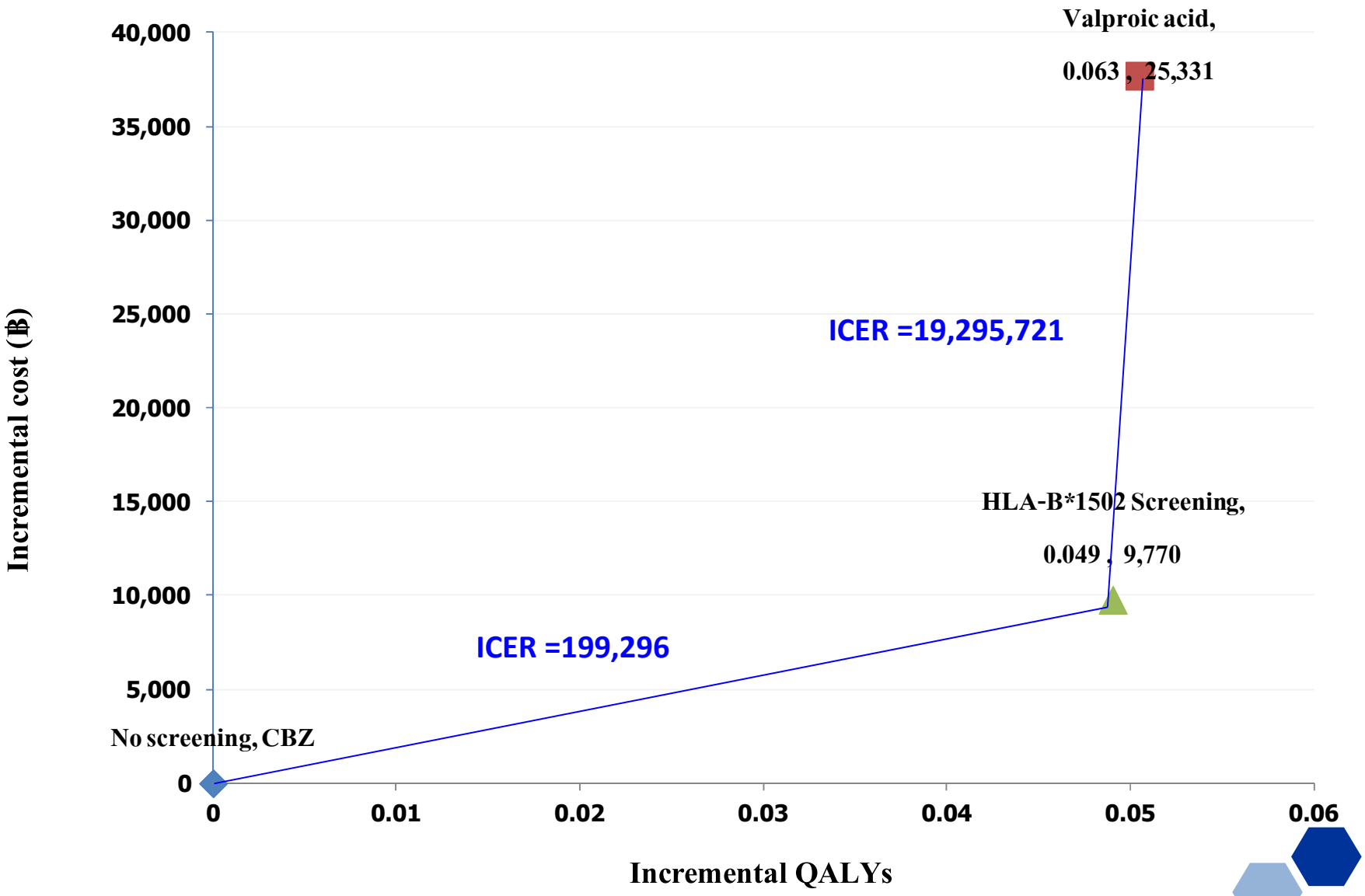
***actual cases calculated from FDA cases report x factor for under-reporting x factor for incorrect submission (ref: Prachachalerm W., 2008)**

