

# University of Colorado Contributions to ICER Reports; What's Next for U.S. Value Assessment?

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# Outline

- Mathematics warm-up and Motivation
- U of Colorado contributions to Institute for Clinical and Economic Review (ICER) reports
- U.S. Coverage and Reimbursement Patterns
- Can additional quantitative decision aids advance the science of U.S. value assessment?



# Mathematical Relationships

- What is the relationship between the area of a perfect square (with side length =  $N$ , where  $N$  is any whole number) and the area of a rectangle with side lengths  $N-1$  and  $N+1$ ?
- Claim: The area of the perfect square equals the area of rectangle plus 1.
  - Visual (partial) proof
  - Algebraic proof

# Visual Proof

- For illustration purposes,  
suppose  $N = 6$

$N = 6$



# Visual Proof

- Area of perfect square =  $N \times N = 36$

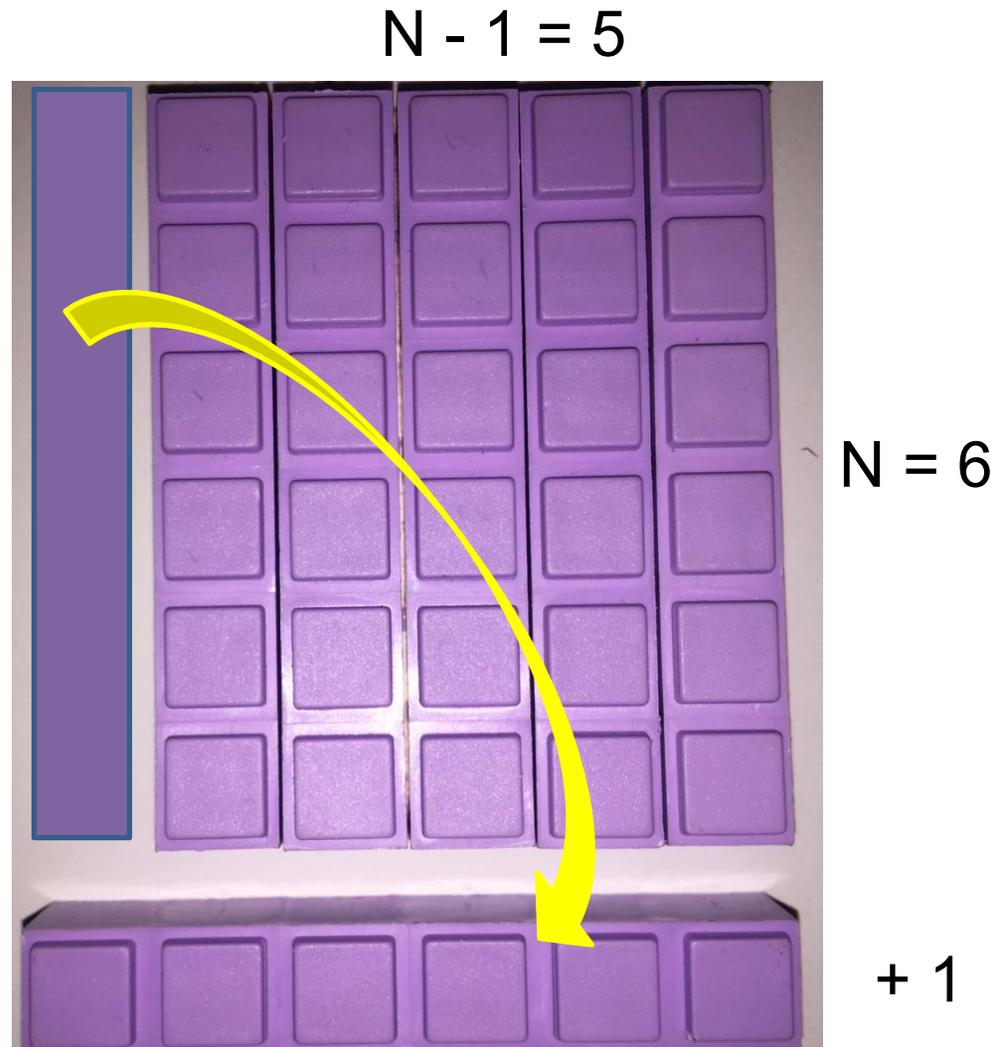


$N = 6$

$N = 6$

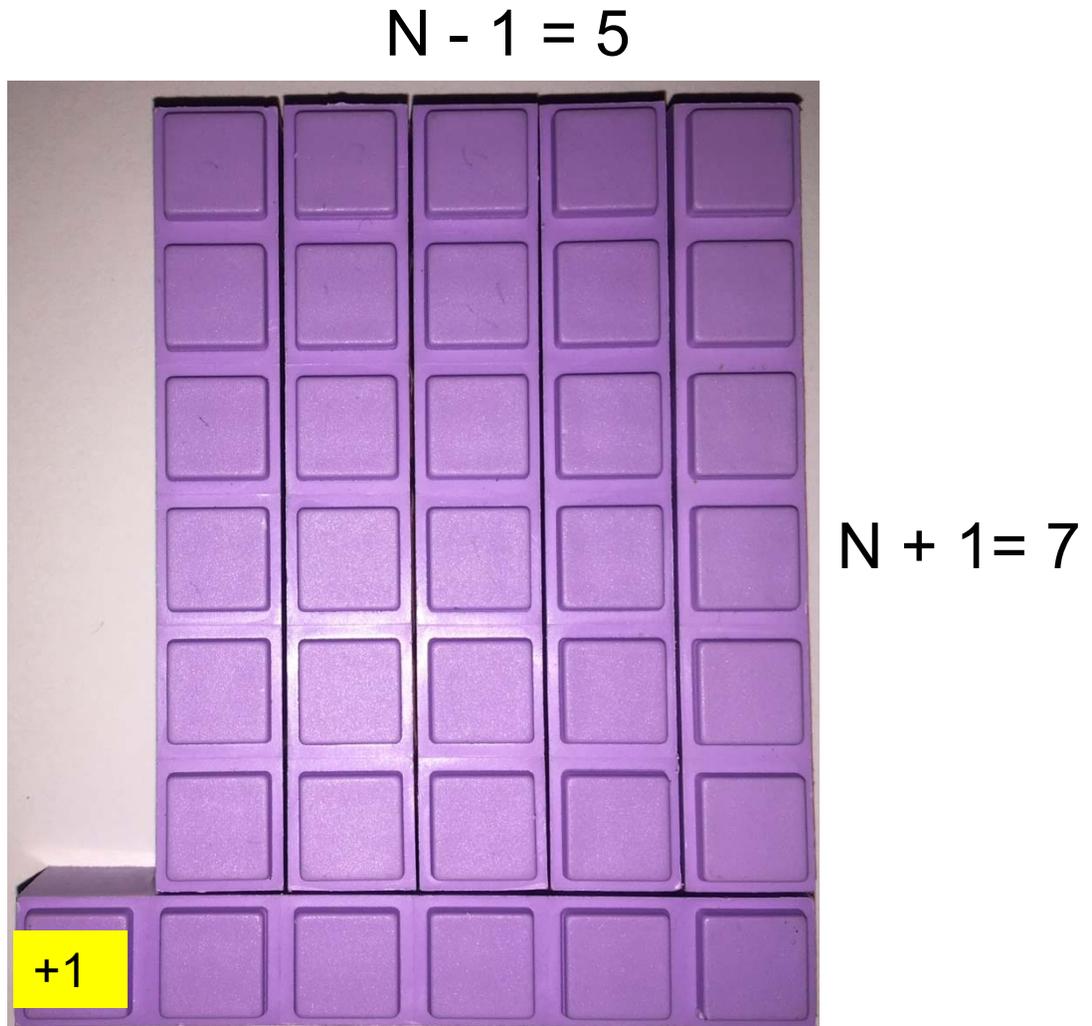
# Visual Proof

- How do we manipulate the perfect square to approximate the rectangle with sides  $N-1$  and  $N+1$ ?



# Visual Proof

- The area of the perfect square is one more than the area of the rectangle with sides  $N-1$  and  $N+1$



