
# GDP Curve: Generalized Dynamic Prevalence Adjustment of Willingness-to-Pay (WTP) to Control for Health Equity in CEA

Vasco Miguel Pontinha, PhD
Assistant Professor

ISPOR Annual 2024
Atlanta, GA

VCU School of Pharmacy

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# Agenda

## Background
- Why Should We Adjust Acceptability Criteria?
- Expected Utility Theory

## Methods
- Identification of Disease Prevalence Data
- Standardization of Prevalence Data

## Results & Discussion
- Prevalence-adjusted Willingness to Pay Thresholds
- Real-world application

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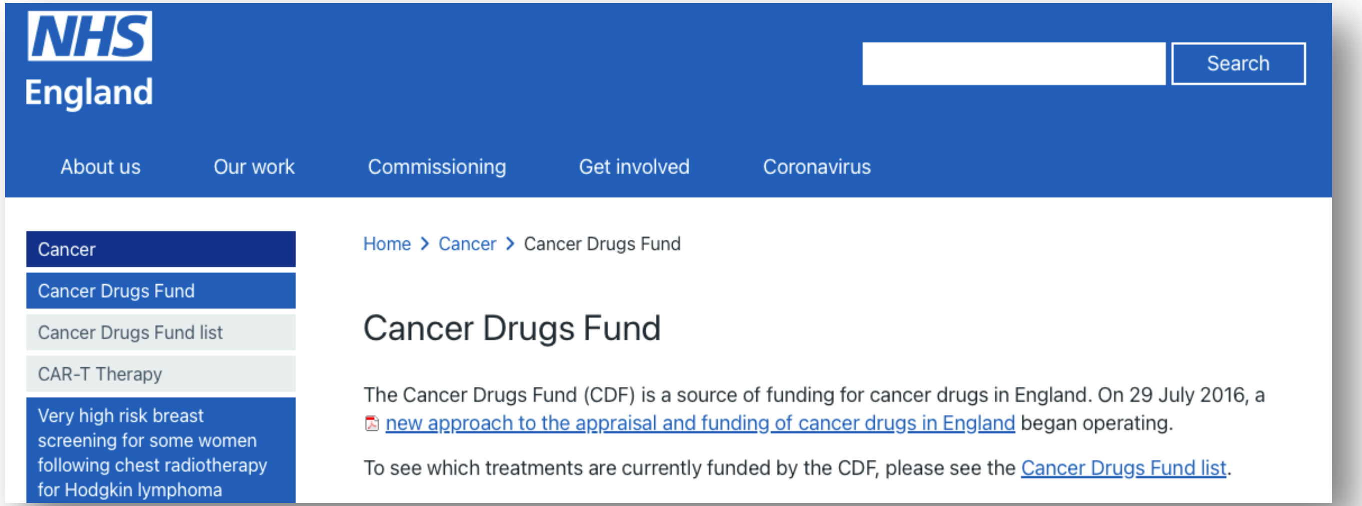
# Why Should We Adjust WTP Thresholds?



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- Cancer
- Cancer Drugs Fund
- Cancer Drugs Fund list
- CAR-T Therapy
- Very high risk breast screening for some women following chest radiotherapy for Hodgkin lymphoma

Home > Cancer > Cancer Drugs Fund

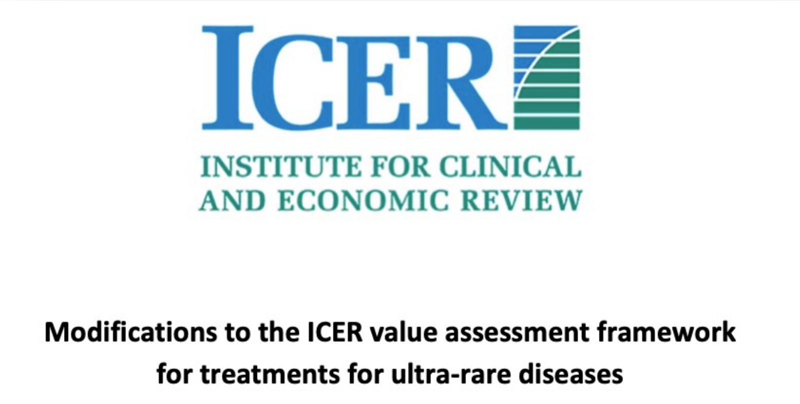
Cancer Drugs Fund

The Cancer Drugs Fund (CDF) is a source of funding for cancer drugs in England. On 29 July 2016, a new approach to the appraisal and funding of cancer drugs in England began operating.