EPILEPSY

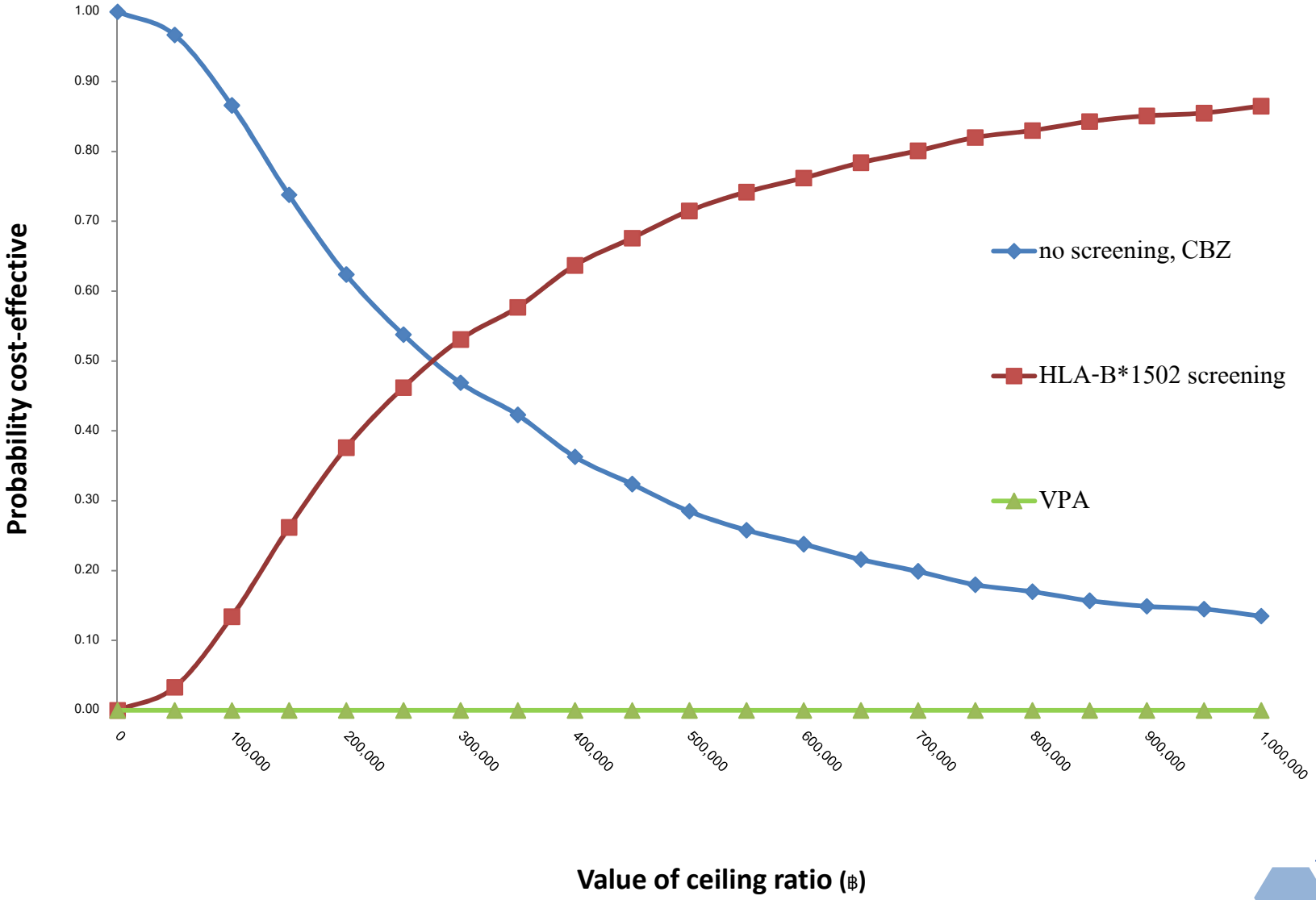
- **ICER**

	CBZ without screening	HLA_B*1502 Screening	VPA without screening
Cost	41,155	50,925	78,851
QALYs	25.168	25.217	25.219
Average ICER		**199,296**	**746,889**
ICER			**19,295,721**

