

# The cost-effectiveness of induction immunosuppression in kidney transplantation

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# Background

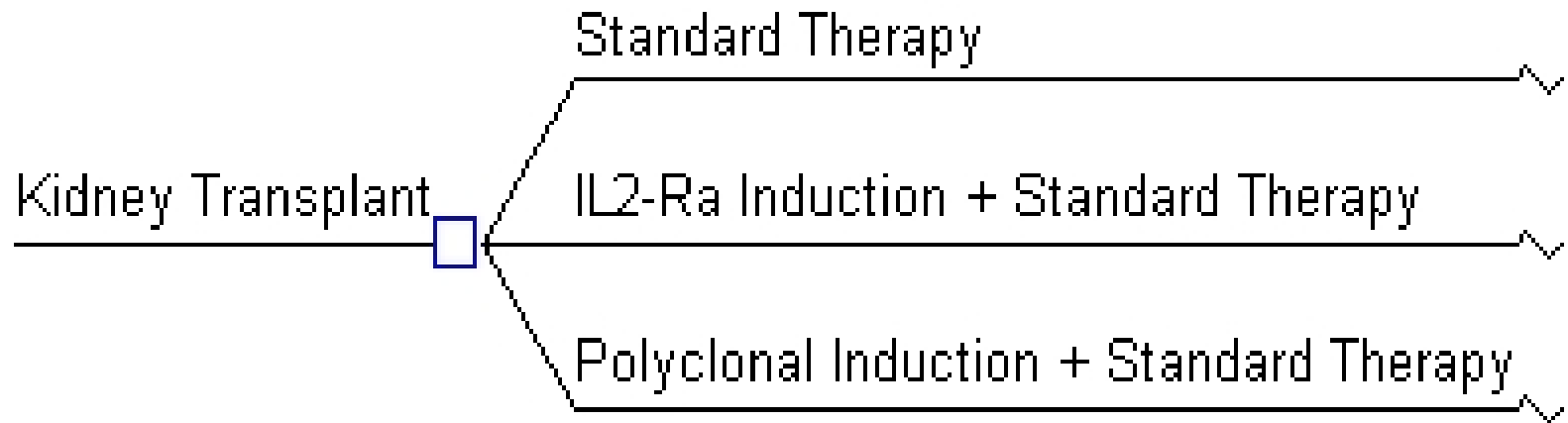
- Induction therapy is specific monoclonal or polyclonal antibody therapy given at the time of transplantation to ↓ acute rejection and delayed graft function
- Monoclonal antibodies include Interleukin 2 receptor antagonists (IL-2Ra) – basiliximab, daclizumab.
  - Consistent beneficial effects compared to standard therapy in systematic reviews
  - Recommended in clinical practice guidelines
- IL-2Ra use in Australia is limited by perceived uncertainty in low risk recipients and cost considerations

# Aim

To compare the cost effectiveness of:

- (i) IL-2Ra induction plus standard therapy versus standard therapy alone (no induction)
- (ii) IL-2Ra induction versus polyclonal induction therapy

# Decision Tree



# Economic Question

From an Australian health system perspective  
over a 20 year time frame

- Costs (AU\$)
- Survival (Life years)
- Quality adjusted survival (QALYs)

# Incremental cost effectiveness ratio (ICER)

$$ICER = \frac{TotalCost_{STANDARD\_THERAPY+IL-2RA} - TotalCost_{STANDARD\_THERAPY}}{Effectiveness_{STANDARD\_THERAPY+IL-2RA} - Effectiveness_{STANDARD\_THERAPY}}$$

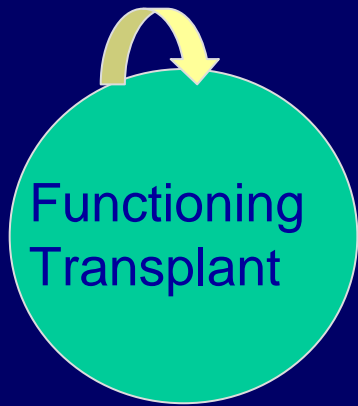
$$ICER = \frac{TotalCost_{IL-2RA} - TotalCost_{POLYCLONAL\_ANTIBODY}}{Effectiveness_{IL-2RA} - Effectiveness_{POLYCLONAL\_ANTIBODY}}$$

# Markov Model

Modelled transplant outcomes in hypothetical cohorts of transplant recipients treated with 3 induction strategies.