To see which treatments are currently funded by the CDF, please see the Cancer Drugs Fund list.

https://www.england.nhs.uk/cancer/cdf/

In the UK, NICE considers significantly higher WTP thresholds for cancer interventions (from £20,000-£30,000/QALY to up to £50,000/QALY)



ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

**Modifications to the ICER value assessment framework for treatments for ultra-rare diseases**

https://icer.org/wp-content/uploads/2020/10/ICER-Adaptations-of-Value-Framework-for-Rare-Diseases.pdf

ICER changed its value assessment framework for rare diseases (up to $500,000/QALY)

Generalized recognition that one single threshold shouldn't apply to conditions with limited therapeutic alternatives and that affect a few number of patients (compared to the general population)

# Why Should We Adjust WTP Thresholds?

**Goal of this research project:**

**ESTABLISH THE THEORETICAL AND METHODOLOGICAL FOUNDATIONS FOR ADJUSTING WTP THRESHOLDS IN ECONOMIC EVALUATION OF HEALTH TECHNOLOGIES**

In the UK, NICE considers significantly higher WTP thresholds for cancer interventions (from £20,000-£30,000/QALY to up to £50,000/QALY)

ICER changed its value assessment framework for rare diseases (up to $500,000/QALY)

Generalized recognition that one single threshold shouldn't apply to conditions with limited therapeutic alternatives and that affect a few number of patients (compared to the general population)

# Background: Expected Utility Theory

$$EU\ (x) = \sum_{o \in O} P_x(o) \times U(o)$$

The expected utility of *x* is the sum of the utility of all outcomes multiplied by their probability

**At the population- or country-level:**
The sum of expected utilities in healthcare is obtained by total expenditures in healthcare weighed by the probability of each health condition

**Attempt to allocate resources to achieve full health (~ utility = 1)**

# Expected Utility (EU) Theory

**Attempt to allocate resources to achieve full health (~ utility = 1)**

$$\text{Let EU} = 1, \text{then}$$

$$K_{health} = \frac{National\ Health\ Spending}{1}$$

**Currently, all diseases are valued at the same K (WTP) ($50,000–$150,000 / QALY)**

**If we allow constant K (WTP) for all diseases:**

- Direct contradiction with the EU theoretical framework, which expects different opportunity costs for different outcomes
- Healthcare spending can potentially explode by allowing the same K (WTP) for the least and most prevalent conditions simultaneously.

# EU Theory and Generalized Dynamic Prevalence (GDP)

Therefore, K (WTP) should be adjusted by the chance of a disease event

***Assumption of absolute risk aversion for adjustment***

$$Adjusted\ K = K' \times R, where\ R\ is\ the\ adjustment\ factor$$

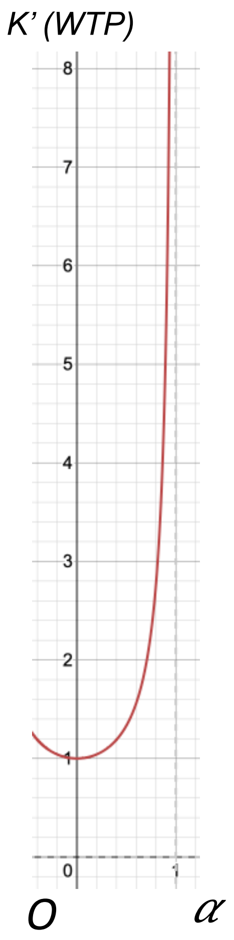
$$Prevalence\ Adjusment\ Factor\ R = \frac{1}{1 - prevalence\ factor^2}$$