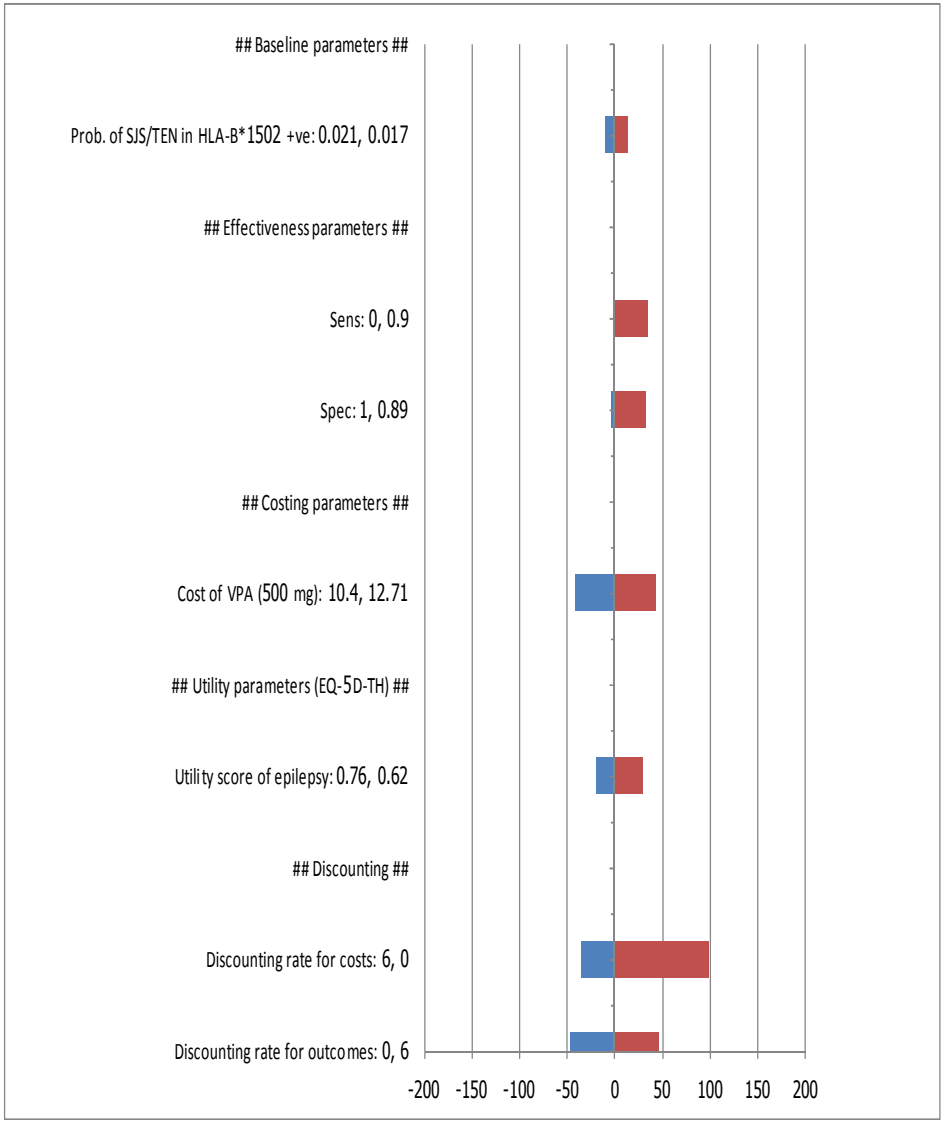
ICER


Valproic acid,
0.063 , 25,331
ICER =19,295,721
HLA-B*1502 Screening,
0.049 , 9,770
ICER =199,296
No screening, CBZ
40,000
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Incremental cost (฿)
0
0.01
0.02
0.03
0.04
0.05
0.06
Incremental QALYs