1. Structured the model to include all potential consequences of treatment and disease process
2. Populated the model with all relevant evidence
3. Tested the uncertainties using sensitivity analyses

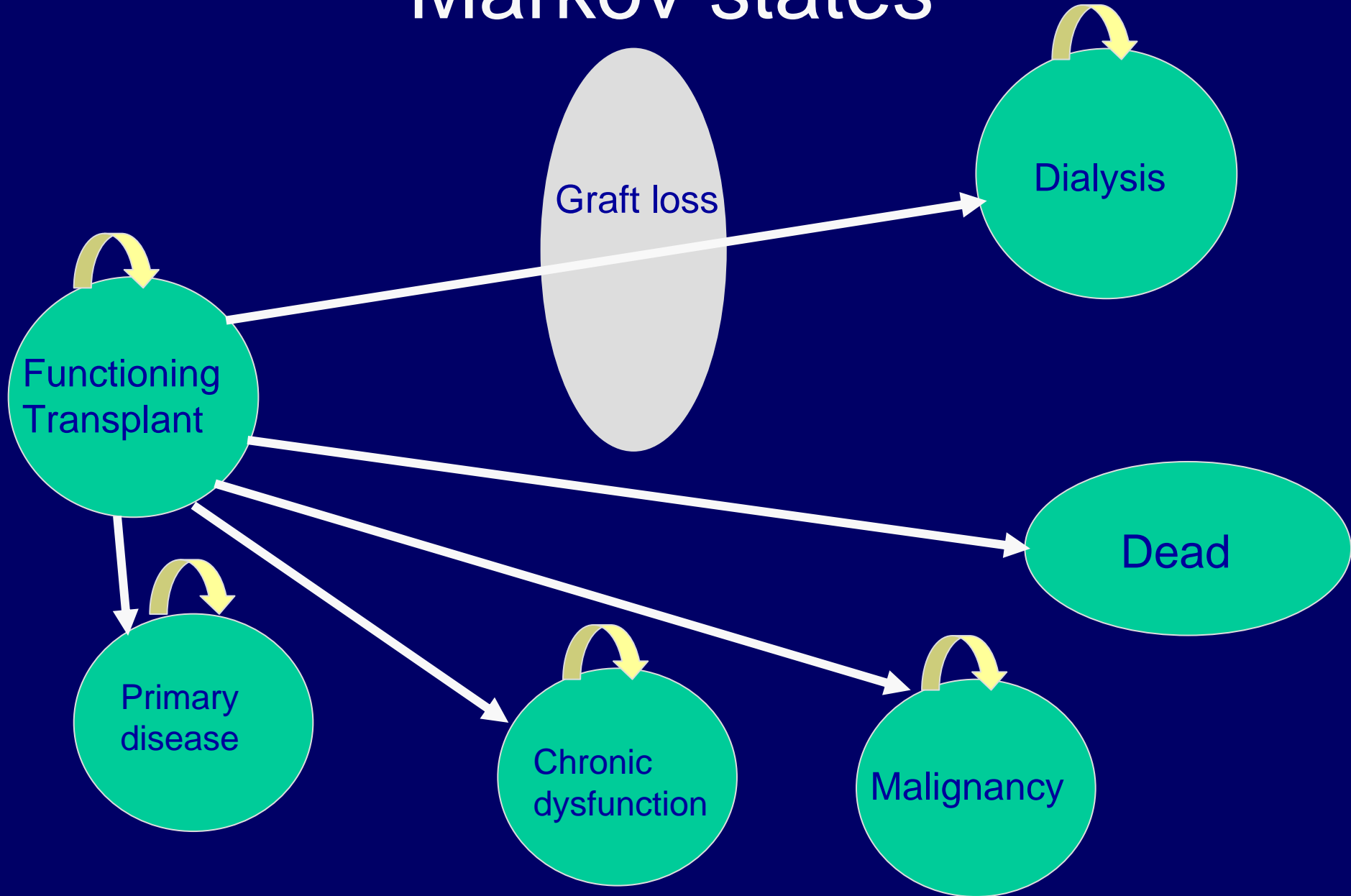
# Markov states



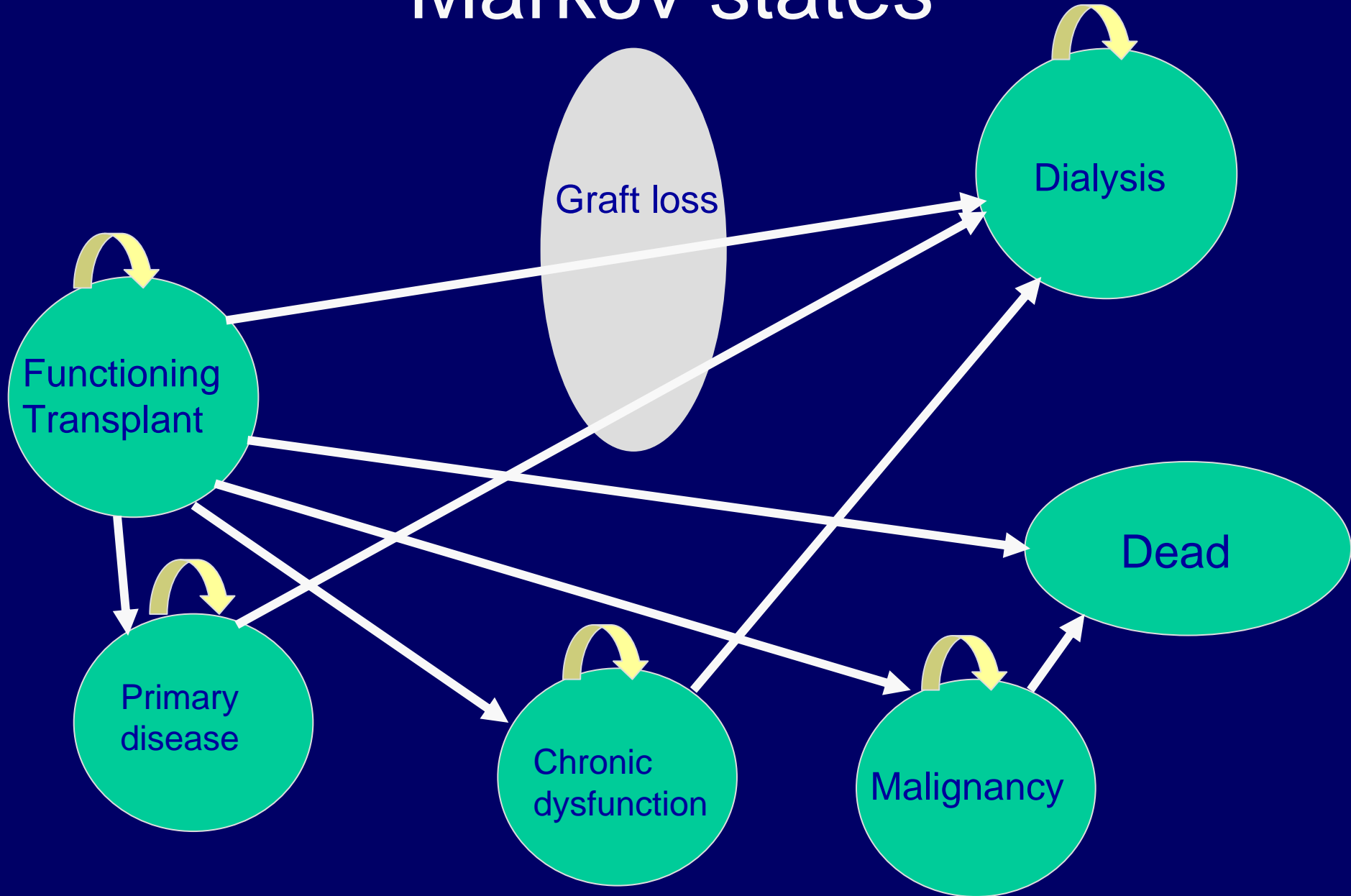
# Markov states



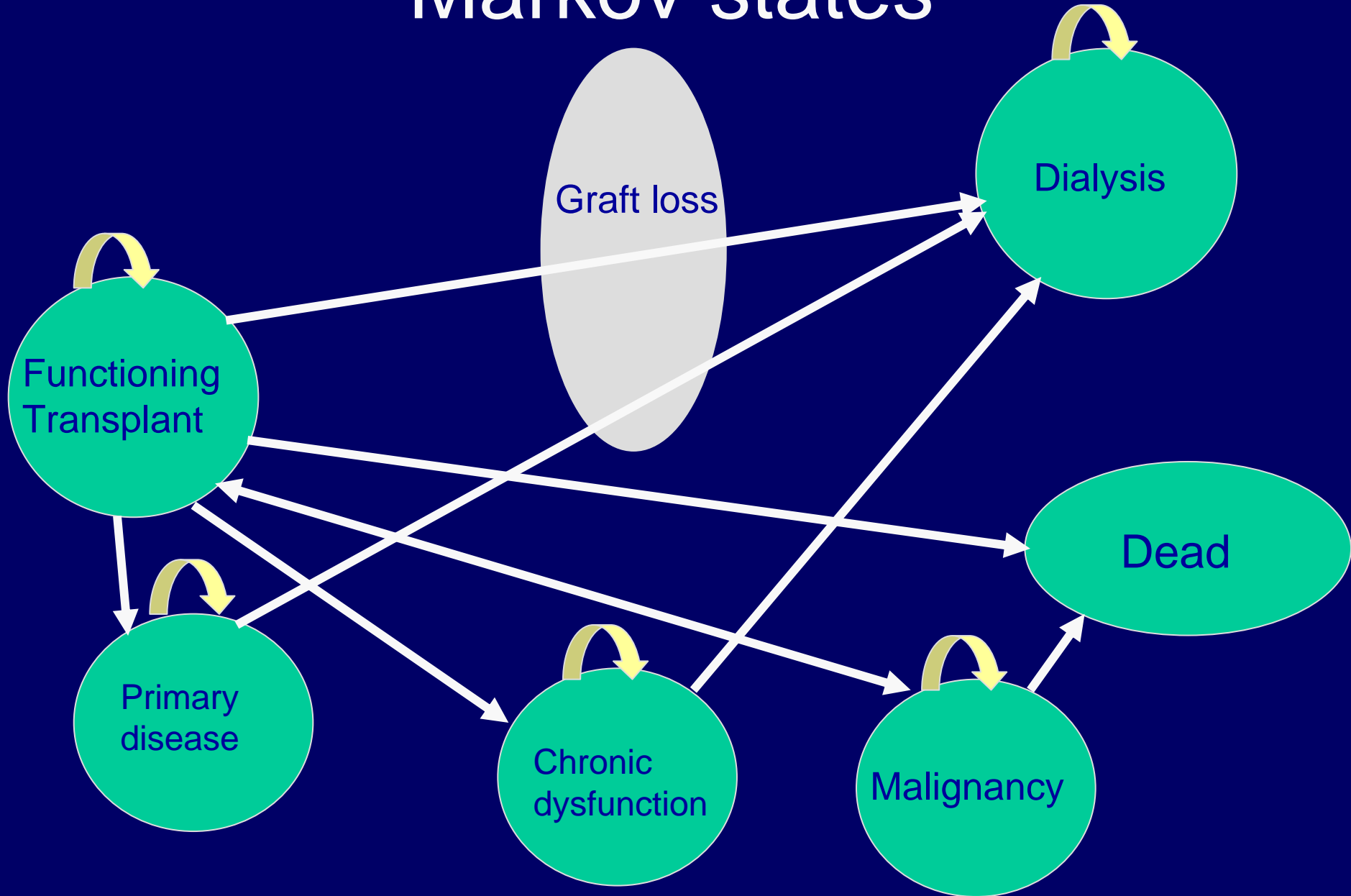
# Markov states



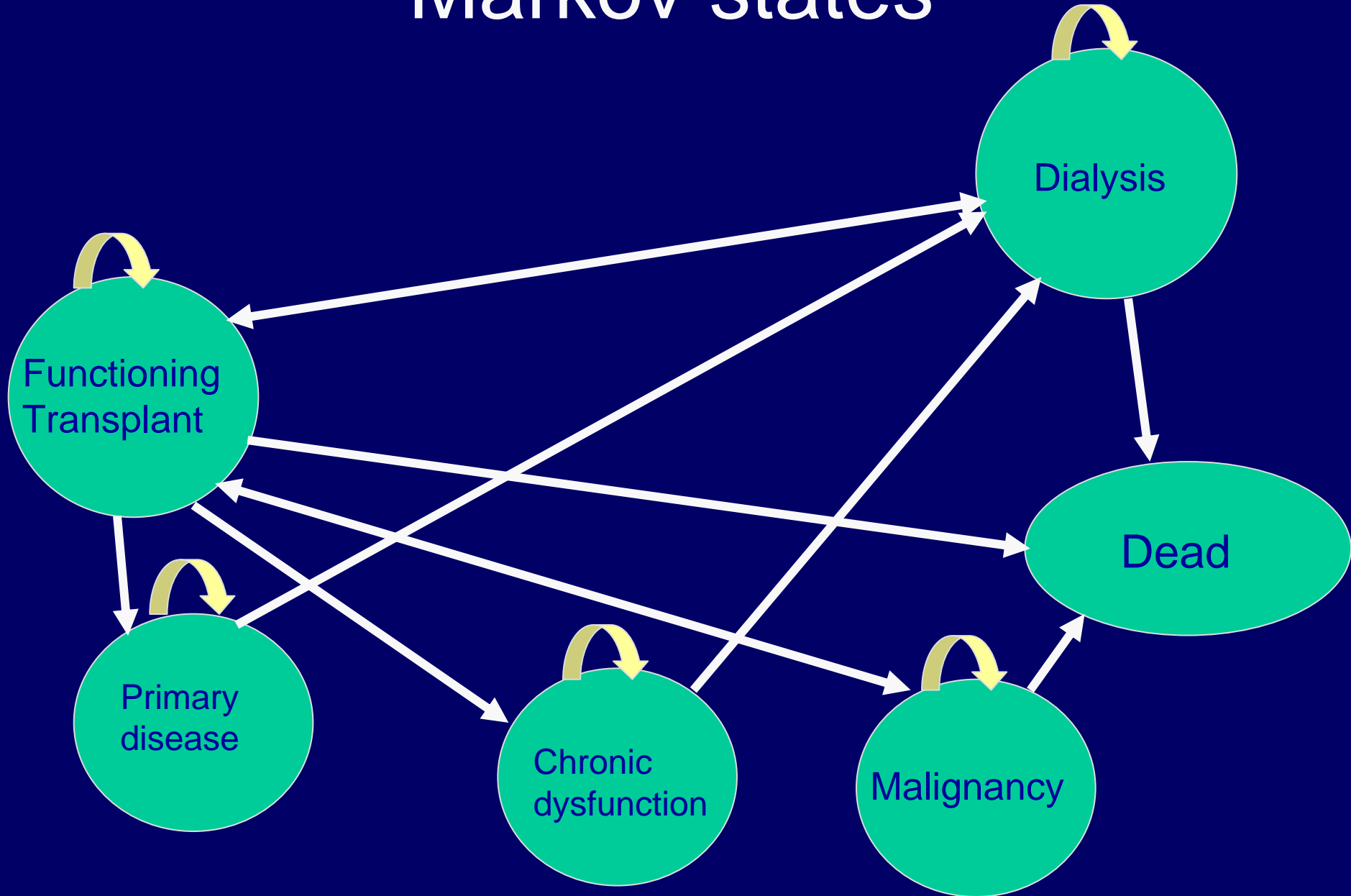
# Markov states



# Markov states



# Markov states



# Model inputs - Quality of life (utility) data

| Health state                                   | QOL   |
|--|-------|
| Functioning transplant no complications yr1+   | 0.77  |
