Cost-Effectiveness of Tolvaptan vs. Angiotensin-Converting Enzyme Inhibitors for US Patients with Autosomal Dominant Polycystic Kidney Disease

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BACKGROUND

- Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a monogenic renal disease that affects approximately 600,000 individuals in the U.S.[1]
- Currently, there are no treatments to cure ADPKD; existing therapies, such as tolvaptan or angiotensin-converting enzyme inhibitor (ACE-I), focus on delaying disease progression

OBJECTIVE

- To determine if tolvaptan (+/- ACE-I) is more cost-effective than ACE-I monotherapy in ADPKD

METHODS

Study Design: A predictive Markov-transition state model simulating two ADPKD patient cohorts in the U.S.

- Either cohort was treated with an ACE-I or tolvaptan (+/- ACE-I)

Time Horizon: 30 years, with 1-year duration to cycle shift

Model Perspective: Societal including direct and indirect costs related to ADPKD[2]

- All annual and indirect costs for specific chronic kidney disease (CKD) stage were added to the price of using tolvaptan (+/- ACE-I) or ACE-I monotherapy in that respective stage
- Indirect Costs: Decreased productivity and caregiver productivity
- Costs were adjusted to 2023 medical-care inflation

Base Case: 50-year-old male and female with hypertensive CKD

Health States: CKD Stage 1-4, end-stage renal disease (ESRD) (CKD Stage 5 + transplants), Death

Comparators[3-6]:

- **Gold Standard**: ACE-I, 100 mg split in 2 doses
- **Comparator:** Tolvaptan, 30 mg tablets four times daily for clinically recommended target dose of 120 mg

Transition Probabilities: Patients remain in current CKD stage, progress to successive CKD stage, or die

- ACE-I: Derived from a cost-effective analysis of ACE-Is vs angiotensin II receptor blockers (ARBs) in ADPKD[7]
- Tolvaptan: a kidney function decline ratio was derived and multiplied by the transition probabilities for ACE-I[7,8]

Cost-Effectiveness Analysis (CEA): 3% discounting was applied to costs and effectiveness

- Conducted CEA to estimate incremental cost-effectiveness ratio (ICER) of tolvaptan (+/- ACE-I)
- vs ACE-I monotherapy per one additional year of prevented death
- A one-way probabilistic sensitivity analysis (OWSA) was conducted, with +/-10% variation in transition probabilities and costs
- A willingness to pay (WTP) threshold of $150,000 was used for comparison
- Effectiveness was measured using quality-adjusted life years (QALYs) and were calculated for each therapy and each CKD stage[9-12]
  - Utility measures for ACE-Is were extracted from a systematic literature review highlighting health-related quality-of-life (HRQOL) utility weights for CKD
  - Utility value was derived from EQ-5D-3L, and a formula was used to calculate the QALY value

Assumptions:

1. Cost of transplants were grouped with ESRD state without preemptive transplantation in CKD stage 4
2. Since ACE-I monotherapy is the standard of care for all patients with ADPKD, patients on tolvaptan were assumed to also be on ACE-I
3. Patients were assumed to be 100% adherent to therapies
4. No reversal of CKD stage transitions