**Hyperbolic function** Range (-∞,0)∪(1,∞), {y|y<0, y≥1}

***GDP Equation:***

$$Adjusted\ K = K' \times \frac{1}{1-\alpha^2}, where\ \alpha\ [0,1]$$

## So, what is $\alpha$ in the GDP equation?

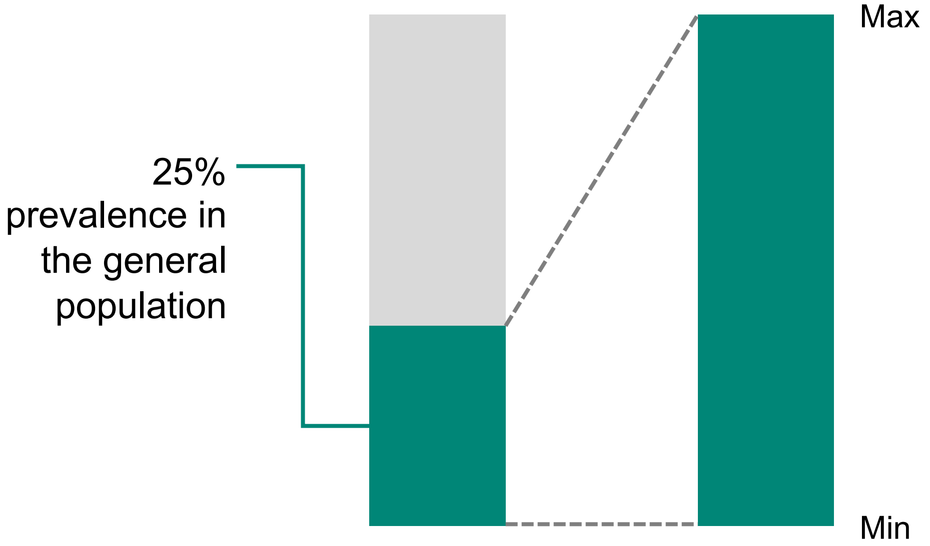



$$f(x) = \frac{1}{1-x^2}$$

# GDP: Prevalence Adjustment Factor (R)

$Prevalence\ Adjusment\ Factor\ R = \frac{1}{1-\alpha^2}$ where $\alpha$ [0,1]

Using absolute prevalence rates would not be appropriate, because the most prevalent condition (hypertension) is ∽ 48% of adults in the US




**$\alpha$ needs to be a standardized value of the prevalence of all diseases in the United States**

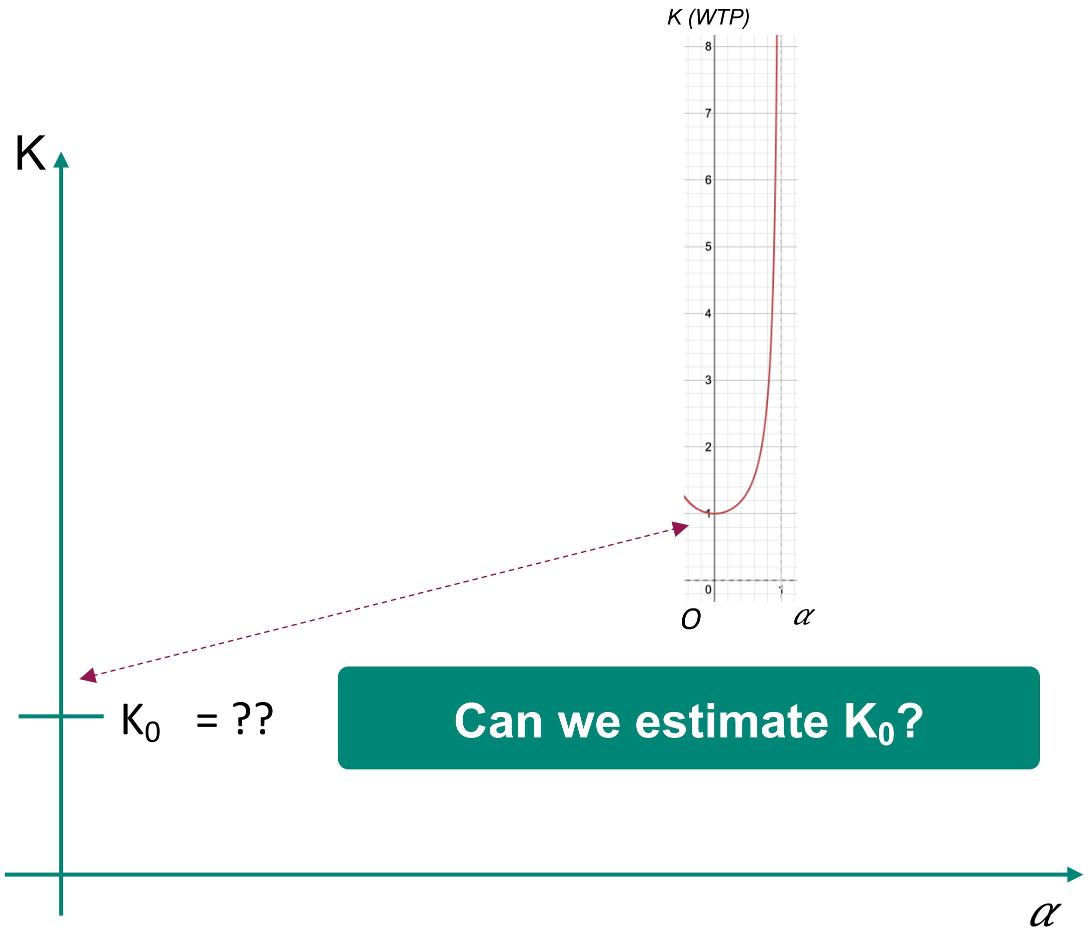
# Generalized Willingness to Pay Threshold

