Limitations of QALYs in Cost-Effectiveness Reviews

William Smith, PhD
Visiting Fellow in Life Sciences
Pioneer Institute

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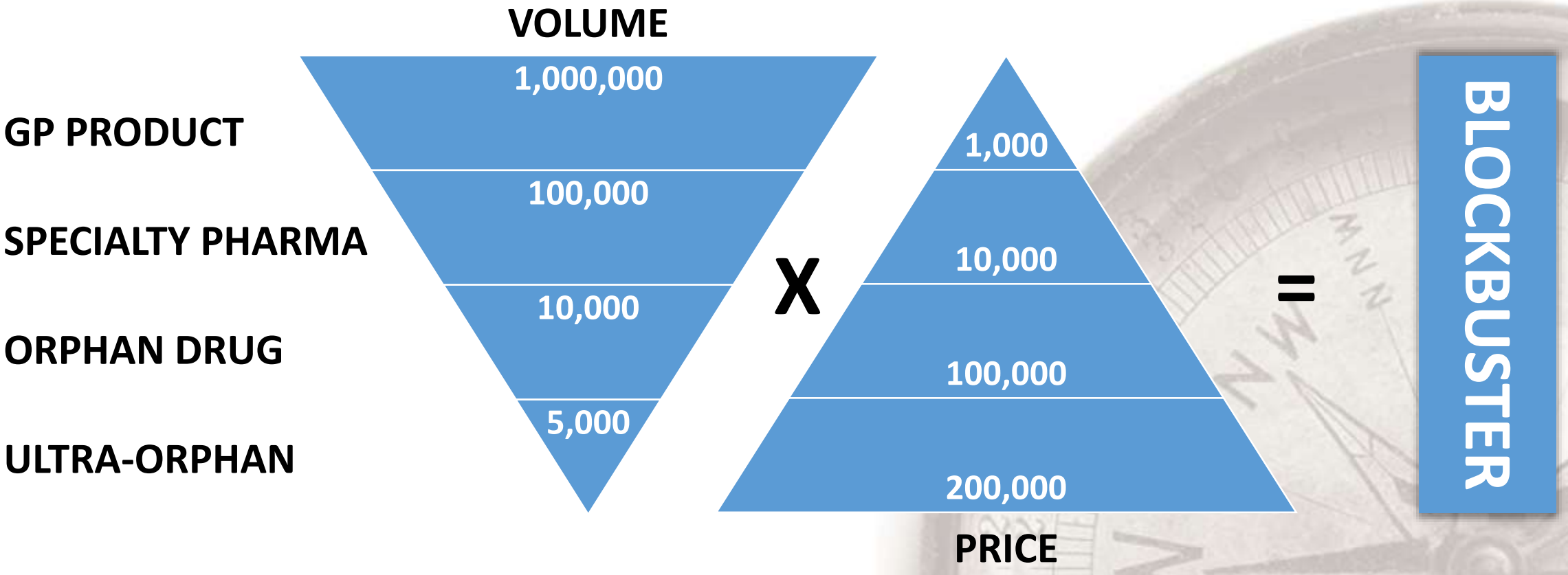
The Reverse Blockbuster Pyramid (Volume vs. Price)



Source: Prof. Mondher Toumi, Univ Lyon and Creativ-Ceutical, Brussels, 12 Jan 2010

Orphan & Rare Disease Drug Trends

Novel Drug Approvals

- In 2018, **34 of FDA/CDER's 59 novel drugs (58%)** were approved to treat rare or orphan diseases. *(Source: FDA)*

Orphan Drug Approvals

- During 2017-2018, FDA approved 174 new orphan drug indications, representing **23% of the total number of orphan indications approved since 1983**. *(Source: IQVIA and Axios)*

The Future is Specialty Drugs

- Specialty is expected to **represent nearly two-thirds of newly launched medicines over the next five years**, and oncology approximately 30%. Orphan drugs could represent 45% of new active substances by 2023. *(Source: IQVIA)*

Rising Costs of Orphan & Rare Disease Drugs

Specialty share of total medicine spending has risen from 11% in 1997 to 43% in 2017. *(Source: IQVIA)*

During the same period, spending on orphan drugs rose from 4% of total medicine spending to 10%. *(Source: IQVIA)*

Median list price for oncology and orphan drugs could exceed $100,000 by 2023. *(Source: IQVIA)*

Important Note: Rising specialty and orphan drug costs have been offset by significant LOEs for major blockbuster drugs. LOEs will account for $95 billion in drug cost reductions over the next five years with $26 billion in 2019 alone, including $9.4 billion in savings from biosimilars. In 2018, therefore, net prices for medicines grew at only 1.5 percent. *(Source: IQVIA)*

Payers Respond To Specialty & Orphan Drug Cost Growth

- Specialty Tiers
- Co-Insurance as a Percentage of Drug's Cost
- Blocking the Use of Coupons From Manufacturers
- Limit Distribution Networks to Exert Greater Price Control
- Prior Authorization & Step Therapy
- Consolidation of Health Plans & PBMs
- Adoption of European-style cost-effectiveness studies (QALYs)

What is a Quality Adjusted Life Year (QALY)?

