PIPC Partnership to Improve Patient Care

Generalized Risk-Adjusted Cost Effectiveness (GRACE)

What is GRACE?

- Generalized Risk-Adjusted Cost Effectiveness (GRACE) is a novel methodology for measuring the cost effectiveness of a healthcare intervention developed by academics at the University of Southern California and University of Rochester.
- GRACE uses a threshold-based approach to evaluate the value of medical technologies and is different than traditional cost effectiveness analyses by making two assumptions that:
    - People with a disease or condition, who are relatively healthy, get less value from treatments than people experiencing severe illness or disability; and
    - A person's willingness to pay for a treatment increases or decreases with their level of disease severity and disability.

How is GRACE different?

- GRACE was designed to address that traditional cost effectiveness analyses assume that all patients – regardless of baseline health – value health gains the same.
- GRACE attempts to mathematically account for this challenge using the concept of diminishing returns, under which GRACE assumes a person with a more severe condition or disability will place higher value on health gain than a healthy person.
- GRACE adjusts willingness to pay (value-based thresholds) based on disease severity and disability. This means GRACE more highly values treatments for patients it determines to have more severe disability or illness, with lower value to treatments for patients considered less sick.
- These adjustments using GRACE imply that traditional cost effectiveness analysis can overvalue diseases classified as "mild" by almost 50%.

How does GRACE measure up?

- Like the QALY, GRACE relies on measures of health outcomes and quality of life that do not account for the perspectives of patients and people with disabilities, and therefore omit many symptoms or impacts important to patients.
- Despite its intent to address issues with the QALY, published studies using GRACE allow for interchangeable comparisons from cost/utility to cost/QALY.
- GRACE uses general surveys of the public to determine level of disease severity and relies on approximations of a "representative individual" that do not incorporate personalized needs or characteristics of individual patients.
- GRACE gives a lower value to improvements in quality of life for people classified as having "mild" diseases based on GRACE, such as migraines or reflux.
- GRACE is new and untested. There are no independent evaluations and few real-world

applications. To implement GRACE would require extensive detailed data on patients' risk profiles, co-existing conditions, and other relevant factors currently lacking and challenging to obtain.

- GRACE does not explicitly incorporate equity concerns related to race, ethnicity, or socioeconomic factors, nor does it account for implicit bias or structural inequities within healthcare systems, disparities in access to healthcare services and treatments, or social determinants of health.

Who is using GRACE?

- Most publications on GRACE are theoretical, authored by its creators.
- No Patient Left Behind (NPLB) applies GRACE and other approaches to cost effectiveness analysis in its report: "Getting the math right when measuring the value of medicines."
- In the 2023 Inflation Reduction Act revised guidance, GRACE was a listed methodology to be evaluated to determine if it violates the law's patient protections and whether GRACE can be used by government to evaluate value of certain pharmaceuticals.

What is the broader community saying?

- National Council on Disability referenced GRACE in its 2022 brief "Alternatives to QALY-Based Cost-Effectiveness Analysis for Determining the Value of Prescription Drugs and Other Health Interventions": *"The GRACE framework comes with its own shortcomings, underscoring the continued need for better data, including new estimates of attitudes toward risk in health outcomes. Like traditional CEA, the GRACE method currently relies on health utilities of a "representative individual" that do not necessarily incorporate issues such health inequities, on which topic the authors suggest future research."*
- Researchers Ryan Fischer, et al., discuss the potential of GRACE to assess the value of rare disease treatment in their article: "Healthcare Stakeholder Perspectives on a Value Assessment Approach for Duchenne Muscular Dystrophy Therapies.": *"The health economists indicated there may be a need to modify cost-effectiveness thresholds; for example, allowing higher thresholds for more severe diseases. New approaches such as disease severity modifiers—as adopted by the National Institute for Health and Care Excellence (NICE)—or novel approaches such as the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) analysis — may be useful.*
- ICER references GRACE in its September 2023 value assessment framework update, including a placeholder for future exploration: "*We will focus on exploring the Generalized Risk-Adjusted Cost-Effectiveness framework …And, as a result of this special focus, ICER may entertain making an interim update to its Value Assessment Framework on this topic prior to the next overall update."*