$$Adjusted\ K = K' \times \frac{1}{1-\alpha^2},\ where\ \alpha\ [0,1]$$

**Standardized prevalence**

**Generalized Willingness to Pay**

*The theoretical WTP threshold for a disease affecting all the US, technically funded by the entire country*




100% prevalent

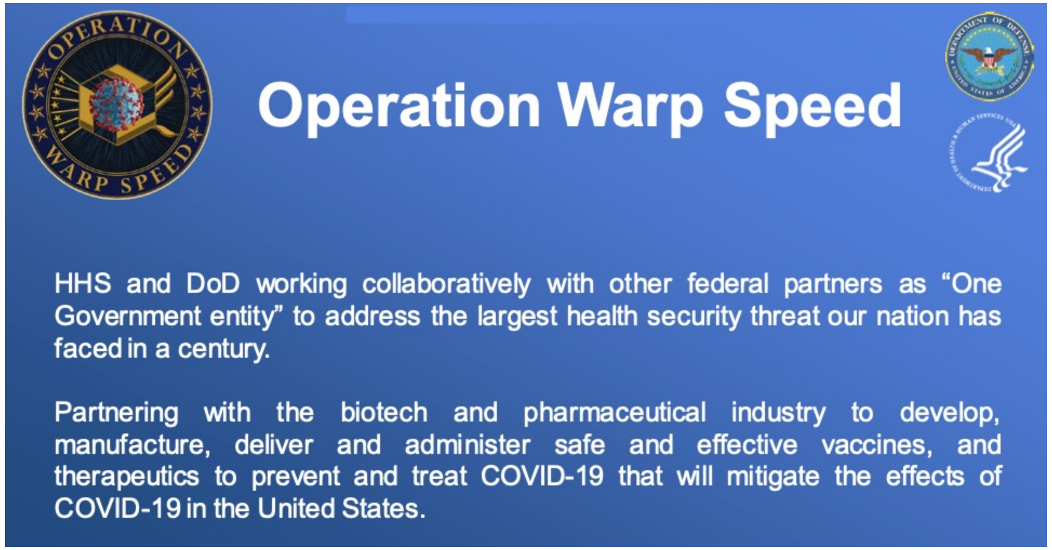
Least prevalent

# (Another) Silver-lining of the COVID-19 Vaccine

- The US government has funded the development, manufacturing, acquisition, and administration of the Covid-19 vaccines

- If we know the COVID-19 ICER from a societal perspective, we could use it to determine $\mathbf{K_0}$

  *i.e., the societal willingness to pay for a condition that affects 100% of the population*




Vaccines and Related Biological Products Advisory Committee October 22, 2020 Meeting Presentation, https://www.fda.gov/media/143560/download

# Covid-19 Vaccine Incremental Cost-Effectiveness Ratio

*The Journal of Infectious Diseases*

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

## Lives and Costs Saved by Expanding and Expediting Coronavirus Disease 2019 Vaccination

**Sarah M. Bartsch,[1] Patrick T. Wedlock,[1] Kelly J. O'Shea,[1] Sarah N. Cox,[1] Ulrich Strych,[2] Jennifer B. Nuzzo,[3] Marie C. Ferguson,[1] Maria Elena Bottazzi,[2] Sheryl S. Siegmund,[1] Peter J. Hotez,[2] and Bruce Y. Lee[1]**