RESULTS

Figure 1. Tornado Diagram

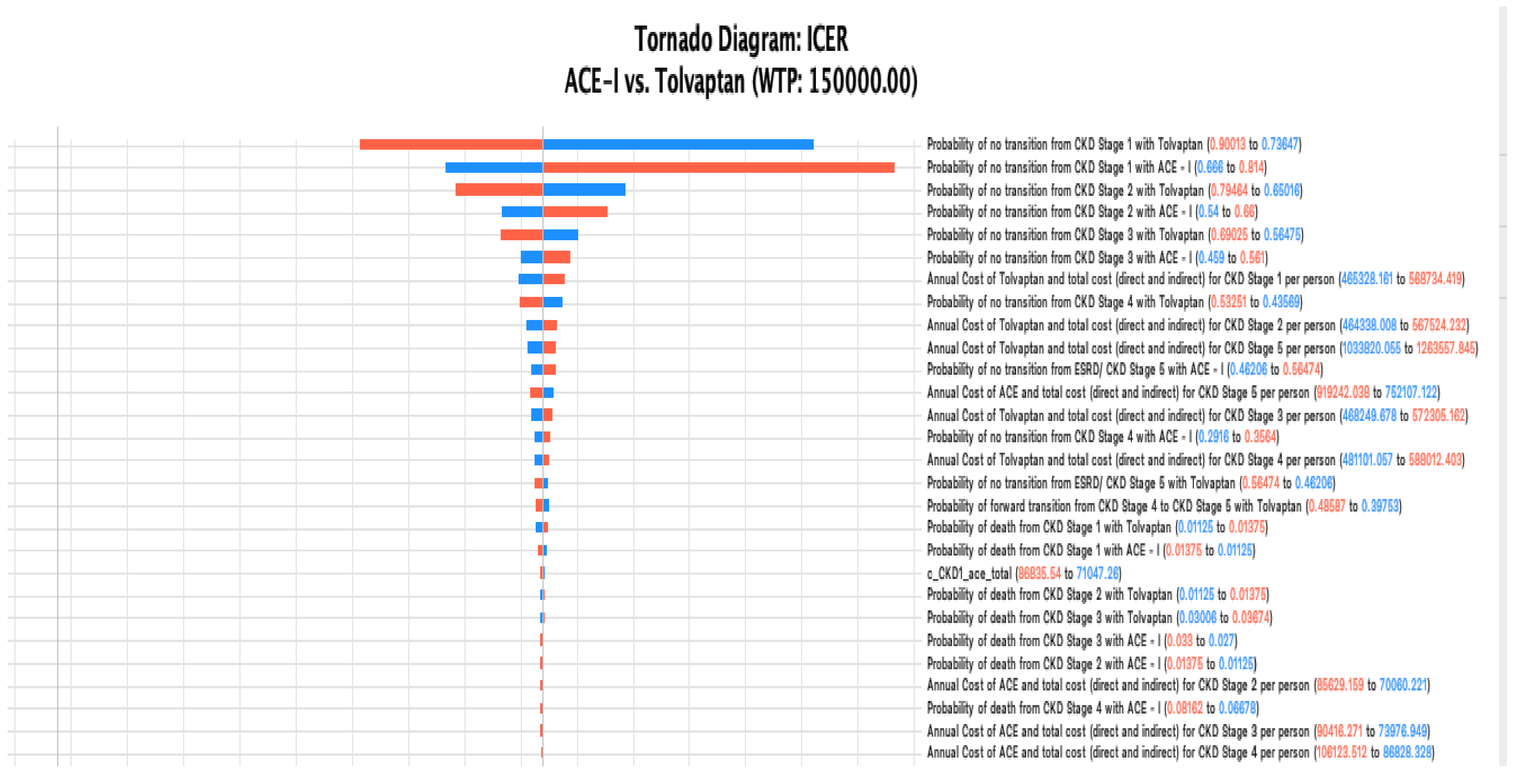
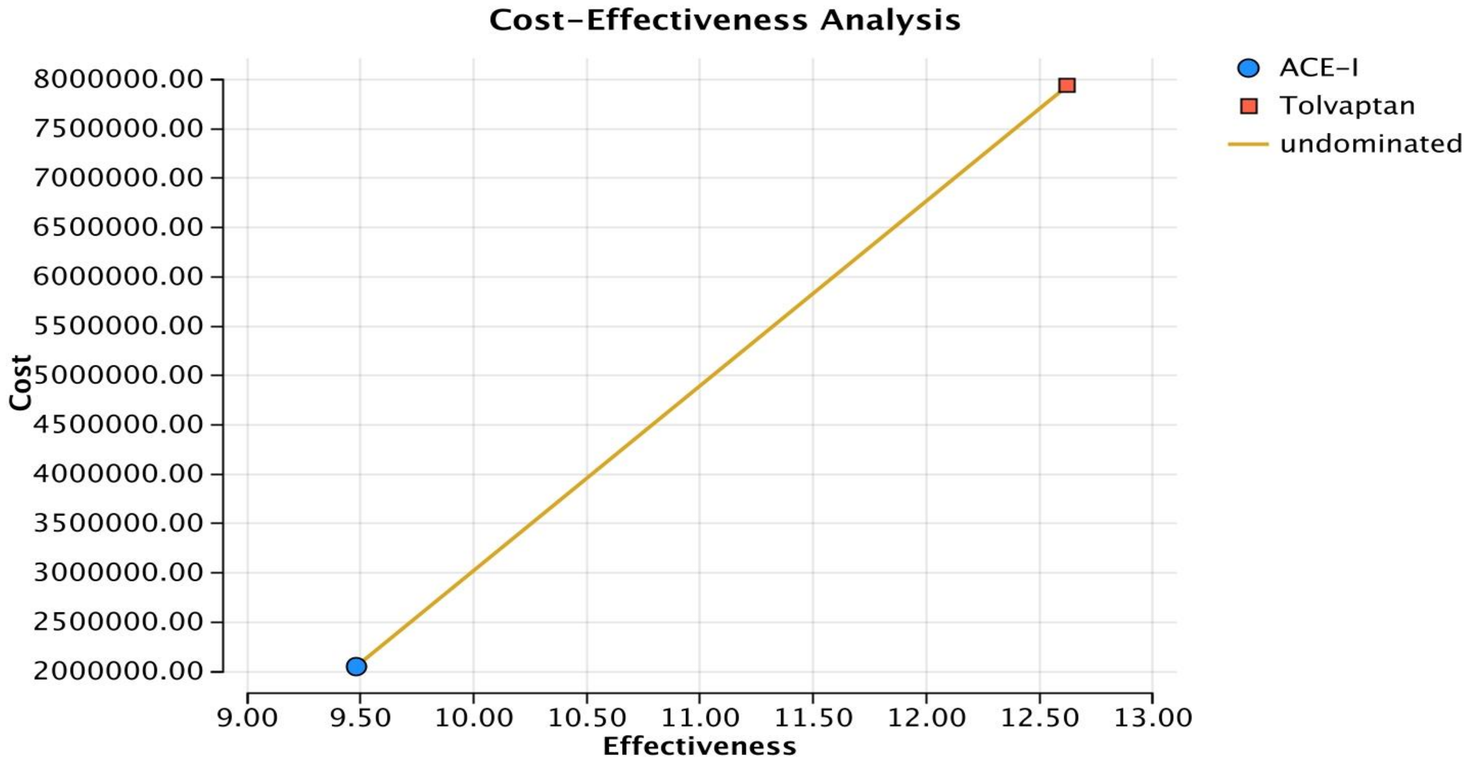


Figure 2. Cost-Effectiveness Plane



- Total annual healthcare costs accrued after 30 years for ADPKD patients using tolvaptan (+/- ACE-I) was estimated to be $7,939,288, compared to ACE-I monotherapy at $2,048,018.
- Life expectancy was increased by 2.97 years among patients taking tolvaptan (+/- ACE-I).
- ICER of $1,875,909/QALY implies tolvaptan is not cost-effective.

LIMITATIONS

- In the absence of accurate tolvaptan transition probabilities from literature, transition probabilities were calculated and based on assumption
- Direct and indirect costs in the model could be overestimated
- The clinical efficacy of tolvaptan and ACE-I were calculated based on literature and may not accurately represent U.S. population

CONCLUSIONS

- Tolvaptan (+/- ACE-I) is not more cost effective than ACE-I monotherapy under the current WTP threshold.
- Tolvaptan offers higher effectiveness, but the substantial incremental cost ($5.8M) outweighs the benefit of additional QALYs.

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