A Brief Tour of the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model

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"A QALY is a QALY…" ?????

- In standard CEA, value of QALY gains is independent of baseline QoL
  - This violates common intuition and numerous survey results
  - People commonly prefer to improve health of the most-worse off
- Math of the CEA model reduces value of QoL improvements for disabled
  - QALY gain $= \Delta LE \times QoL + \Delta QoL \times LE$
  - U.S. Affordable Care Act bans use of CEA because of this discrimination
- CEA says that tradeoff between QoL and LE is the same at all QoL levels
  - Intuition says that those in worst QoL will be more willing to give up LE to improve QoL
- CEA says that only average health outcomes matter
  - If people care about risky outcomes, this misstates value of treatments

Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model Generalizes CEA

- Standard CEA assumes diminishing returns to consumption (C) but not QoL. $V(C,H) = U(C)H$
- GRACE makes one simple generalization, allowing for diminishing returns in QoL as well as for C.
- $V(C,H) = U(C)W(H)$ where $W(H)$ has positive but diminishing marginal utility.
- This also introduces risk aversion in QoL, so uncertainty in outcomes matters.

Five changes in proper conduct of CEA emerge

- Value for low-severity illnesses declines
- Rapidly increasing value as illness severity increases
- Major benefits shown for improvement in QoL for disabled people
- Tradeoff between LE and QoL changes with illness severity
- Uncertainty in treatment outcomes matters

Willingness to Pay in Standard CEA

- $\omega_C =$ elasticity of utility with respect to consumption
- $C =$ consumption (income minus medical spending)
- Willingness to pay for better health defined by the “opportunity cost”
- $K = \frac{C}{\omega_C}$ in CEA
- $.33 \leq \omega_C \leq .5$
- Therefore $2C \leq K \leq 3C$

WTP in GRACE

- $K_{GRACE} = C\left[\frac{\omega_H}{\omega_C}\right] R = K\omega_H R$
- WTP varies directly with severity of untreated illness (R)
- WTP for trivial illnesses is lower than K
  - $\left[\frac{\omega_H}{\omega_C}\right] < \frac{1}{\omega_C}$ since $0 < \omega_H < 1$ with positive but diminishing marginal utility for QoL
- CEA overvalues treatments for mild illnesses
- CEA undervalues treatments for highly severe illnesses

Polling Questions

1. **If your level of income fell by 10 percent, by what percentage would your overall happiness (utility) fall?**
2. **If your level of health status fell by 10 percent, by what percentage would our happiness (utility) fall?**

GRACE adds two additional factors

- ω_H = elasticity of utility with respect to QoL
- R = measure of illness severity
- Define $H = H_0(1 - \ell^*)$
  - Severity of illness is ℓ^* where $0 \leq \ell^* < 1$
- $R = \frac{Marginal\ Utility\ when\ sick}{Marginal\ Utility\ at\ H_0}$
- The value of R:
  - Depends considerably on r_H^*
  - To date, r_H^* remains unmeasured
  - Probably, $0 < r_H^* < 1$

Table 3
Baseline QoL levels for a set of example diseases.

ℓ^*	Example Diseases
0.0–0.1	Peptic Ulcer Disease; Stress Urinary Incontinence; Benign Prostatic Hyperplasia
0.1–0.2	Grave's Disease; Hypertension with no complications; Sleep Apnea
0.2–0.3	Familial Hypercholesterolemia; Peripheral Arterial Disease; End-Stage Knee Osteoarthritis
0.3–0.5	Type 1 Diabetes; Acute Lung Injury; Moderate to Severe Rheumatoid Arthritis
0.5–0.7	TIA[a] and Carotid Stenosis; TBI[b]; Nursing Home Residents at Risk of Pressure Ulcers
0.7–1.0	Alzheimer's disease; Metastatic Colorectal Cancer; Acute Pulmonary Embolism

Notes: Example diseases are taken from the Tufts Cost-Effectiveness Analysis Registry.
[a] Transient ischemic attack.
[b] Traumatic brain injury.

