

## BACKGROUND

The shortcomings of current methods:

- Traditional cost-effectiveness analysis (CEA) assumes risk-neutrality over health, and omits value elements such as disease severity, value of hope, and equity, **potentially undervaluing treatments for severe illnesses**<sup>1,2</sup>

The potential solution:

- Generalized Risk-Adjusted Cost-Effectiveness (GRACE) **relaxes this assumption** by accommodating non-linear returns to health (diminishing returns) within current framework, also factoring these omitted value elements<sup>2</sup>

Barriers to proper GRACE implementation:

- Effective implementation requires utility estimates that capture risk preferences varying over health levels—**current applications rely on visual analog scale (VAS)-based functions from a general population**, requiring analysts to map other measures (e.g., EQ-5D) to VAS<sup>3</sup>
- As many analysts do not have VAS-based data, estimating utility functions over more commonly available measures, such as time trade-off (TTO; used for EQ-5D values) can remove a cumbersome mapping step when indexes align

## OBJECTIVE

- Our study aims to estimate utility functions over multiple health indexes (VAS and TTO) directly from non-small cell lung cancer (NSCLC) patients, enabling both simplified and patient-centric GRACE analysis

## METHODS (OVERVIEW)

Overview:

- Patients with NSCLC recruited via online groups; demographic & clinical characteristics to be recorded

- Patients complete survey with 6 hypothetical VAS-based health gamble scenarios + 6 standard TTO questions

How It Works:

- Survey elicits preference between certain and risky health outcomes when offered various treatment options

- The point where patients are indifferent between certain and risky options reveals a certainty equivalent (CE)

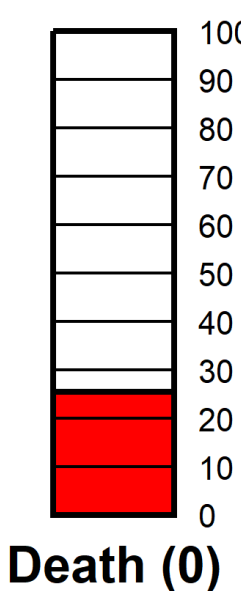
- CEs will be used to estimate utility functions over health via four parametric models under expected utility theory

- Standard TTO questions to be fielded at each corresponding CE to link VAS index to TTO within study

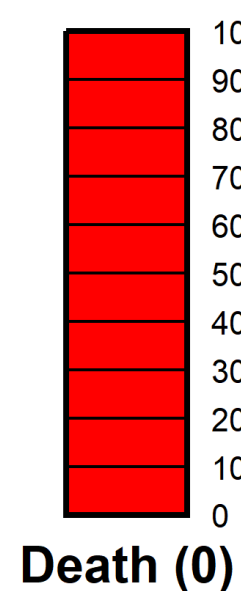
## METHODS (SURVEY DESIGN)

	I prefer Treatment A	I prefer Treatment B	
Treatment A: Certain outcome = 21		X	Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 24		X	Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 27	X		Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 29	X		Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 32	X		Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 35	X		Treatment B: 20 (50% chance) 40 (50% chance)
Treatment A: Certain outcome = 38	X		Treatment B: 20 (50% chance) 40 (50% chance)

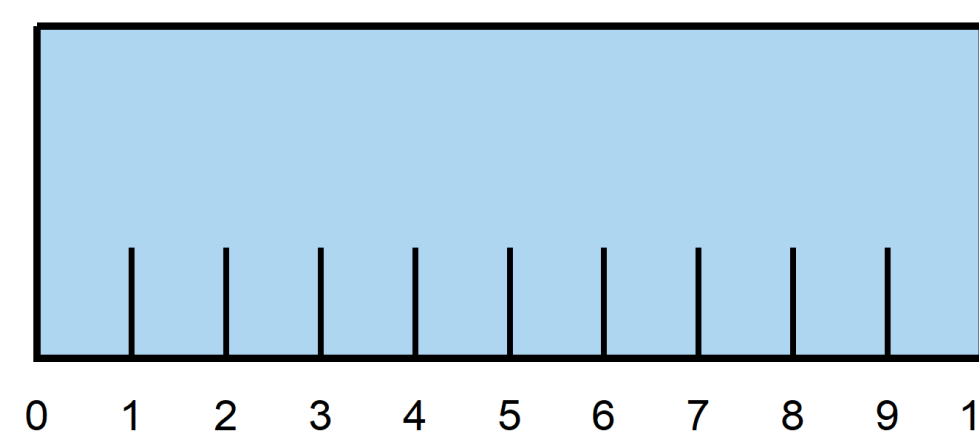
Perfect Health (100)