Probabilistic sensitivity



One-way sensitivity



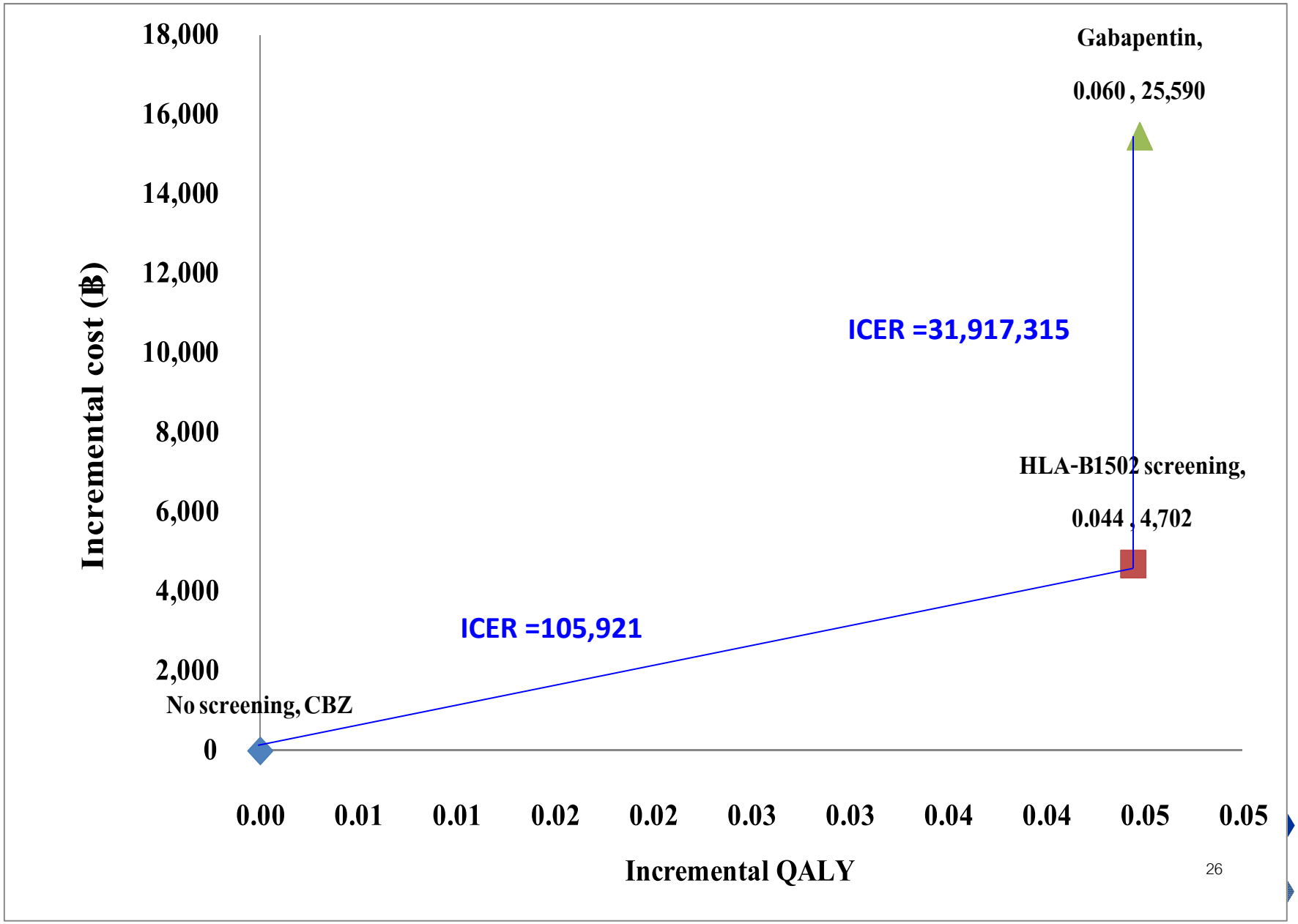
- Important parameter
  - Discounting rate
  - Cost of VPA
  - Sensitivity
  - Specificity