R varies with degree of risk aversion in QoL

R-Multipliers for alternative values of r_H^* and ℓ^*

	r_H^*						
ℓ^*	0	0.25	0.5	0.7	0.8	0.9	1
0	1	1	1	1	1	1	1
0.1	1	1.03	1.05	1.08	1.09	1.1	1.11
0.3	1	1.09	1.2	1.28	1.33	1.39	1.43
0.5	1	1.19	1.41	1.62	1.74	1.87	2
0.7	1	1.35	1.83	2.32	2.62	3.01	3.33
0.9	1	1.78	3.15	5.01	6.29	7.91	9.95

Baseline disability also enters

- Define $d^* =$ proportional health loss from pre-existing disability. Baseline health is $H = H_0(1 - d^*)$
- In this situation, $K_{GRACE} = K\omega_C R\left\lceil \frac{1}{1-\psi d^*} \right\rceil$
  - ψ adjusts for diminishing marginal utility of H
- GRACE places higher value on improving QoL for disabled people than standard CEA does.
- This (at least partly) resolves the ACA concerns about CEA discrimination against disabled people

WTP for QoL extensions rise with illness level

Think of this tradeoff, δ, as WTP in LE for QoL gains

- Commonly occurs in healthcare
- Standard CEA assumes that δ is the same for all levels of illness.

A similar question: In which situation would you prefer 500 more SF of living space?

- In a small 1000 SF apartment
- In a large "McMansion" house

Some Common Examples:

Chemotherapy and/or Radiation Therapy:
Temporary but major reductions in Quality of Life (QoL) from side effects of drugs (nausea, hair loss, fatigue….) in exchange for extended life expectancy (LE)

Open heart surgery:
Improved QoL from reduced angina, increased functionality vs. surgical fatality risk of 3-5% or more.

QoL gain from total knee replacement vs. post-operative death risk of 1:167.

Reduced low back pain vs. surgical mortality risk of 1:770.

Treatment outcome uncertainty also matters

- Reduced variance creates value to risk-averse consumers
  - "Value of Insurance"

- Greater positive skewness increases value
  - "Value of Hope" – greater chance of wonderful improvement

- The "uncertainty" effect matters most when there is little average difference in treatment outcomes.

$$\epsilon \approx 1 + \left[\frac{\mu_H}{\mu_B}\right]\left[-\frac{1}{2} r_H^* \left(\frac{1}{\mu_H}\right)^2 \Delta\sigma_H^2 + \frac{1}{6}\pi_H^* r_H^* \left(\frac{1}{\mu_H}\right)^3 \Delta[\gamma_1 \sigma_H^3] + \ldots\right]$$

Incentives for Innovation

- Standard CEA says that value of adding a specific amount of health is the same no matter what the level of untreated health.
- GRACE says that improving health of the sickest is most valuable.
- If implemented in value-based pricing, GRACE would change “signals” sent to innovators
  - Biopharmaceutical
  - Medical device
  - Medical treatment strategies (not subject to IP laws…)

Summary

Key Differences between GRACE and CEA

- WTP for minor diseases is lower in GRACE
- WTP for serious diseases is higher in GRACE, rising rapidly with severity
- WTP for QoL improvements for disabled rises rapidly with severity
- Uncertainty of treatment outcomes also enters measures of value
- GRACE sends different “signals” to innovators about what is most valuable to society.

Thank you for your attention

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Operationalizing GRACE

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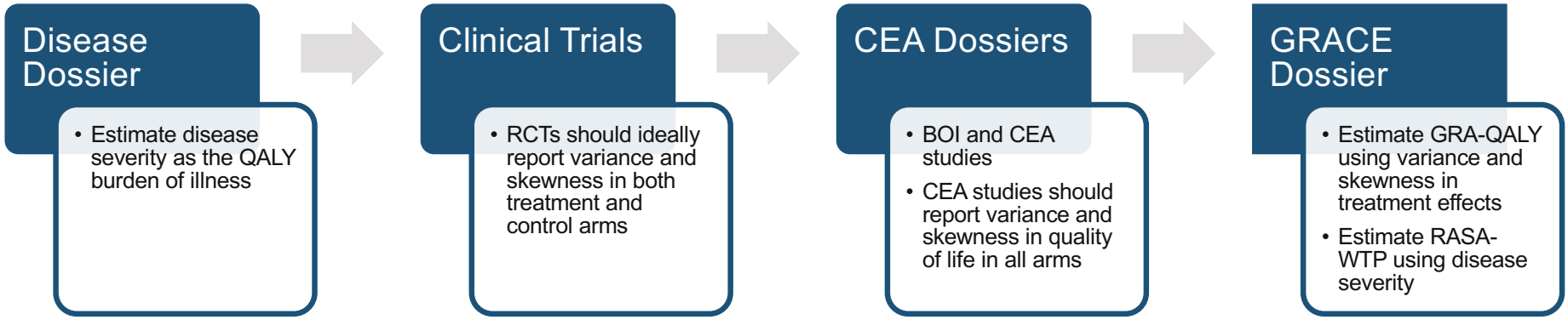
HEOR data-generation can be readily adapted to GRACE