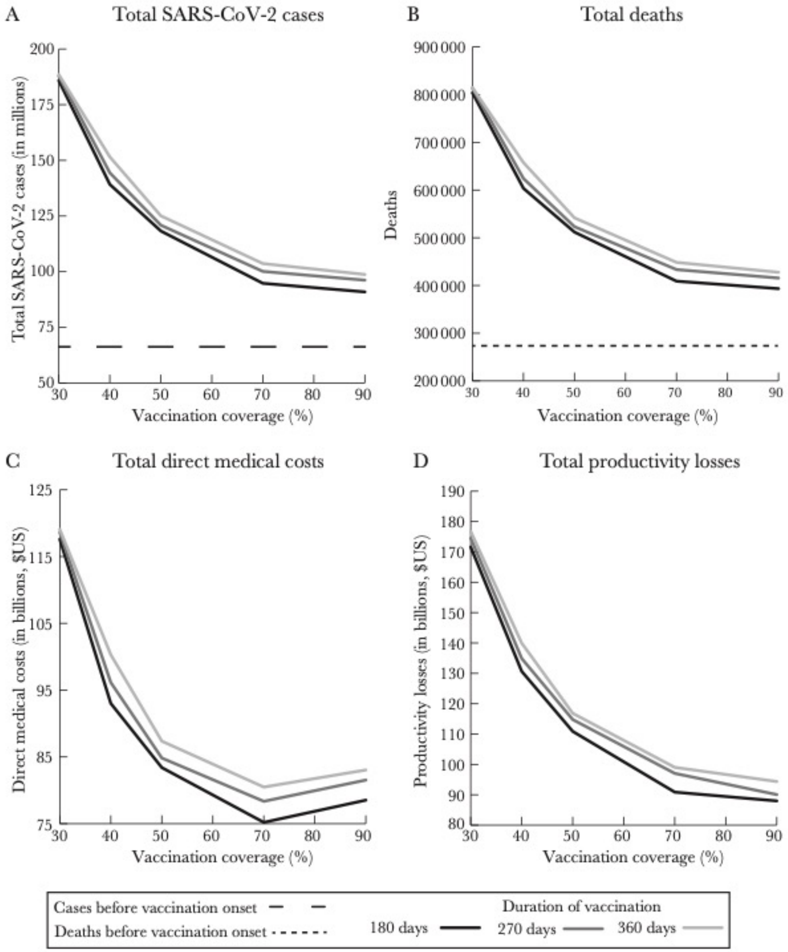
[1]Public Health Informatics, Computational, and Operations Research, Graduate School of Public Health and Health Policy, City University of New York, New York City, New York, USA, [2]National School of Tropical Medicine and Departments of Pediatrics and Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, USA, and [3]Johns Hopkins Center for Health Security, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