NEUROPATHIC PAIN

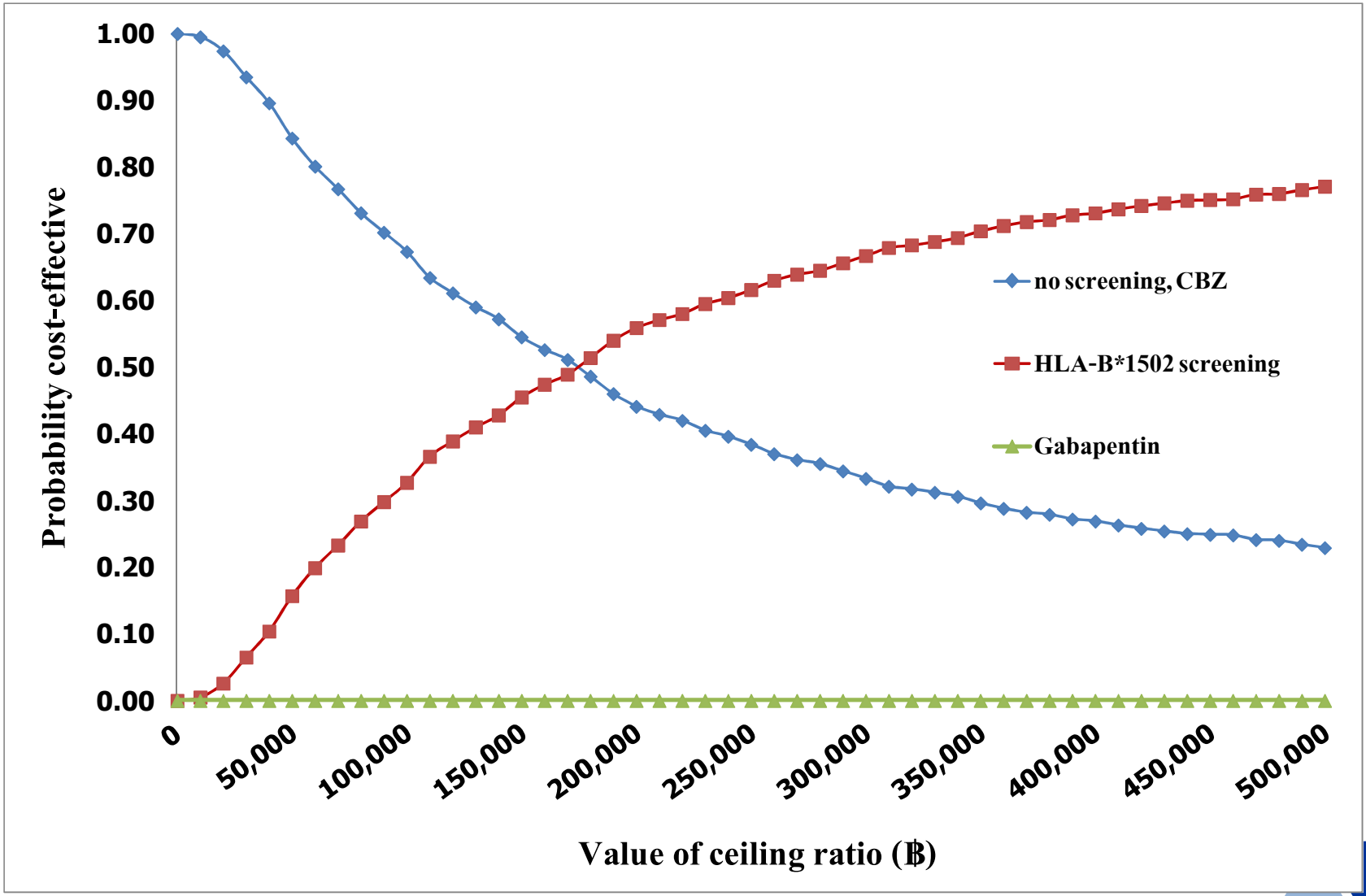
- **ICER**

	CBZ without screening	HLA_B*1502 Screening	VPA without screening
Cost	18,194	22,895	33,659
QALYs	25.65	25.69	25.69
Average ICER		**105,921**	**345,789**
ICER			**31,917,315**

