"What If?" Clinical Impact and Cost-Effectiveness of a Novel Therapy to Prevent Advanced Frailty Among People with HIV

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BACKGROUND AND OBJECTIVE

- People with HIV experience higher rates of physical frailty at younger ages than people without HIV.
- Potential frailty prevention medications are under investigation.
- Our objective was to evaluate a novel therapy to prevent advanced frailty (defined as having 4-5 Fried Frailty criteria) among PWH under various cost and efficacy scenarios.
- We focused on preventing advanced frailty as targeted prevention given to people likely to worsen could be more efficient than distribution to all PWH.

METHODS

- We used a microsimulation model to estimate the clinical impact and economic value of an advanced frailty prevention therapy given to PWH with frailty, simulating individuals as they transition between frailty states.
- We defined base-case efficacy as a 30% reduction in transitions to worsened frailty states, based on reductions from exercise programs.
- We compared a simulation with no preventive therapy to six alternative simulations, a low-, moderate-, and high-efficacy and cost therapy assuming advanced frailty was either reversible or irreversible.
- We conducted sensitivity analyses with parameters derived from published studies and literature.

Table 1A. Cohort Characteristics

Characteristic	Value	Derived From
Mean (SD) Age (y)	54 (7)	ACTG HAILO Study
% Female	30%	
% Frail (3 criteria)	100%	Assumption

Table 1B. Key Model Input Parameters

Advanced Frailty State	Value	Derived From
Quality-of-life utility decrement	0.095	MWCCS
Mortality hazard ratio	4.2	Hanlon, *Lancet*, 2018
Additional annual costs ($) *(Women/Men)*	15,700/10,600	Ensrud, *Ann Intern Med*, 2023

Novel Therapy to Prevent Advanced Frailty	Efficacy	Annual Cost ($)	
Low-Efficacy, Low-Cost	6% (2%-10%)	150 (50-450)	Assumptions
Moderate-Efficacy, Moderate-Cost	30% (20%-50%)	1,000 (500-3,000)	
High-Efficacy, High-Cost	70% (50%-80%)	4,500 (1,500-5,500)	

Treatment efficacy is defined as percent reduction in annual transition to a worsened state of frailty. Ranges shown in the table represent distributions used for parameters in sensitivity analyses. Costs are in 2025 USD.

RESULTS

Base-case analysis

- In the base case, we projected that the therapy would reduce years with advanced frailty by 0.4 years and increase quality-adjusted life expectancy by 0.2 QALYs (Table 2).
- The therapy would be cost-effective for payers willing to pay above $112,000/QALY. If recovery from advanced therapy were not possible, the therapy would be cost-effective for payers willing to pay above $74,000/QALY.

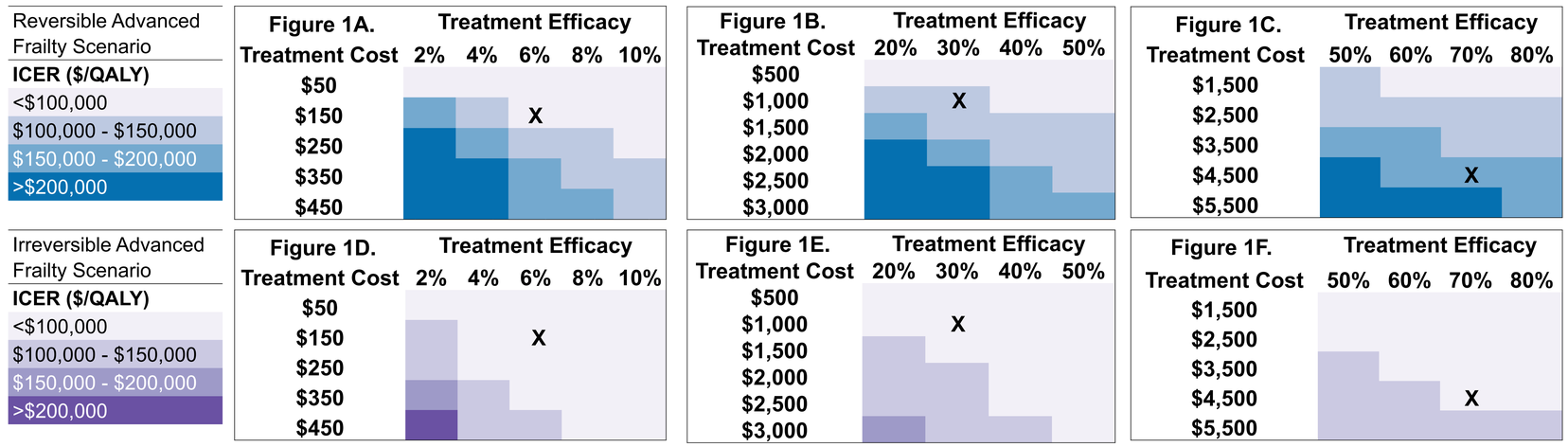
Table 2: Clinical and Survival Benefits and Cost-Effectiveness of a Frailty Prevention Therapy

	Years with Advanced Frailty	Life Expectancy	Quality-Adjusted Life-Expectancy	Average Lifetime Cost	ICER, $/QALY
Base Case (Recovery from Advanced Frailty Possible)					
Status Quo	1.1	14.7	9.7	$752,000	-
Novel Therapy to Prevent Advanced Frailty	0.7	15.0	9.9	$778,000	$112,000
Scenario Without Recovery from Advanced Frailty					
Status Quo	4.8	13.2	8.5	$695,000	-
Novel Therapy to Prevent Advanced Frailty	3.5	13.8	9.0	$733,000	$74,000

These analyses assume that the novel therapy to prevent advanced frailty has moderate efficacy and cost (30% efficacy, annual cost of $1,000). ICERs (incremental cost-effectiveness ratios) are calculated as the ratio of incremental cost to incremental QALYs gained with the therapy.

Two-way sensitivity analysis

- A frailty prevention therapy would be cost-effective at ≤$150/year (6% efficacy), ≤$500/year (30% efficacy), or ≤$1,500/year (70% efficacy) (Figure 1A-C).
- Without recovery from advanced frailty, the therapy would be cost-effective at ≤$350/year (6% efficacy), ≤$1,500/year (30% efficacy), or ≤$4,500/year (70% efficacy) (Figure 1D-F). The X in Figures 1A-F represent the base case assumption for each scenario.



LIMITATIONS

- Studies used to parameterize the model may not be representative of all PWH.
- As no therapy to prevent advanced frailty yet exists, we used data from similar therapies and studies of PWH to populate likely values.

CONCLUSIONS

- A novel therapy to prevent advanced frailty could extend the lifespan of PWH
- The therapy likely would need to be inexpensive to achieve cost-effectiveness, but a more expensive therapy may be cost-effective if given to PWH at risk of irreversible advanced frailty.
- These results offer a pricing framework to inform decisions if a therapy for the prevention of advanced frailty becomes available.

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