Above Brand

Estimate Relative Risk Preferences

- Existing DCE methods can estimate “relative risk-aversion” and “relative prudence” in the generally insured population, which could vary with geography

Within Brand



GRACE requires three sets of new parameters

Some parameters are unique to GRACE and do not appear in traditional cost-effectiveness

Burden of illness measures

Variance and skewness of outcomes

Risk preferences over health-related quality of life

Producing the raw materials for GRACE

Burden of Illness

Why it matters

- Disease severity affects the value of health improvements

What is needed

- Baseline quality of life in untreated sick state, treated sick state, and (optionally) pre-illness state with permanent disability
- E.g., quality of life can be measured using QALYs or any other health index
- GRACE is agnostic about the way quality of life is measured

How often it is needed

- These parameters are needed for every indication and treatment
- Typically, they are already estimated in traditional burden of illness studies

Producing the raw materials for GRACE

Variance and Skewness of Outcomes

Why it matters

- Risk-averse patients care about variability in outcomes

What is needed

- Variance and skewness in quality-of-life outcomes
- These parameters must be calculated separately for the treatment and for the standard of care
- E.g., if quality of life is measured using QALYs, these parameters could be recovered from existing cost-effectiveness simulation models
- GRACE is agnostic about the way quality of life is measured

How often it is needed

- These parameters are needed for every indication and treatment
- Typically, they can be measured in the cost-effectiveness simulations that are already conducted

Producing the raw materials for GRACE

Risk Preferences Over Health-Related Quality of Life

Why it matters

- The degree of relative risk-aversion and relative prudence affects the way patients value variability in outcomes and disease severity

What is needed

- Estimates of relative risk-aversion and relative prudence over health-related quality of life
- GRACE is agnostic about the way quality of life is measured

How often it is needed

- These parameters could be estimated just once or twice and applied globally
- Ideally, they would be measured in different populations of people to ascertain heterogeneity

Methods for measuring risk preferences over health

Risk preferences can be measured using established survey methods

An existing literature uses discrete choice experiments to measure risk preferences over consumption

- These methods have been used to measure risk preferences over health

An alternative literature has developed survey methods for directly measuring "happiness"

- These methods could be used to measure risk preferences over health, although this would be a novel application

Methods for measuring risk preferences over health

Discrete choice experiments are an established way to measure risk preferences

Concept

- Present respondents with choices between sure levels of health and gambles over health
- Specify a form for an underlying utility function
- Estimate the parameters of that utility function using the choices that respondents make