# Algebra Proof

- Claim: The area of the perfect square (sides  $N \times N$ ) equals the area of the rectangle (sides  $N-1 \times N+1$ ) plus 1.
- Does  $N \times N \stackrel{?}{=} (N-1) \times (N+1) + 1$
- $N^2 \stackrel{?}{=} N^2 + N - N - 1 + 1$
- $N^2 = N^2$  Q.E.D. ✓

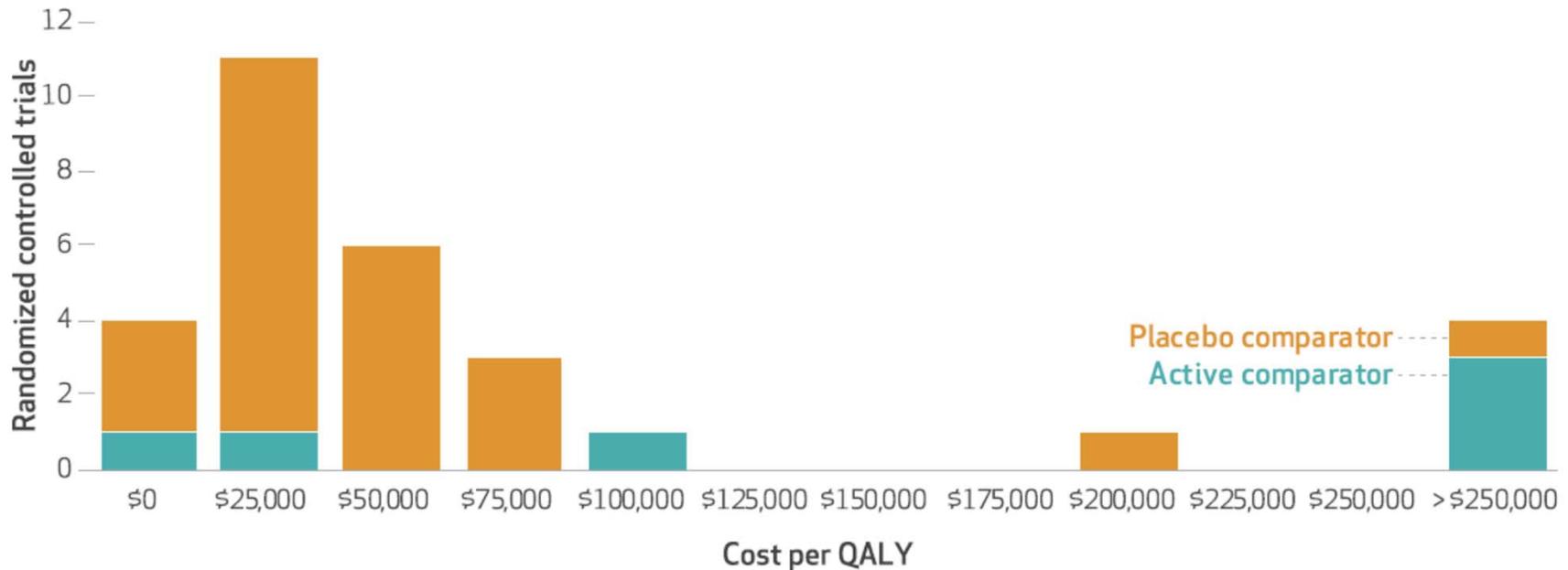
# Motivation

- Claim 1. Value =  $\frac{\Delta Cost}{\Delta QALY}$  (i.e. traditional cost-effectiveness) alongside a cost-effectiveness threshold
- Claim 2. If value is synonymous with cost-effectiveness in the U.S. and we have value-based system(s), then we should observe a tight clustering of cost-effectiveness for commonly prescribed (and paid) medicines.

# Claim 2 does not hold

## EXHIBIT 1

Distribution of the incremental cost per quality-adjusted life-year (QALY) gained from the model estimates



- Of 25 commonly prescribed CVD drugs, 5 (20%) had cost-effectiveness findings above commonly cited thresholds.

Campbell JD, Belozeroff V, Whittington MD, Rubin RJ, Raggi P, Briggs AH. Prices For Common Cardiovascular Drugs In The US Are Not Consistently Aligned With Value. Health Affairs (Millwood) 2018, 37(8):1298-1305.