| Functioning transplant no complications yr0    | 0.75  |
| Functioning transplant first month             | 0.68  |
| Functioning transplant with chronic rejection  | 0.67  |
| Maintenance dialysis                           | 0.57  |
| Acute rejection in first year (bad transplant) | 0.50  |
| CMV disease (sick)                             | 0.47  |
| Cancer palliative care (+ transplant)          | 0.40* |
| Dead with functioning graft / dead dialysis    | 0     |

# Model inputs – cost data

| <b>Variable</b>         | <b>Components</b>                       | <b>DRG / MBS / PBS code</b> | <b>AU\$</b> | <b>ALOS</b> |
|-------------------------|---|-----------------------------|-------------|-------------|
| (1) Cost of Tx          | Hospital stay / operation for recipient | A09B                        | 29,681      | 8.58        |
|                         | Donor admission / cadaver nephrectomy   | L04A/B/C                    | 9,568       |             |
| (2) Cost of IL-2Ra      | Basiliximab 20mg x 2                    | (WSAHS)                     | 6,540       | n/a         |
| (3) Cost of f/up Yr0    | Immunosuppressive drugs                 | 8648E/8650G                 | 23,056      | n/a         |
|                         | Doctor visits x 24                      | 116                         | 1,637       |             |
|                         | Blood tests                             | 66512/65070                 | 1,690       |             |
|                         | Concomitant meds                        | 1326T/1695F                 | 7,063       |             |
| (4) Cost of CMV disease | Hospital stay                           | T61A                        | 34,950      | 30          |
|                         | Diagnostic tests                        | 72836/70351                 | 789         | Range       |
|                         | Ganciclovir + Valganciclovir IV         | 6136Y/6357N                 | 5,004       | (6-71)      |