**(See the Editorial Commentary by Heaton, on pages 931–3.)**

**Societal Incremental Cost-Effectiveness Ratio**

**$6,982 / QALY**

*with vaccination rates between 70-90%*



# G-PACE: Generalized Willingness to Pay Threshold

**G-PACE**

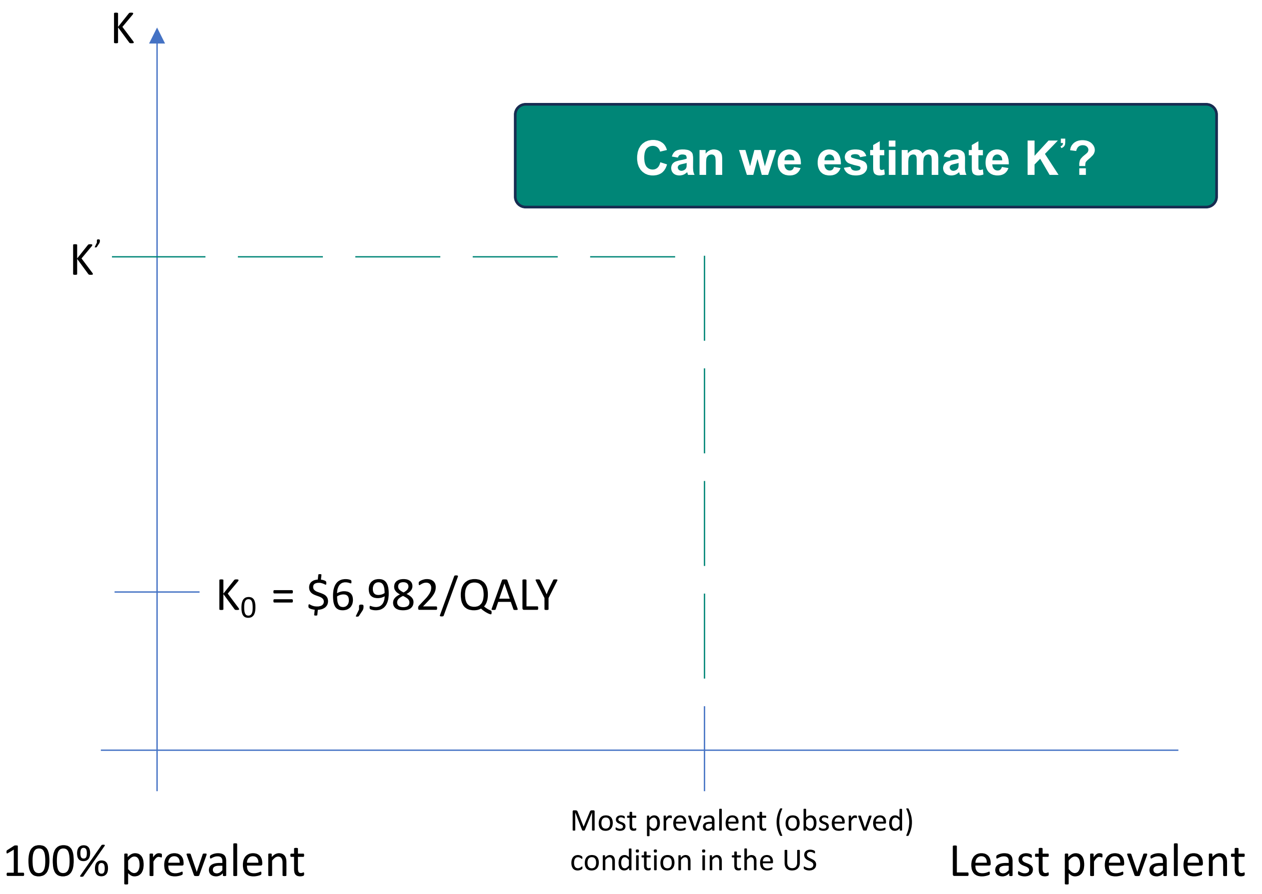
$$Adjusted\ K = K' \times \frac{1}{1-\alpha^2}, where\ \alpha\ [0,1]$$

**Standardized prevalence**

**Generalized Willingness to Pay**

*The theoretical WTP threshold for a disease affecting all of the US, technically funded by the entire country*