# Claim 2 does not hold

EXHIBIT 2

Trends in hazard ratios over time in randomized controlled trials of thirty commonly prescribed cardiovascular drugs, by year of trial publication and type of comparator

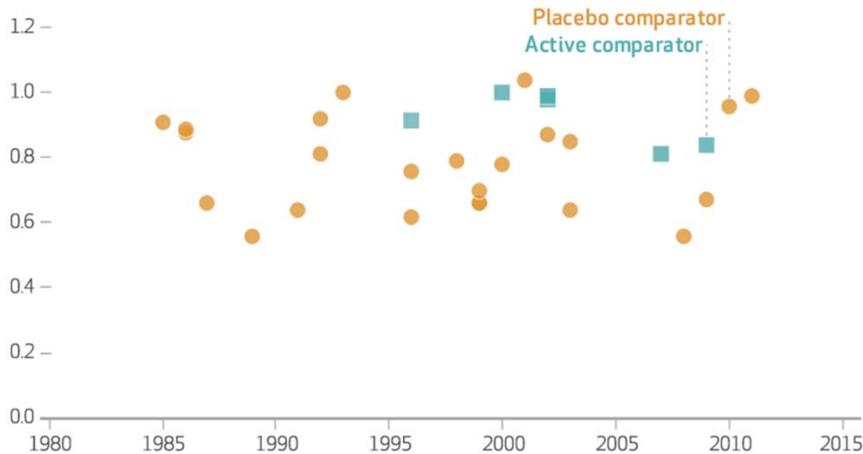
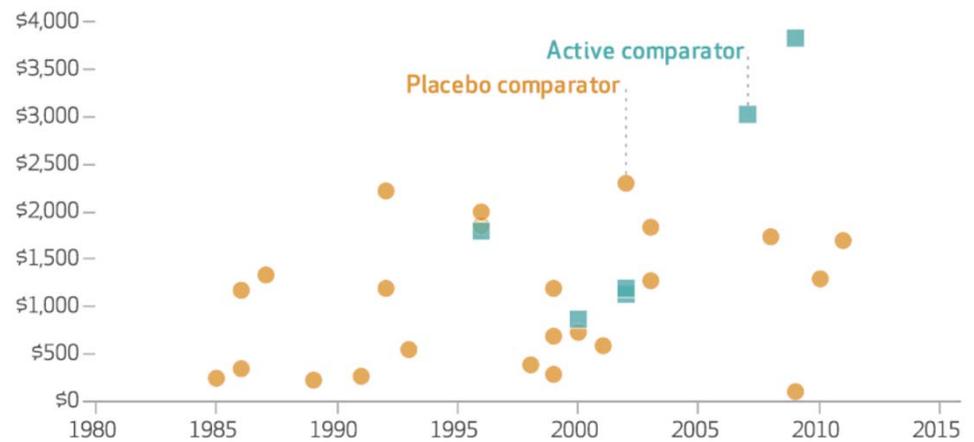


EXHIBIT 3

Trends in annual drug costs over time in randomized controlled trials of cardiovascular drugs, by year of trial publication and type of comparator



- Hazard ratios are flat over time (HRs are less favorable for active comparator trials)
- Annual drug prices increase over time (prices are higher for active comparator trials)
- *Claim 1, value = cost-effectiveness, needs further investigation*

Campbell JD, Belozeroff V, Whittington MD, Rubin RJ, Raggi P, Briggs AH. Prices For Common Cardiovascular Drugs In The US Are Not Consistently Aligned With Value. Health Affairs (Millwood) 2018, 37(8):1298-1305.

# CU Contributions to ICER reports

- Cost-effectiveness evidence for:
  - asthma biologics (2 reviews);
  - rheumatoid arthritis targeted immune modulators;
  - ovarian cancer PARP inhibitors;
  - B-cell malignancy chimeric antigen receptor t-cell (CAR-T) therapies
  - endometriosis (elagolix);
  - and ongoing assessments in secondary prevention of cardiovascular disease

# CU Team

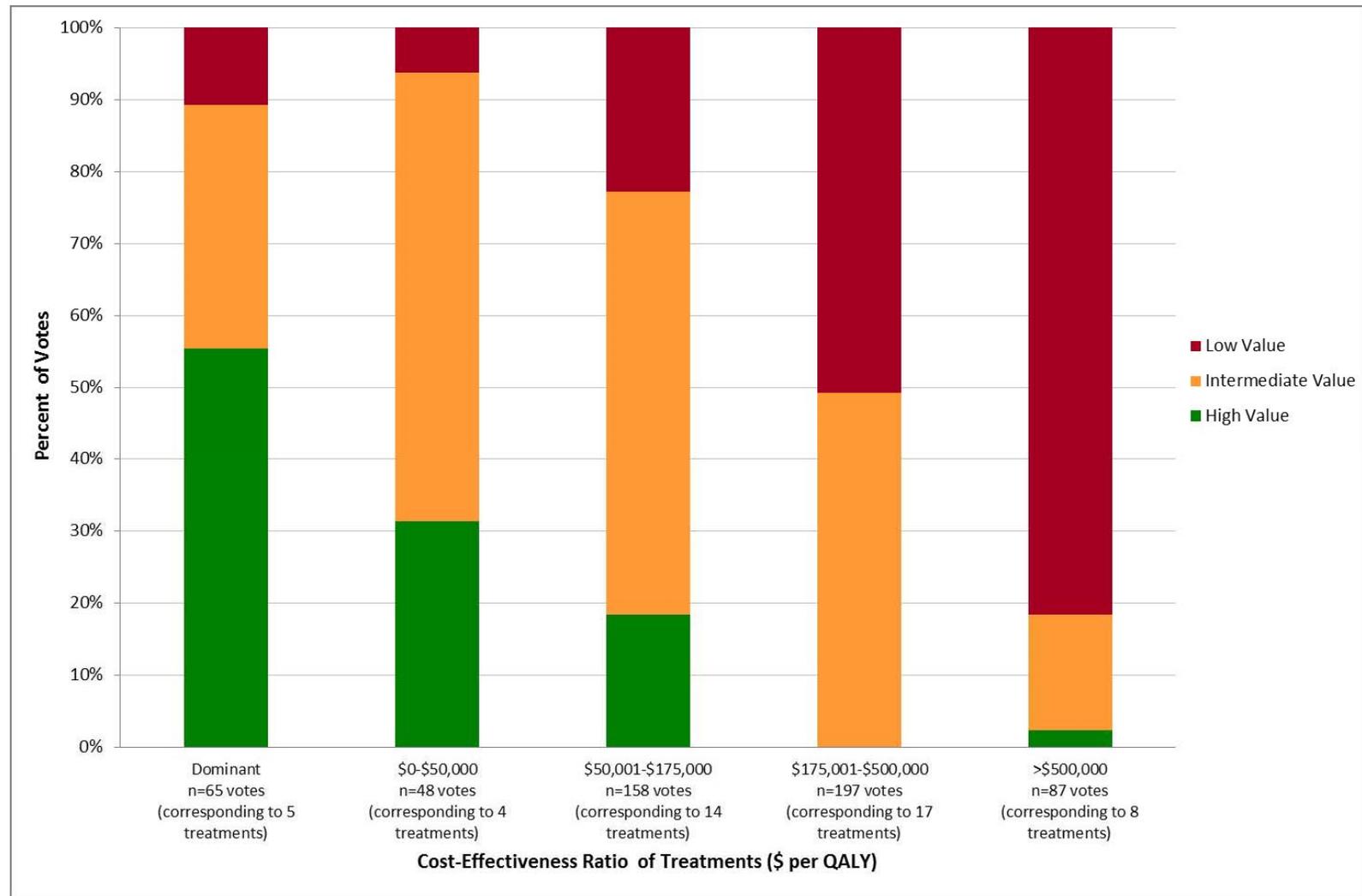
- 3 Faculty
  - Jon Campbell
  - R Brett McQueen
  - Mel Whittington
- PhD grad students
- Other staff have included a professional research assistant and post-doctoral fellow