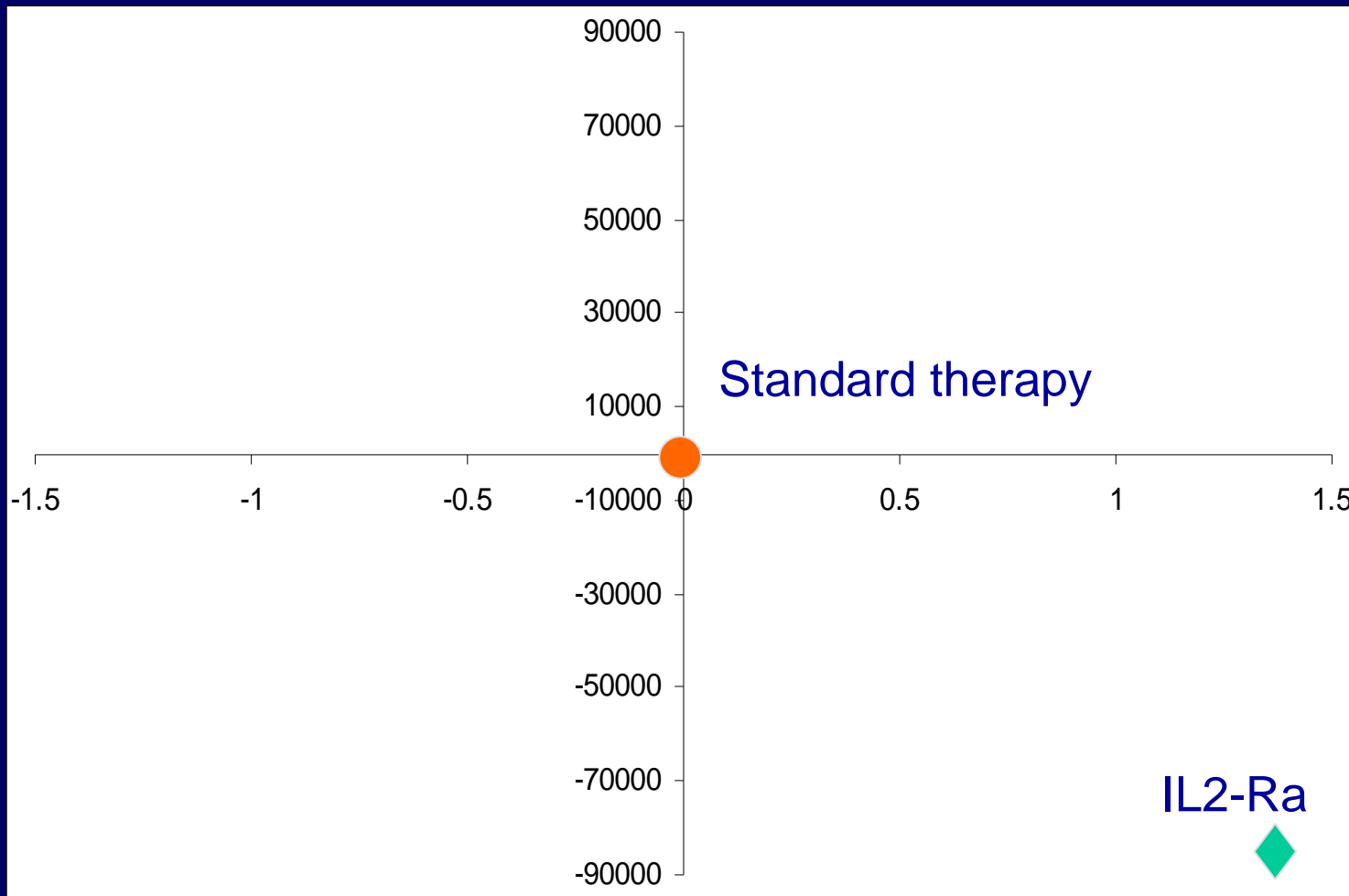
## Results - (after 20 years)

| Strategy             | Cost (AU\$) | Life Years | QALYs |
|----------------------|-------------|------------|-------|
| Standard therapy     | 345,649     | 7.05       | 3.86  |
| IL-2Ra induction     | 266,347     | 7.26       | 5.28  |
| Polyclonal induction | 263,820     | 6.91       | 5.08  |

# Cost-effectiveness plane

## (i) IL2-Ra vs standard therapy

△ COSTS (\$)



△ OUTCOMES (QALYs)