**Can we estimate K'?**



# Societal Incremental Cost-Effectiveness Ratio for The United States Private Insurance Market

Annals of Internal Medicine — ORIGINAL RESEARCH

**A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States**

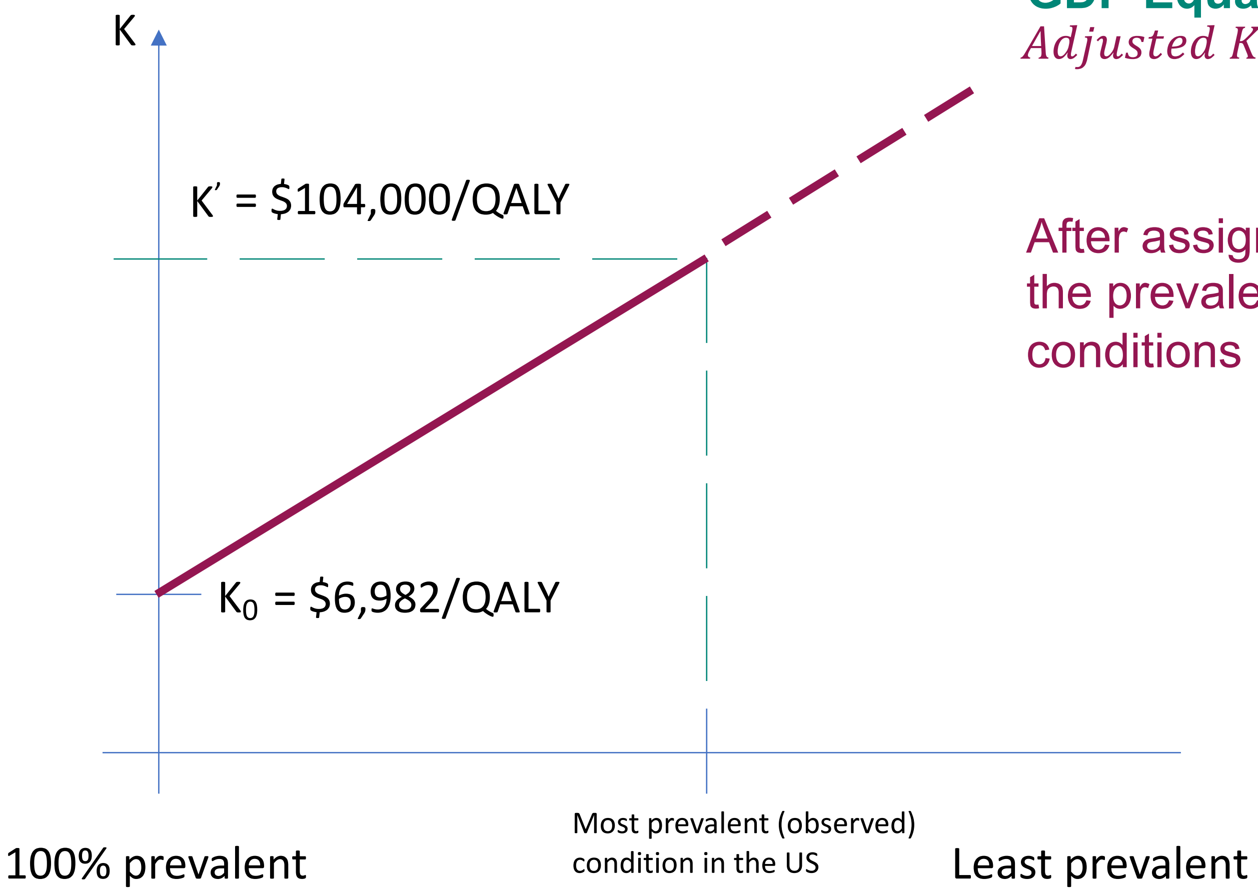
**David J. Vanness, PhD; James Lomas, PhD; and Hannah Ahn, MS**

**Estimate a U.S. cost-effectiveness threshold**, obtained by simulation of short-term mortality and morbidity attributable to persons dropping health insurance due to increased health care expenditures passed through as premium increases.

**Incremental Cost-Effectiveness Ratio**
**$104,000 / QALY**
The point after which, most people stop buying health insurance

Vanness DJ, Lomas J, Ahn H. A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States. Ann Intern Med. 2021 Jan;174(1):25-32. doi: 10.7326/M20-1392. Epub 2020 Nov 3.

# Generalized Willingness to Pay Threshold




**GDP Equation**

$$Adjusted\ K = K' \times \frac{1}{1-\alpha^2}$$

After assigning these data points, we will estimate the prevalence-adjusted Ks for the remaining conditions in the US using G-PACE

# Approach

**Identification of Disease Prevalence Data**
**Standardization of Prevalence Data**

**Plot of WTP Thresholds plot according to varying disease prevalence**

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# **Methods:** Identification of Disease Prevalence Data

- Medical diagnosis were assumed to be represented by the International Classification of Diseases, Tenth Revision (ICD-10) codes

- Disease prevalence (informed by ICD-10 codes) data were retrieved from the Medical Expenditures Panel Survey (MEPS) Medical Condition File 2021

  *MEPS is a combination of surveys of families and individuals, their medical providers (doctors, hospitals, pharmacies, etc.), and employers across the United States.*

- Prevalence data were estimated according to relative frequencies of ICD-10 codes

# **Methods:**
# Standardization of Prevalence Data

## Box-Cox Transformation

$$T(Y) = \frac{(Y^{\lambda} - 1)}{\lambda}$$

Several Box-Cox transformations were tested: natural normalizations, as well as other values for $\lambda$: [-3, -2, -1, 0, 1, 2, 3]

Daimon T. Box–Cox Transformation. International Encyclopedia of Statistical Science, 2011

## Evaluation of Box-Cox Transformation

Normality assessed by the Shapiro-Wilk and Kolmogorov-Smirnov tests as well as histograms and QQ plots were computed to evaluate the normality of the standardizations post-transformations

Razali, N. M., & Wah, Y. B. (2011). Power comparisons of Shapiro-Wilk, Kolmogorov-Smirnov, Lilliefors and Anderson-Darling tests. J Stat Model Anal 2 (1): 21–33.