# Economic model team contributions to ICER process

- Month 1
  - ICER announces topic; conversations with stakeholders begin
  - Contribute to draft scope
- Month 2
  - Contribute to final scope posted
  - Data requests drafted for manufacturers and others
- Month 3
  - Contribute to model analysis plan
  - Develop model
  - Join stakeholder calls
- Month 4
  - Present preliminary model to manufacturers and join calls with stakeholders
  - Validate model
  - Contribute to draft evidence report
- Month 5
  - Contribute to finalizing draft evidence report and draft model
- Month 6
  - Respond to public comments
  - Revise contributions to report and model
- Month 7
  - Contribute to finalizing report and model
  - Present economic findings at public meeting
- Month 8
  - Contribute to final report and model

<b>Disease State</b>	<b>Therapeutic Options</b>	<b>Comparator</b>	<b>Eligible Population</b>	<b>Incr. QALYs</b>	<b>Incr. Cost-Effectiveness Ratio (\$/QALY)</b>
Asthma	Mepolizumab; Nucala®	Standard of care (SoC) alone.	Individuals ages $\geq 12$ with severe eosinophilic asthma	1.53 / 1.63	\$385,546 / \$344,000
Rheumatoid Arthritis	Targeted immune modulators (Tocilizumab monotherapy; Actemra®)	Adalimumab monotherapy (Humira®)	Adults with moderately-to-severely active RA and inadequate response to conventional DMARDs.	0.4	Cost saving and increased QALYs
Ovarian Cancer	PARP inhibitors (Olaparib; Lynparza®)	Placebo (i.e. observation only).	Adult women with platinum-sensitive ovarian cancer; with complete or partial response to the most recent regimen and candidates for maintenance therapy.	0.59	\$324,116
B-Cell Lymphoma	CAR-T (Axicabtagene ciloleucel; Yescarta®)	Chemo-therapy (from SCHOLAR-1) for the treatment of DLBCL.	Adults ages $\geq 18$ with relapsed/refractory B-cell lymphoma after two or more lines of systemic therapy.	3.4	\$136,078

# Are ICER voting panels basing value votes on cost-effectiveness?



Neumann PJ et al. Should A Drug's Value Depend On The Disease Or Population It Treats? Insights From ICER's Value Assessments. Health Affairs Blog Nov 6, 2018 10.1377/hblog20181105.38350

# Are ICER voting panels basing value votes on cost-effectiveness?

- ICER devotes a section of their reviews to “Potential Other Benefits and Contextual Considerations” including domains with yes/no votes from the panel
- Criteria influencing value votes include:
  - cancer
  - ultra-rare diseases
  - reduced caregiver burden
  - improved productivity
  - disease severity
  - lack of evidence
  - uncertain benefits compared to alternatives
  - safety concerns

# Should we tinker with the threshold rather than incremental analyses?

## Value-Based Pricing for Emerging Gene Therapies: The Economic Case for a Higher Cost-Effectiveness Threshold

Louis P. Garrison, PhD; Tristen Jackson, PharmD, MS;  
Douglas Paul, PharmD, PhD; and Mike Kenston, BS, MBA

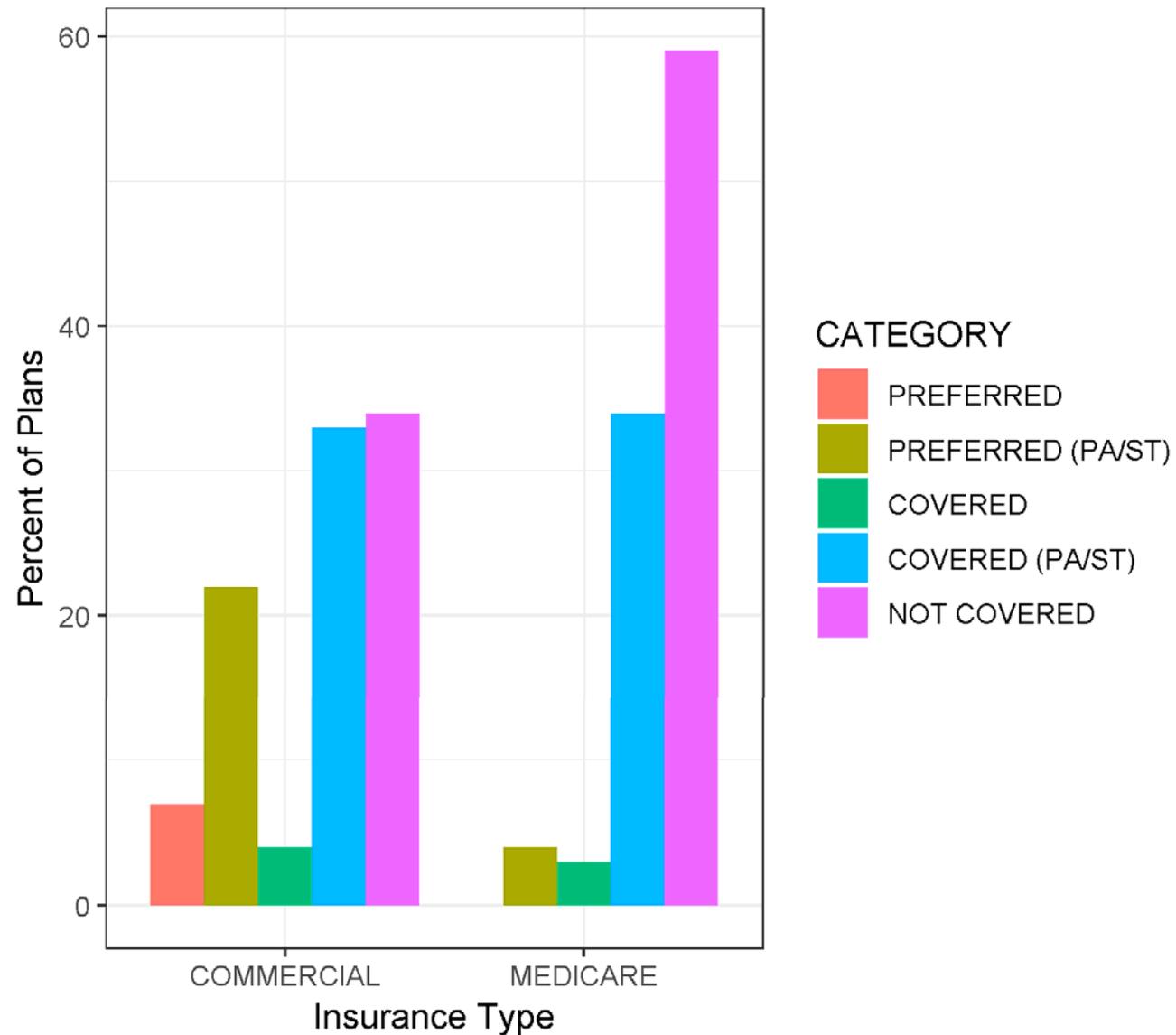
- Health Technology Assessment
  - Ultra-rare, value of statistical life (up to \$500k/QALY)
- Method Approaches
  - Opportunity cost, 3x GDP (\$20k to \$180k/QALY)
- Technology Examples (wide range)