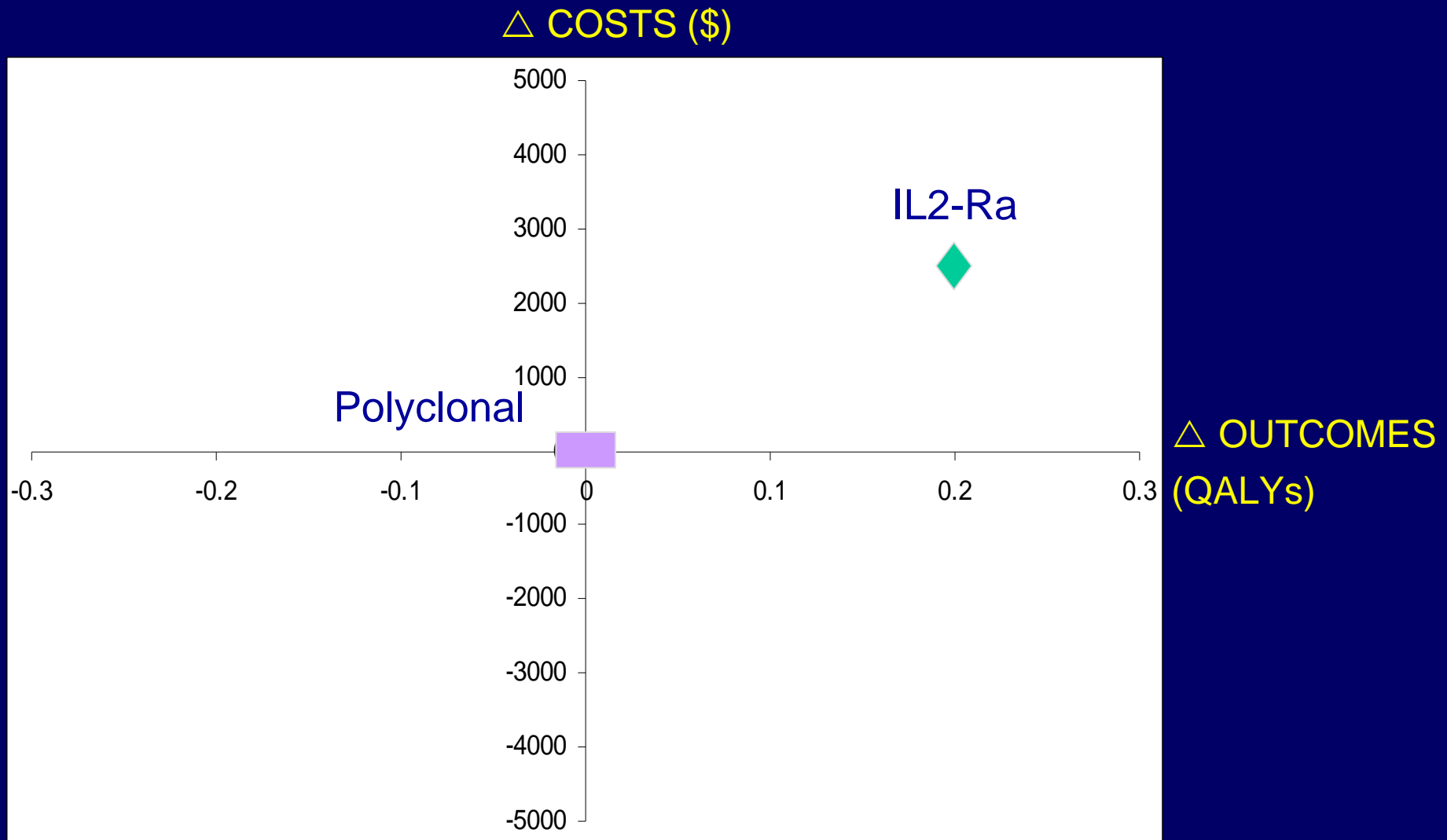
# Results

## (i) IL2-Ra vs Standard Therapy

Induction therapy with IL2-Ra is both more effective and less expensive.

**Standard therapy is 'dominated'**

# Cost-effectiveness plane (ii) IL2-Ra vs polyclonal



# Results

## (ii) IL2-Ra vs Polyclonal Induction

$$ICER = \frac{TotalCost_{IL-2RA} - TotalCost_{POLYCLONAL\_ANTIBODY}}{Effectiveness_{IL-2RA} - Effectiveness_{POLYCLONAL\_ANTIBODY}}$$

