Decomposing Value in Cost-Effectiveness Analysis Using Machine Learning

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Background and Motivation

Cost-effectiveness analysis (CEA) supports decision-making under uncertainty by estimating the economic value of health interventions

- Probabilistic sensitivity analysis (PSA) propagates joint uncertainty across model inputs.
- Outputs include distribution of value (e.g., INMB, value-based price)

Limitation: PSA tells us *how uncertain value is*, but not *why it varies*

- Which parameters drive value?
- Which input matter most for decision-making?
- How do interactions shape economic value?

Gap: No systematic framework exists to decompose value under joint uncertainty

Research Questions

1. Which parameters drive variation in economic value under joint uncertainty?
2. How do model input interact or shape value-based price (VBP)?
3. Can machine learning provide a transparent decomposition of value?

Methods

Application

Cost-effectiveness analysis of: Long-acting injectable PrEP (cabotegravir) vs daily oral PrEP (TDF/FTC)

Model

- Cohort-based Markov model with Health States: HIV-, HIV+, AIDS, Death (Figure and Table 1)
- US healthcare perspective with a 3% discount rate

Analytical Framework

Step 1: Generate Training Data (PSA as Data-Generating Process)

- Run 1,000 Monte Carlo simulations
- Each simulation i produces:
  - **Inputs (X):** sampled model parameters -- **Output (Y):** corresponding value-based price (VBP)
- **Each PSA draw becomes one observation in the dataset:** Final dataset (X_i, VBP_i)

Step 2: Train Machine Learning Emulator

- Model: **XGBoost regression**
- **Objective:** learn mapping $(X \rightarrow VBP)$
- **Data split:** 80% training and 20% testing (cross-validation)

Step 3: Decompose Value Using Shapley-Based Methods

- Use **Shapley value decomposition (SHAP values)** from cooperative game theory
- For each simulation: Decompose predicted VBP into additive contributions of each parameter (Table 2)

Figure 1: Markov Model Structure

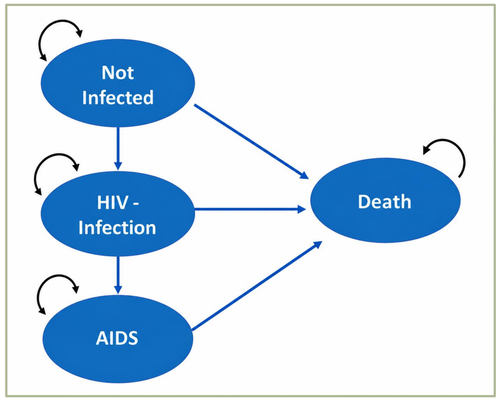


Table 1: Key Model Inputs

	Protective population Value (SD)	Distribution	Nonprotective population Value (SD)	Distribution	References
Transition probabilities					
Long-acting PrEP					
Not infected to HIV	0.57% (0.0074)	Beta	0.71% (0.008)	Beta	[5]
Not infected to death	0.0148% (0.001)	Beta	0.0148% (0.001)	Beta	WHO
HIV to AIDS	8.1% (0.027)	Beta	8.1% (0.027)	Beta	[22]
HIV to death	0.0261%	α	0.0261%	α	[5, 23]*
AIDS to death	0.4% (0.006)	Beta	0.4% (0.006)	Beta	[24]
Traditional PrEP					
Not infected to HIV	1.76% (0.013)	Beta	3.48% (0.018)	Beta	[5]
Not infected to death	0.0148% (0.0012)	Beta	0.0148% (0.0012)	Beta	WHO
HIV to AIDS	8.1% (0.027)	=	8.1% (0.027)	=	[22]
HIV to death	0.0261%	=	0.0261%	=	[5, 23]*
AIDS to death	0.4% (0.006)	=	0.4% (0.006)	=	[25–27]*
Utilities					
Long-acting PrEP					
Not infected	0.911 (0.055)	Beta	0.912(0.055)	Beta	[25–27]*
HIV	0.789 (0.047)	Beta	0.789 (0.047)	Beta	[25–27]*
AIDS	0.702 (0.042)	Beta	0.702 (0.042)	Beta	[25–27]
Traditional PrEP					
Not infected	0.90837 (0.054)	α	0.909(0.054)	α	[25–27]*
HIV	0.789 (0.047)	Beta	0.789 (0.047)	Beta	[25–27]*
AIDS	0.702 (0.042)	Beta	0.702 (0.042)	Beta	[25–27]
Cost					
Per cycle (monthly)					
LA PrEP	4208$ (1,052)	Gamma	4208$ (1,052)	Gamma	ViiV Healthcare
Daily oral PrEP	1759$ (440)	Gamma	1759$ (440)	Gamma	TDF/FTC
Visit cost (lab test)	233$ (58)	Gamma	233$ (58)	Gamma	[28]
HIV care	1991$ (498)	Gamma	1991$ (498)	Gamma	[28]
AIDS care	2863$ (716)	Gamma	2863$ (716)	Gamma	[28]