A QALY is a cost-effectiveness methodology measuring the ability of a new therapy to extend life and improve the quality of life. QALYs use a scale of 0–1, with 0 representing death and 1 representing a year of life lived in perfect health.

Example: Oncology drug that provides additional 6 months of life and has significant side effects. Scores .5 on both longevity and quality of life.

QALY methodology provides for a "threshold" value for a full year of life lived in perfect health. In the US, the Institute for Clinical and Economic Review (ICER) uses a threshold of $100,000-$150,000. For our oncology example, .5 x $100,000-$150,000 would provide a cost-effectiveness range of $50,000-$75,000. If the therapy costs less than $50,000, it would be considered a high value therapy versus intermediate and low value ranges.

QALYs used extensively in Europe, e.g. NICE in the UK.

U.S. Payers Consider Use of QALY Cost-Effectiveness Studies Through ICER

The Limitations of QALYs

Ethical

Methodological

Contextual

RECOMMENDED READING: Pettit DA et al., "The Limitations of QALY: A Literature Review," *Journal of Stem Cell Research & Therapy* 2016. 6:4.

Limitations of QALYs → Ethical

- Should patients be **denied drugs** pending QALY review?
- Does the QALY review **interfere with physician judgment**?
- Does the QALY threshold **establish an arbitrary price** on human life?
- Are QALY reviews simply fig leaves for **healthcare rationing**?
- Are QALY reviews **insensitive to the real world experiences** of patients?

Limitations of QALYs → Methodological

Are QALY reviews conducted with adequate data, e.g. not Germany?

Do QALY reviews lead to inefficiencies in healthcare spending, e.g. bias toward hospital procedures with its $991 million threshold?

How often should ICER reviews be updated?

Reviews don't consider personalized medicine.

Should quality of life measurements be determined by patients?

Should physicians, especially specialists, have a greater role in QALY reviews?

Do QALY reviews fail to capture non-health benefits of drug therapies, e.g. productivity, earnings, caregivers, etc.?

Is the use of meta-data analysis a sound way to reach conclusions about specific drugs?

Limitation of QALYs → Contextual

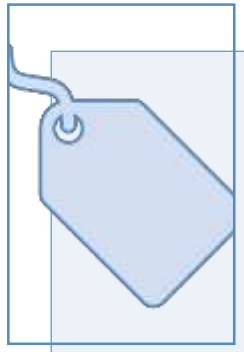
- Is the QALY **biased against oncology patients** as it uses longevity criteria?
- Is the QALY **biased against disabled patients** or even an ADA violation?
- Is the QALY **biased against older patients**?
- Is there a **bias against preventative medicine**?
- Rare disease patients and the **limits of a one-size-fits-all approach**.

The ICER Framework for Ultra-Rare Disease Drugs

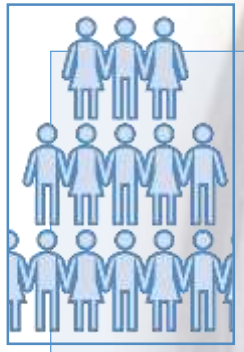
The More Things Change, the More They Stay the Same

- **New Framework will only apply to patient populations of 10,000 or less.**

QALY value price benchmarks for ultra-rare drugs will remain in the $100,000-$150,000 range but ICER will "adapt its analysis to provide willingness to pay threshold results" up to $500,000.



Rare disease medicines with per QALY ratings between $175,000 and $500,000 would no longer be rated as "low value" and an independent appraisal committee will vote on the "long-term value for the money" for each therapy on a low, intermediate and high value scale.



For ultra-rare disease drugs, ICER will conduct a "societal perspective analysis" to measure potential savings in areas such as "patient and caregiver productivity, education, disability, and nursing home costs." These are described as "contextual considerations."

Limitations of ICER's Ultra-Rare Disease Framework

- Ultra-rare disease definition **not aligned with U.S. laws and regulations**
- Contextual factors are presented along side medical costs analysis **but not built into the model**
- General framework – but especially ultra-rare disease framework – **ignores coming advances in personalized medicine** and ability to predict efficacy and non-efficacy
- **Limited data** from clinical trials

Health Affairs Study: ICER Reviews and Orphan Rare Disease Drugs

Study analyzed 555 ICER appraisal committee votes on 48 treatments from 2014 to 2018, with 13 cancer therapies and five rare disease drugs.

Four of the five rare disease drugs scored above $500,000 per QALY and were voted "low value," although the fifth rare disease therapy for inherited retinal disease with a QALY of $644,000 received two votes of "high value," seven for "intermediate" and three for "low value."

Cancer treatments received somewhat favorable reviews as therapies with QALYs in the range of $175,000 to $500,000 were rated of "intermediate value" in 63% of cases with the remaining 37% rated "low value."

See: Neumann et al., "Should a Drug's Value Depend Upon the Disease Or Population It Treats? Insights from ICER's Value Assessments," Health Affairs Blog, November 6, 2018. DOI: 10.1377/hblog20181105.38350

HHS Secretary on QALYs in Public Programs

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Contact Information

William S. Smith
Visiting Fellow on Life Sciences | Pioneer Institute
wsmith@pioneerinstitute.org
Office: (617) 723-2277 | Mobile: (202) 570-6968

@PioneerBoston

PioneerInstitute.org

@PioneerInstitute