$$ICER = \frac{\$266,347 - \$263,820}{5.28 - 5.08}$$

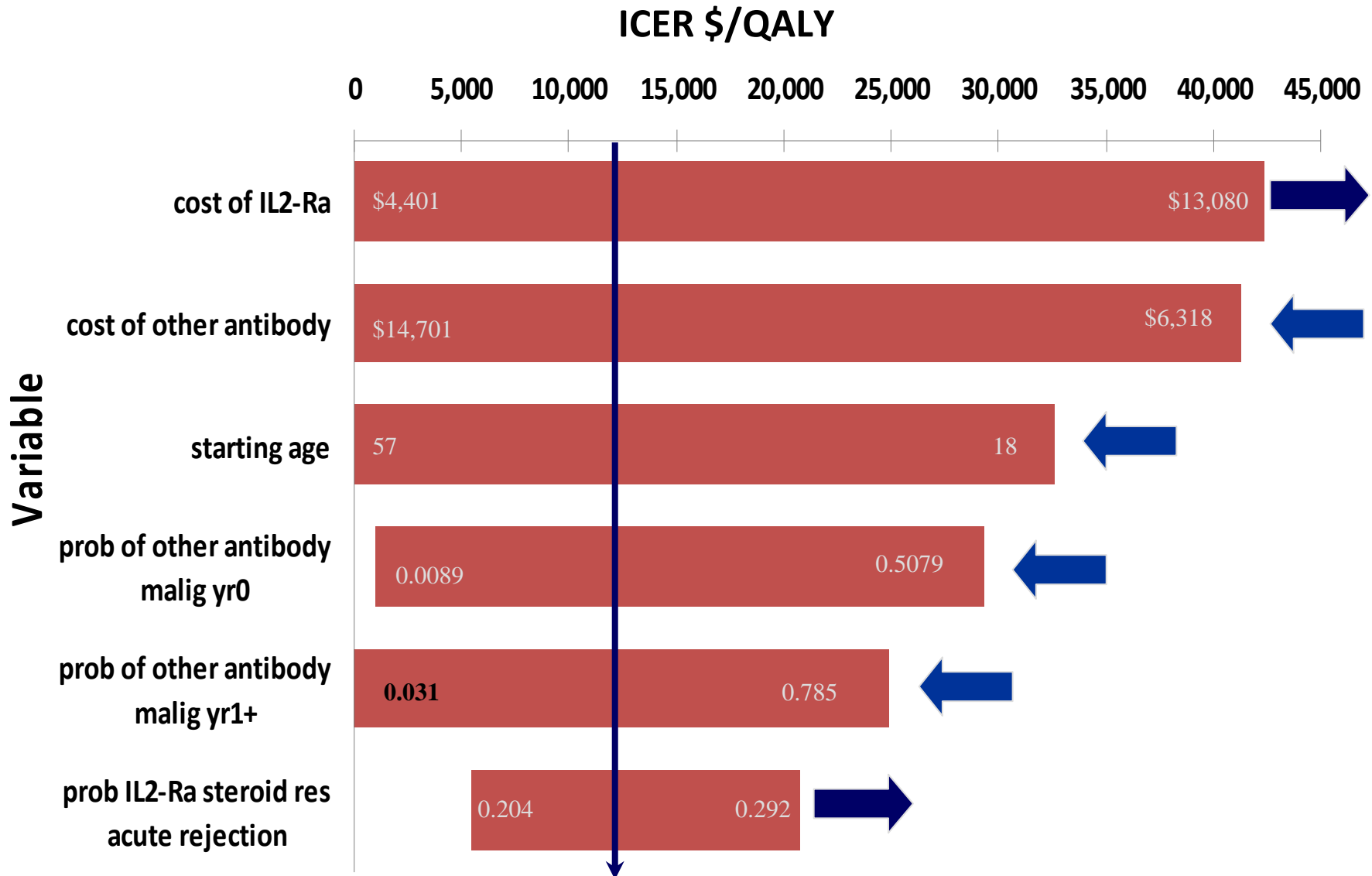
ICER = \$12,736/QALY gained using IL2-Ra instead of polyclonal induction

# Sensitivity analysis

## IL2-Ra vs standard therapy

- All variables tested across range
  - 95% CI for transition probabilities and utilities
  - Plausible range for costs (multiplier formula)
- IL2-Ra was more effective and less expensive than standard therapy

# One-way sensitivity analysis IL2-Ra vs Polyclonal



# Conclusions

## (i) IL2-Ra vs standard therapy

### IL2-Ra:

- Is \$79,302 less expensive
- Leads to 0.21 additional life years (2.5 months)
- Leads to 1.42 additional quality adjusted life years (17 months)

## (ii) IL2-Ra vs polyclonal induction

### IL2-Ra:

- Is \$2,527 more expensive
- Leads to 0.35 additional life years (4.3 months)
- Leads to 0.20 additional quality adjusted life years (2.5 months)
- ICER \$12,736/QALY

# Additional slides



# Transition probabilities

| Variable name   | Base Case | Range           |
|---|-----------|-----------------|
| Starting age  | 46        | 18-70           |
| Probability of no events post Tx Standard therapy                   | 0.407     | 0.3562 – 0.4578 |
| Probability of no events post Tx IL2-Ra therapy                     | 0.562     | 0.5109 – 0.613  |
| Probability of acute rejection – standard therapy                   | 0.3727    | 0.3427 – 0.4027 |
| Probability of acute rejection – IL2-Ra therapy                     | 0.2703    | 0.2431 – 0.2974 |
| Probability of steroid resistant acute rejection – Standard therapy | 0.2824    | 0.2245 – 0.3404 |
| Probability of steroid resistant acute rejection – IL2-Ra therapy   | 0.2481    | 0.2036 – 0.2924 |
| Probability of CMV disease – standard therapy                       | 0.0842    | 0.0596 – 0.1088 |
| Probability of CMV disease – IL2-Ra therapy                         | 0.0748    | 0.0508 – 0.1605 |

# Who was Markov?

- Andrey Andreyevich Markov b.1856 - 1922
- A Russian mathematician - Professor at St Petersburg University
- Studied the theory of probability → Markov chains
- Political activist – known as “Andrew the Furious”