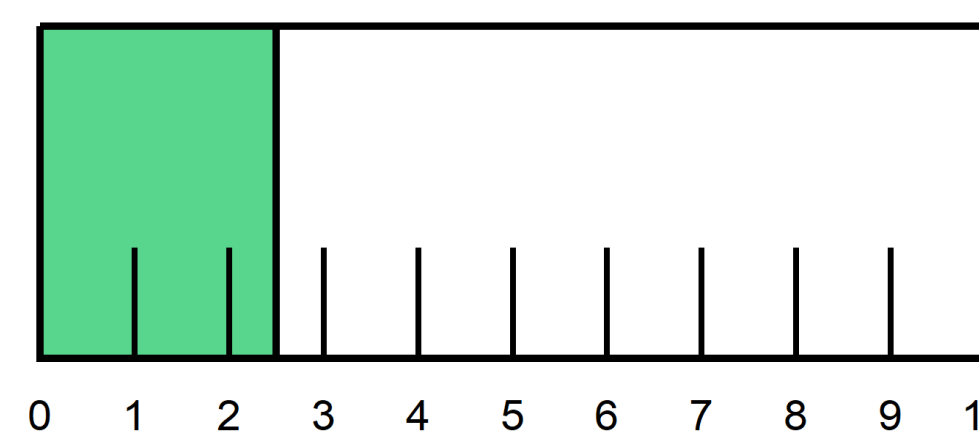
Perfect Health (100)



Option A: 10 Years in Current Health (25.5)



Option B: 2.5 Years in Perfect Health (100)

Risk Preference Section (Based on VAS)

- For 6 hypothetical health gamble scenarios leveraged from Mulligan et al. 2024, certainty equivalents (CEs) elicited via choice between certain outcome (A) or risky prospect (B)<sup>3</sup>
- In both, subjects are told to imagine health as increasing in a number ranging from 0 (death) to 100 (perfect health)
- Respondents are also told to imagine being 40 years old with usual health equal to 100, and to imagine further that their health deteriorates to specified level 20 out of 100
- Responds are told that treatments would change their health for one year, after which time it would return to 100
- Switch point from treatment B to A indicates CE → **In this example, CE would be 25.5 (midpoint of 24 and 27)**

Time Trade-Off (TTO) Section

- 6 standard TTO questions will be fielded; one at each of the CEs identified for each patient in the risk preference section
- Establishes a direct link between VAS and TTO indexes;** allowing estimation of TTO-based utility functions
- Enables easy implementation (e.g., just plug in commonly available EQ-5D values into these newly derived utility functions, then take resulting value and run model with that)
  - Instead of mapping to VAS first → removes 1 step

## METHODS (ANALYTIC APPROACH)

- CEs from survey to be used to structurally estimate parametric utility functions under expected utility theory as shown:
- Using Constant Relative Risk Aversion (CRRA) as an example, utility ( $W$ ) over health ( $H$ ) can be represented as:

$$W(H) = H^{1-\rho}$$

- Since utility from CE is same as that of gamble:

$$H_{CE}^{1-\rho} = \frac{1}{2} \bar{H}^{1-\rho} + \frac{1}{2} \underline{H}^{1-\rho}$$

- Here,  $H$ ,  $\bar{H}$ , and  $\underline{H}$  depict health level, and that of the good and bad outcome, respectively
- Next,  $\rho$  can be estimated using nonlinear least squares (NLLS) via the estimating equation:

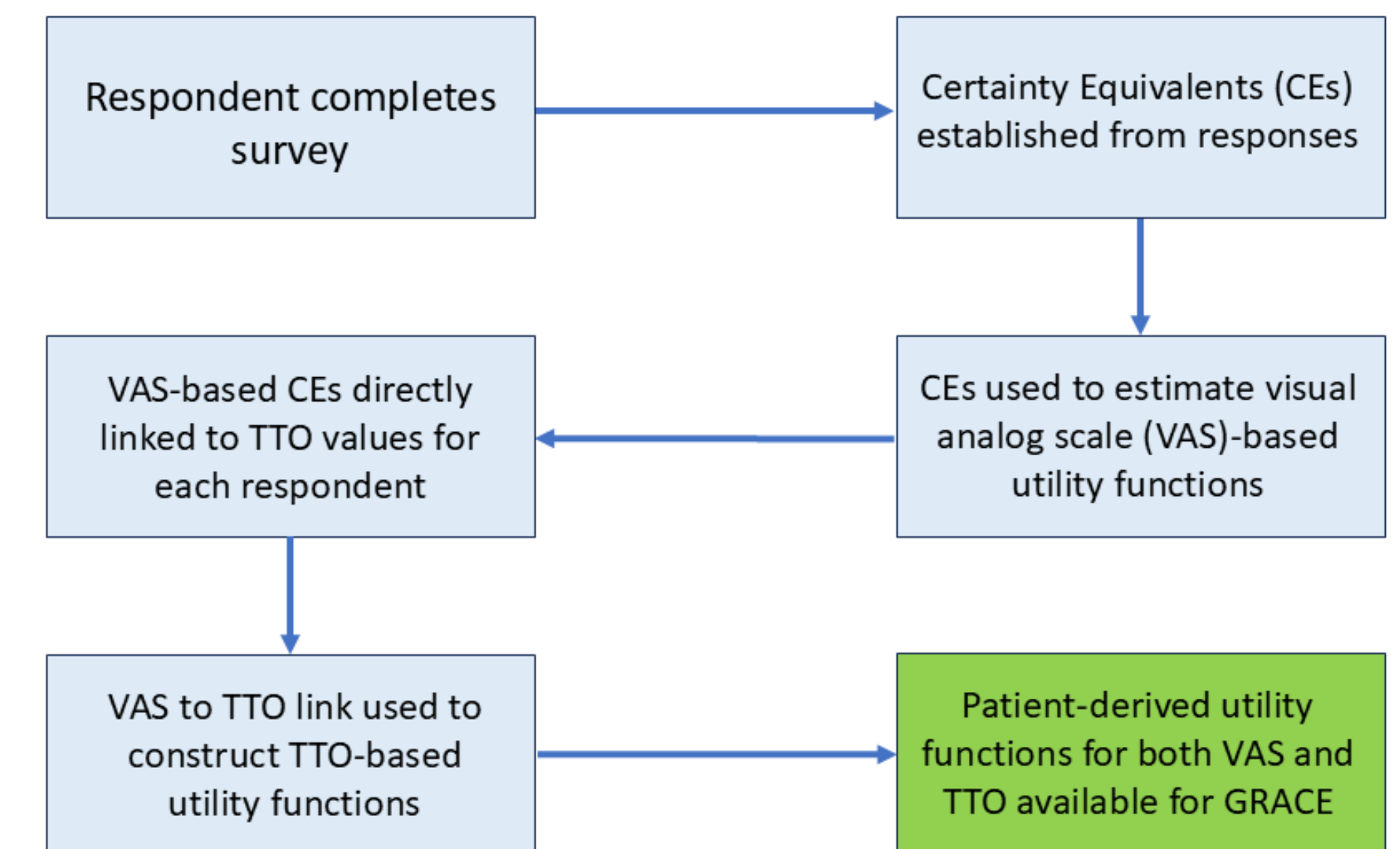
$$H_{CE,i} = \left( \frac{1}{2} \bar{H}^{1-\rho} + \frac{1}{2} \underline{H}^{1-\rho} \right)^{\frac{1}{1-\rho}} + \epsilon_i$$

- When  $\rho$  is estimated, so is the utility function:

$$W(H) = \frac{H^{1-\rho}}{1-\rho}$$

- Now with estimates of  $\rho$  in hand, **utility can be estimated for any health-related quality-of-life (HRQoL) value**
- Same approach for estimating utility under hyperbolic absolute risk aversion (HARA), 1 and 2-parameter expo-power structures
- Regress TTO values on VAS CE estimates to obtain coefficient → Use to estimate TTO-based utility functions

## ORDER OF OPERATIONS



## EXPLORATORY OUTCOMES

- Upon estimating utility functions, relative risk aversion can be derived via:
 
$$r = -\frac{W''(H)}{W'(H)} H$$
- Relative risk prudence derived via:

$$\pi = -\frac{W'''(H)}{W''(H)} H$$

## PILOT FINDINGS &amp; NEXT STEPS

- Median completion time of **20 minutes** in informal piloting
- Respondents found questions clear, but felt survey fatigue during TTO portion → randomizing and assigning 3 of 6 TTO questions per respondent is a possible alternative
- Next:** Pilot within patient population and refine survey

## EXPECTED RESULTS AND IMPLICATIONS

- Patient-derived utility functions over health, measured by both VAS and TTO indexes to be generated for GRACE
- HRQoL values can be sourced from published literature and matched to the appropriate utility function based on the health index used (e.g. EQ-5D to TTO function)

## REFERENCES

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- Mulligan K, Baid D, Doctor JN, Phelps CE, Lakdawalla DN. Risk preferences over health: Empirical estimates and implications for medical decision-making. J Health Econ. 2024;94:102857. doi:10.1016/j.jhealeco.2024.102857

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