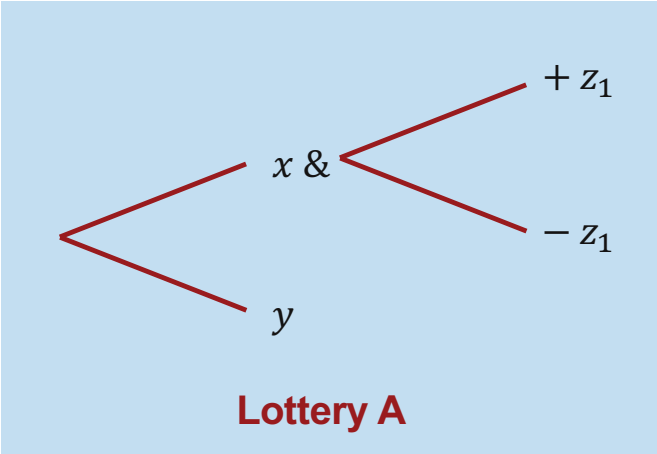
Prior studies can serve as models

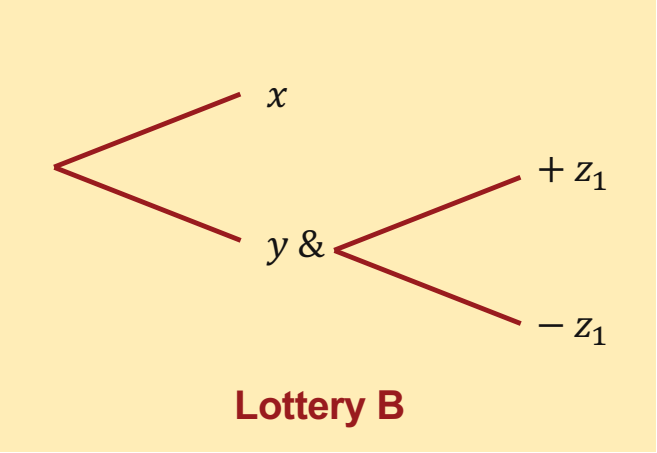
- Charles Noussair et al. (2013, *Review of Economics and Statistics*) present methods for estimating relative risk-aversion and relative prudence over money
- Arthur Attema et al. (2016, *Journal of Health Economics*) present methods for estimating relative risk-aversion over health-related quality-of-life

Methods for measuring risk preferences over health

Discrete choice experiments build upon choices between sure bets and risky gambles

Measuring Prudence ($x \neq y$):





Measuring risk aversion is similar, except the comparison is between a sure bet and a lottery, rather than a sure bet versus a sure bet followed by a lottery.

Methods for measuring risk preferences over health

Happiness regressions provide a novel way of measuring risk preferences

Concept

- An existing literature has developed methods for asking people about their level of happiness directly (e.g., Richard Easterlin, *PNAS*, 2003)
- Ask people about happiness, health, and income
- Use the results to directly estimate a utility function
- The resulting estimates identify the parameters of the utility function, along with risk-aversion (see Lakdawalla/Phelps, *European Journal of Health Economics*, 2021)

Methods for measuring risk preferences over health

Happiness regressions provide a novel way of measuring risk preferences

Estimation Approach

$$\ln(Happy_i) = \beta_1 \ln(H_i) + \frac{1}{2}\beta_2(\ln(H_i))^2 + \beta_3 \ln(C_i) + \frac{1}{2}\beta_4(\ln(C_i))^2 + \epsilon_i$$

GRACE will be no harder to implement than standard CEA once we have risk parameter estimates

GRACE parameters are already accessible to researchers

- Burden of illness parameters are already part of a CEA dossier
- Variance and skewness of outcomes can usually be estimated using the same CEA models that are already being developed
- Relative risk preferences need to be estimated, but this is a fixed-cost, not one that must be borne for every new technology
- With these estimates in hand, the Incremental Generalized Risk-Adjusted Cost-Effectiveness Ratio (IGRACER) can be estimated
    - Just multiply the parameters as shown in Lakdawalla/Phelps (*EJHE*, 2021)

How to learn more about GRACE

Four articles in print: (Lakdawalla and Phelps)

Health Technology Assessment with Risk Aversion in Health

JHE
July 2020

Health Technology Assessment w/ Diminishing Returns to Health: The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model

VIH
February 2021

A Guide to Extending and Implementing Generalized Risk-Adjusted Cost-Effectiveness (GRACE)

EJHE
September 2021

Generalized Risk-Adjusted Cost-Effectiveness (GRACE): Ensuring Patient-Centered Outcomes in Healthcare Decision Making

ISPOR Value & Outcomes SPOTLIGHT
September 2021

(First Prize in PhRMA Foundation Value Assessment Challenge)

COMING SOON! (Phelps and Lakdawalla)
The Generalized and Risk-Adjusted Cost Effectiveness (GRACE) Model: Overview and Implementation (textbook, expected publication in 2022)

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