Concrete Example
Average VBP: ~$28,000
Predicted VBP: ~$40,000
→ **+ $12,000 explained by SHAP**

Table 2: Decomposing VBP: SHAP Contributions for a Single Simulation

Parameter	SHAP Contribution	Interpretation
HIV acquisition probability under oral PrEP	+$7,500	Higher values increase VBP
HIV acquisition probability under long-acting PrEP	-$4,000	Higher values decrease VBP
Cost of Oral PrEP	+$3,800	Higher costs decrease VBP
Utility of being uninfected under long-acting PrEP	+$4,700	Higher values increase VBP
Total	+$12,000	

Figure 2: Observed vs Predicted Value-Based Price

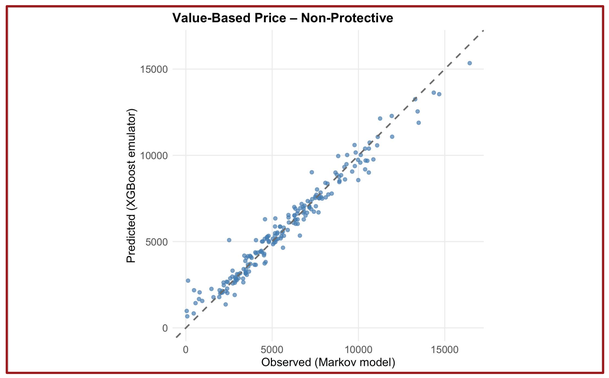
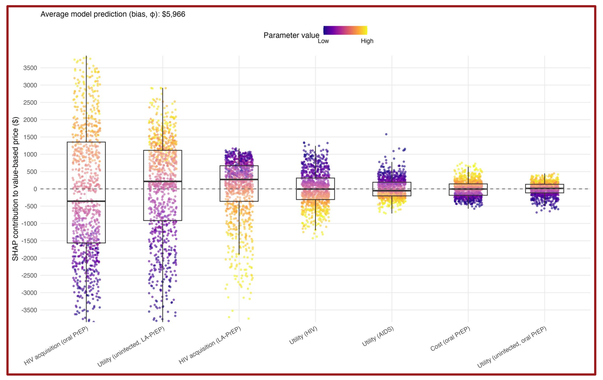


Figure 3: SHAP Decomposition of Value-Based Price



Methods (continued):

Interpretation:

- Each parameter shifts VBP above or below the mean
- Contributions sum to the predicted value: Mean VBP + sum of parameter contributions (Table 2)
- Effects are conditional on all other inputs and captures nonlinearities and interactions

Results

Model Performance

- Strong agreement between observed and predicted VBP (Figure 2)
- Indicates the emulator accurately captures how inputs translate into value

Key Drivers of Value-Based Price for Long-Acting PrEP (Figure 3)

- HIV acquisition probability under oral PrEP (reflecting effectiveness of comparator)
  - ➢Higher probability of infection under oral PrEP increases VBP
  - ➢High values increase VBP by up to ~60% above the mean, while low values decrease it by up to ~60% below the mean (±$3,500)
- Utility of being uninfected under long-acting PrEP (reflecting improved convenience and reduced adherence burden relative to daily oral PrEP)
  - ➢Higher values increase VBP; lower values decrease VBP
  - ➢ High values increase VBP by up to ~40-45% above the mean, while low values decrease it by up to ~60% below the mean (-$3,500 to +$2,500)
- HIV acquisition probability under long-acting PrEP (reflecting effectiveness of the intervention)
  - ➢Higher probability of infection under long-acting PrEP decreases VBP
  - ➢High values decrease VBP by up to ~50% below the mean, while low values increase it by up to ~15-20% above the mean (-$3,000 to +$1,000)
- Cost of oral PrEP (Truvada)
  - ➢Higher costs (of comparator) directly increase VBP
  - ➢High costs increase VBP by up to ~10% below the mean, while low costs decrease it by up to ~15-20% above the mean (-$500 to +$1,000)

Conclusions

- VBP is primarily determined by relative protection and quality-of-life gains, not cost alone
- This framework transforms CEA from a black box into an interpretable model by decomposing value under joint uncertainty

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