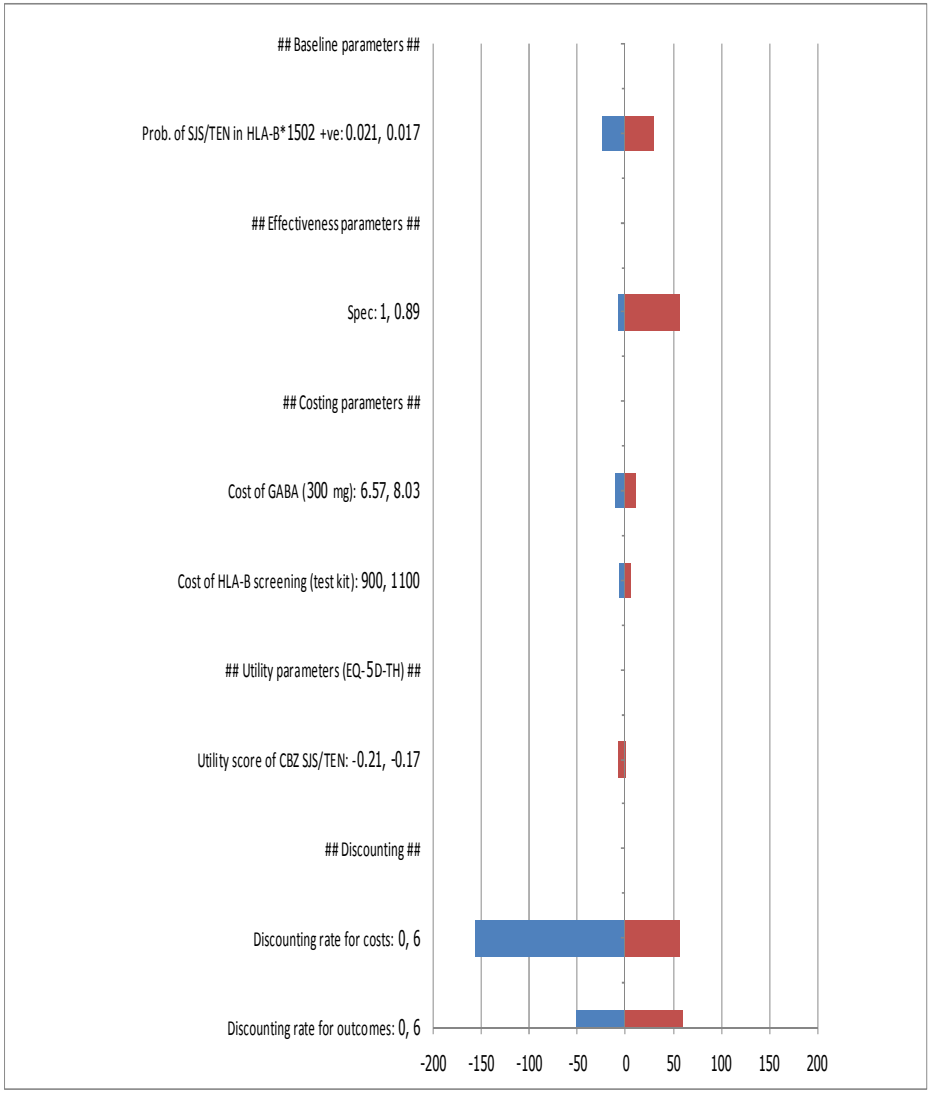
ICER


18,000
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
Incremental cost (฿)
Gabapentin,
0.060 , 25,590
ICER =31,917,315
HLA-B1502 screening,
0.044 , 4,702
ICER =105,921
No screening, CBZ
0.00
0.01
0.01
0.02
0.02
0.03
0.03
0.04
0.04
0.05
0.05
Incremental QALY

Probabilistic sensitivity



One-way sensitivity



- Important parameter
  - Discounting rate
  - Specificity
  - Probability of SJS/TEN in HLA-B*1502 positive
  - Cost of GABA

Feasibility and Budget impact

- Estimation for new cases of CBZ in Thailand
- Laboratory distribution in Thailand
- Budget impact analysis

Estimation for new cases of CBZ in Thailand

- Direct usage data (new cases) are not available – 2 methods used to estimated the data

Method	Range of estimation
Estimated from survey data	~ 14,183 – 55,314/ year
Inferred from SJS/TEN reported in Thailand	~ 20,435 – 70,000/ year

Laboratory distribution in Thailand

- Equipment (PCR) machines are available
- DMSC: Multiplex allele specific PCR (validated in house method)
- 12 Regional Medical Sciences center
- Trained for DMSc-1502 or equivalent test
- 1 week turn around time is possible with current logistic (3 days is possible with more costs spend on logistics)
- Inter laboratory QC is in place (KKU, MU, CU, Rajvithi)

Budget impact analysis

	Min	Max
Total test (no. of new case)	14,183	55,314
Budget impact (Baht)	14,183,000	55,314,000

- Based on DMSc-1502 @ 1,000 Baht/test cover logistics and training cost

Conclusion

- HLA-B*1502 screening might reduce 90% of SJS/TEN cases per year from CBZ
- HLA-B*1502 screening represents good value for money for preventing severe drug reactions from the use of CBZ in Thailand


Thank you!