# What about U.S. coverage and reimbursement patterns?

- Managed Markets Insight & Technology LLC.  
<https://www.formularylookup.com/>
  - February 2019
- Summarize the U.S. coverage of therapies CU team has contributed to ICER reviews and compare coverage with cost-effectiveness
  - Preferred (with or without prior authorization or step therapy)
  - Covered but not preferred (with or without prior authorization or step therapy)
  - Not covered

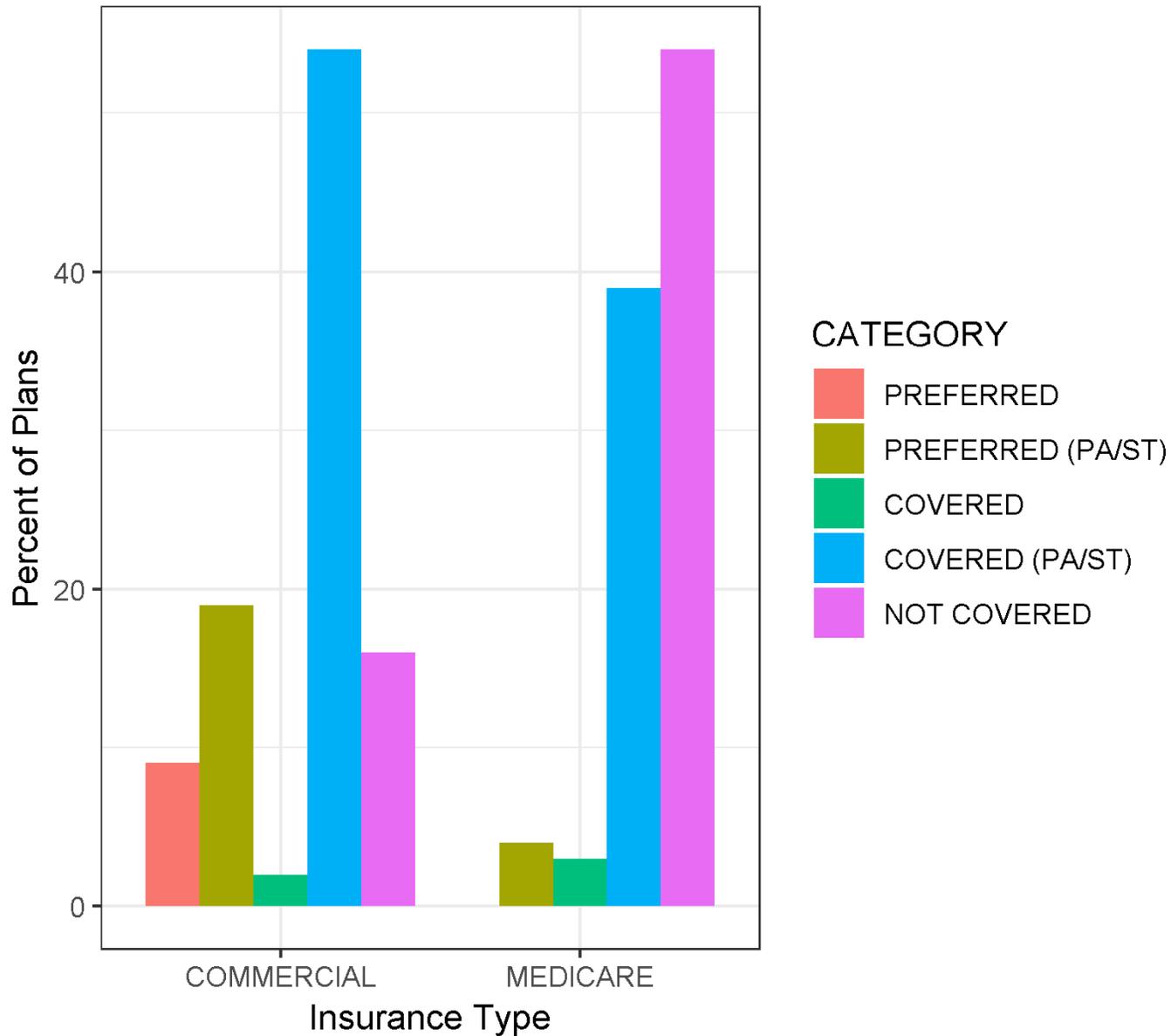
# Mepolizumab; Nucala®

\$344,000/QALY



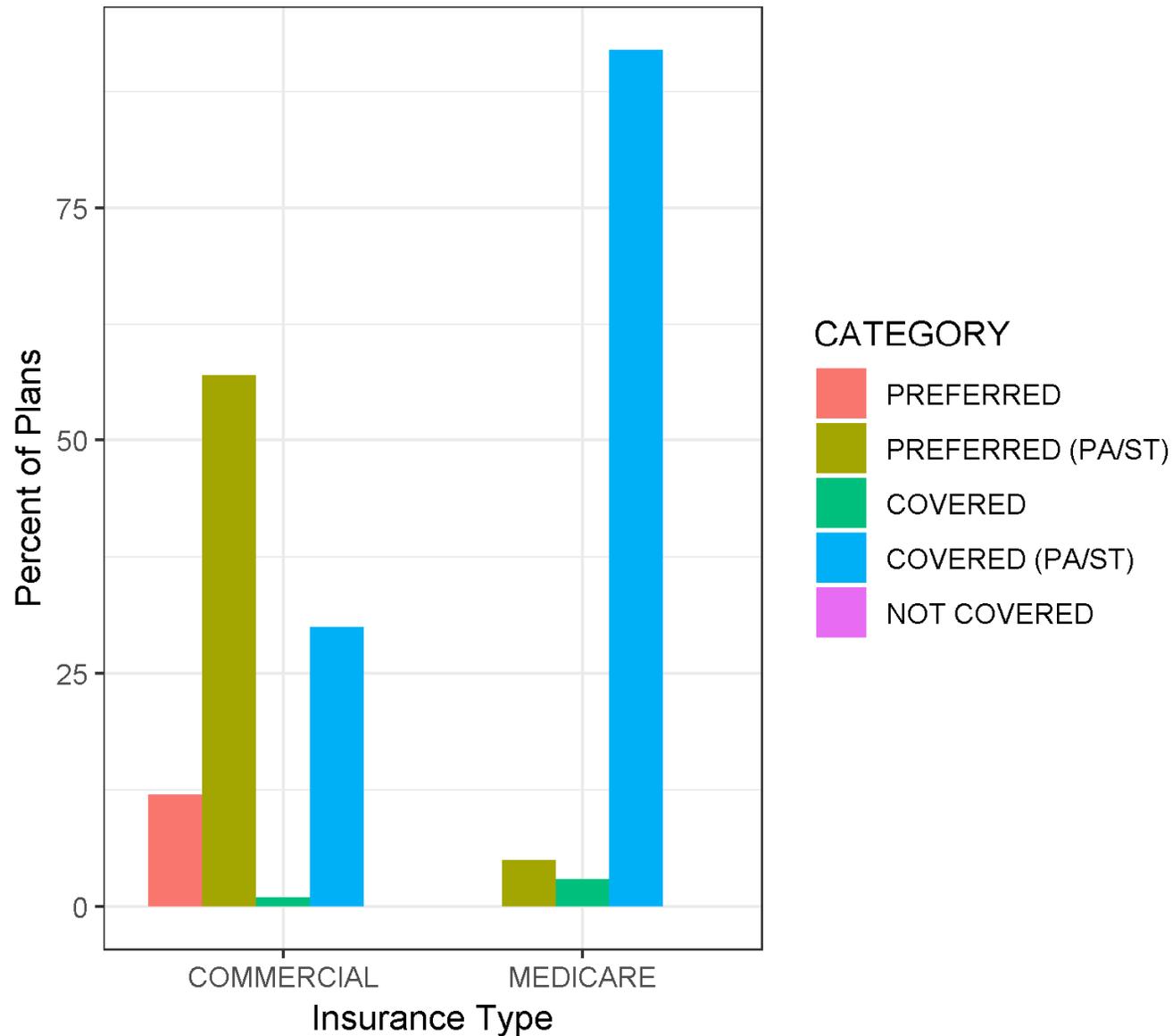
# Tocilizimab; Actemra®

Dominates Humira® (lower cost and higher QALY)



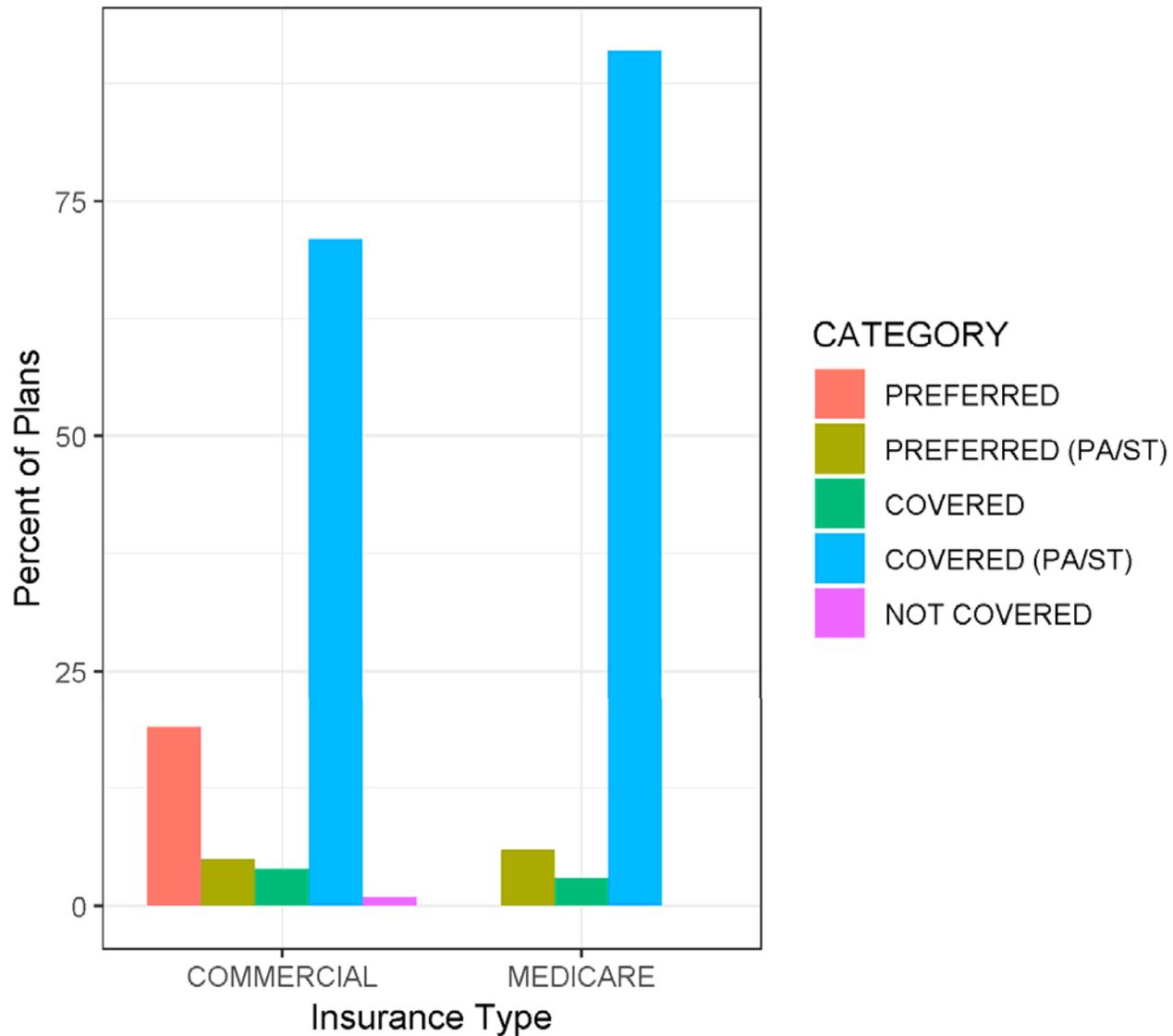
# Adalimumab; Humira®

Dominated by Actemra® (higher cost and lower QALY)



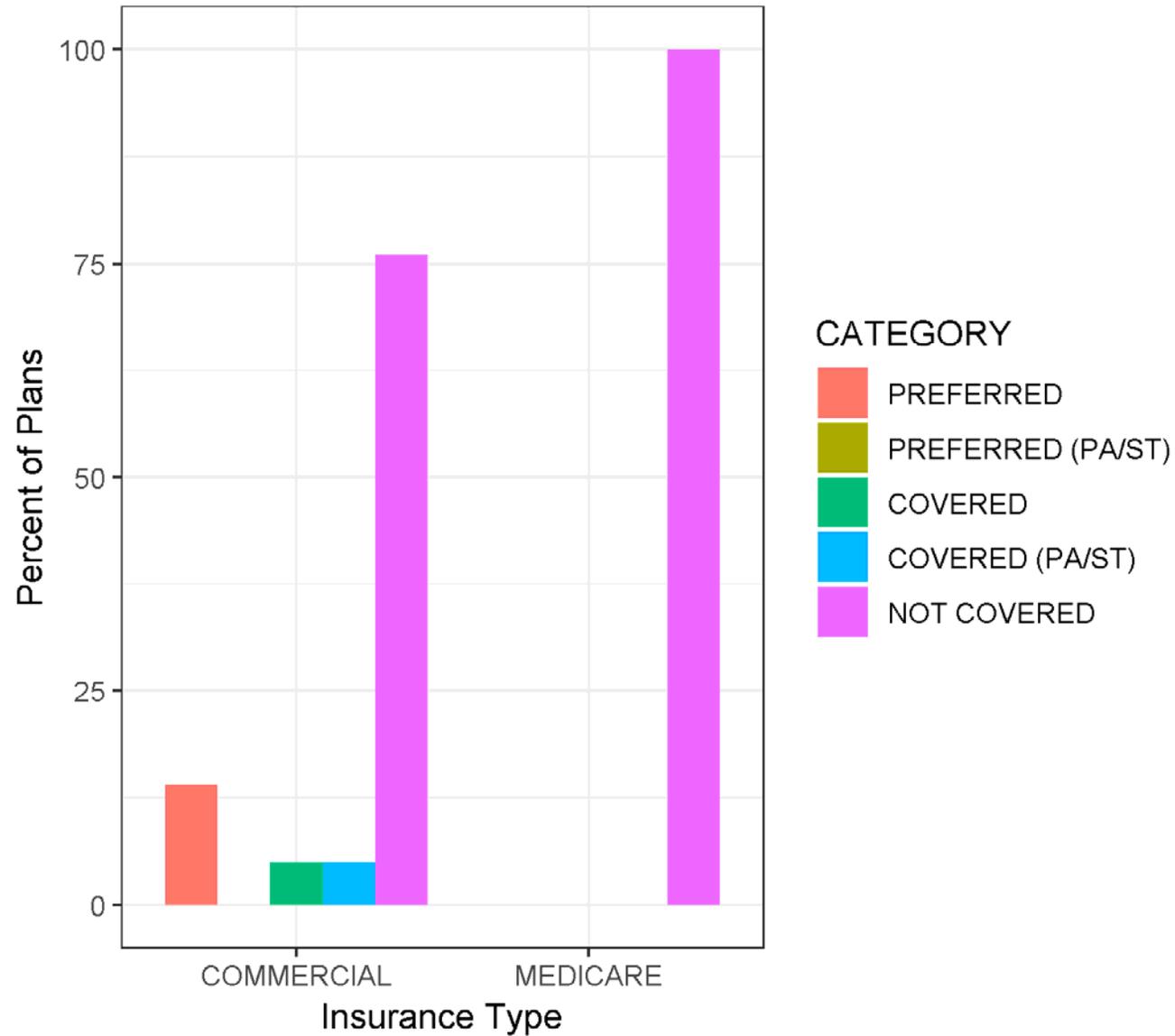
# Olaparib; Lynparza®

\$324,000/QALY

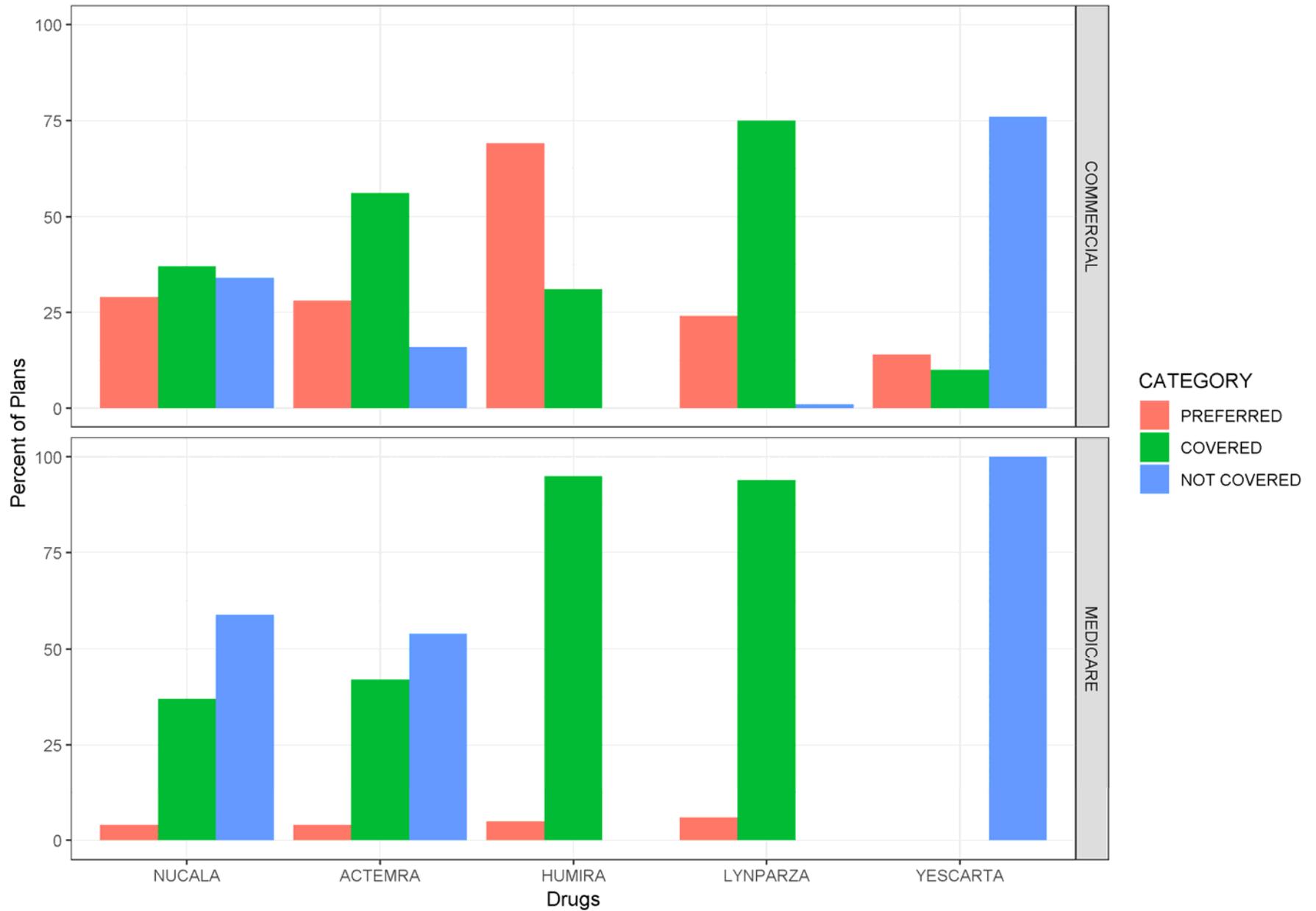


# Axicabtagene ciloleucel; Yescarta®

\$136,000/QALY



# Coverage Summary



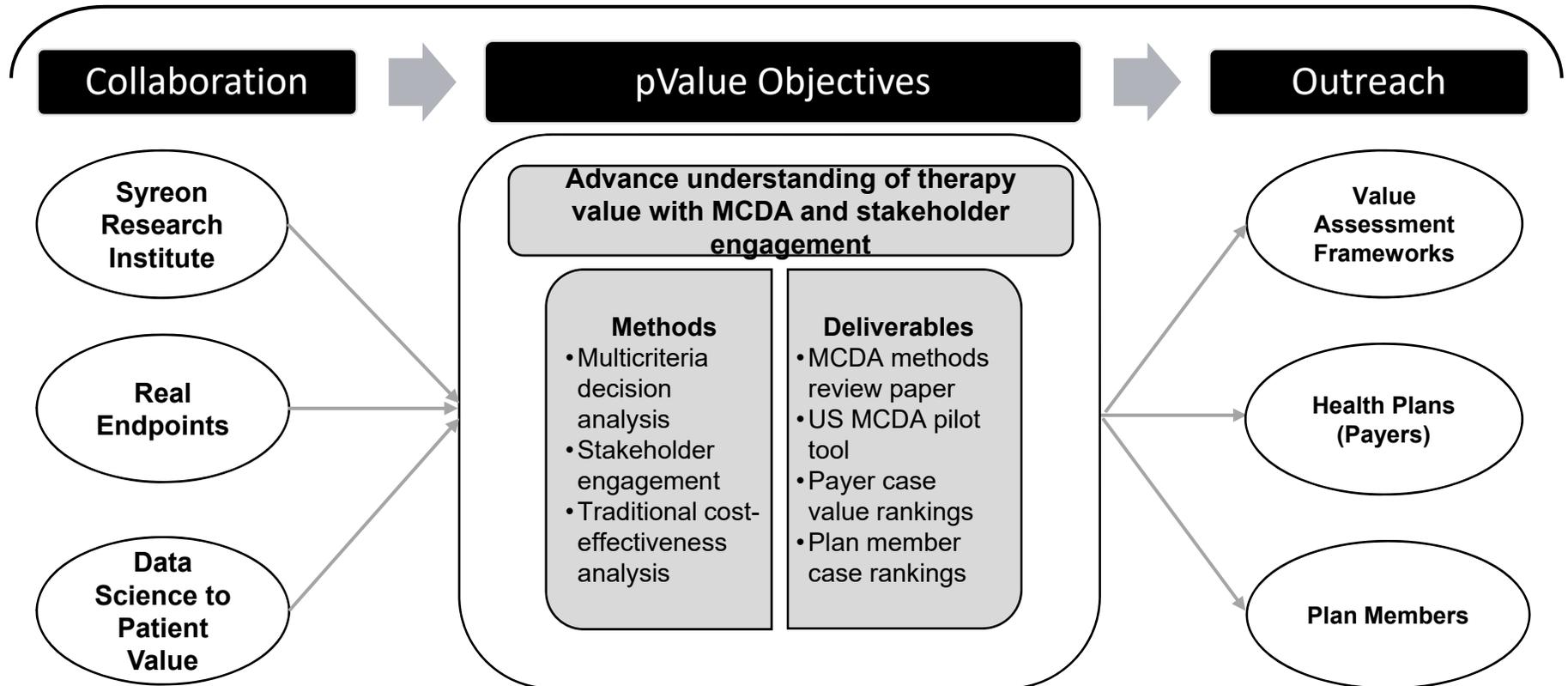
# Claims Revisited

- Health systems that strive to achieve good value will be more efficient
- Coverage heterogeneity across plans suggests different evidence weights
  - U.S. Coverage decisions are evidence-based, but what evidence and what weights?
- Cost-effectiveness is not synonymous with U.S. view of value but is a good starting point
  - \$5,000/QALY vs. \$50,000/QALY vs. \$500,000/QALY vs. \$5,000,000/QALY

# Hypothesis

- Additional quantitative decision aids, namely multicriteria decision analysis (MCDA), will advance the science of value assessment to guide coverage and reimbursement decision making.
  - MCDA explicitly evaluates multiple (conflicting) criteria in decision making.
  - MCDA offers a promising compliment to traditional value assessment by explicitly weighting and including multiple value components outside the cost-per-QALY metric.

## pValue Center of Excellence collaborators, objectives, and outreach



# Conclusions

- Cost-effectiveness is not the full picture of value but remains a starting point for value assessment
  - Math continues to help us solve problems
  - Definitions and intent of analyses are critical for interpretation and use
- ICER and others are working to advance the field of value assessment through CEA modifications and CEA compliments
- Let us be constructive in our critiques and continue to test possible solutions

# Acknowledgements

- U of Colorado Colleagues
  - Investigators: R Brett McQueen; Melanie Whittington
  - PhD Graduate Student: Chong Kim
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- pValue Funders and Collaborators
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  - Date Science to Patient Value (U of Colorado School of Medicine)
  - Syreon Research Institute
  - Real Endpoints

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