# Results:
## Prevalence Data from 2021 MEPS Medical Conditions File

**Number of Medical Diagnoses (unique ICD-10 Codes)**

289 unique ICD-10 Codes, [20.16% - 0.0075%]

**Diagnosed Sample Size**

17,373 individuals (unweighted)

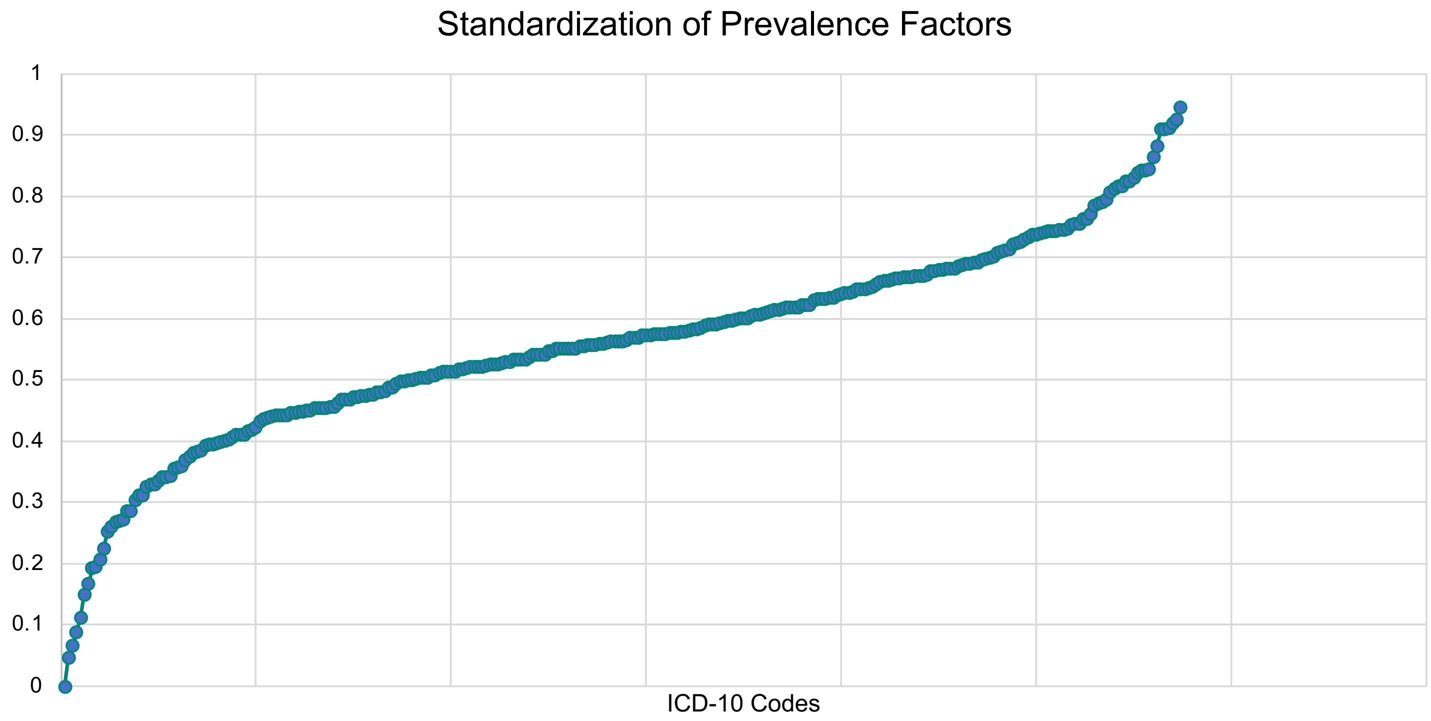
223,877,274 individuals (weighted sample size)

# **Results:** Standardization of Prevalence Data

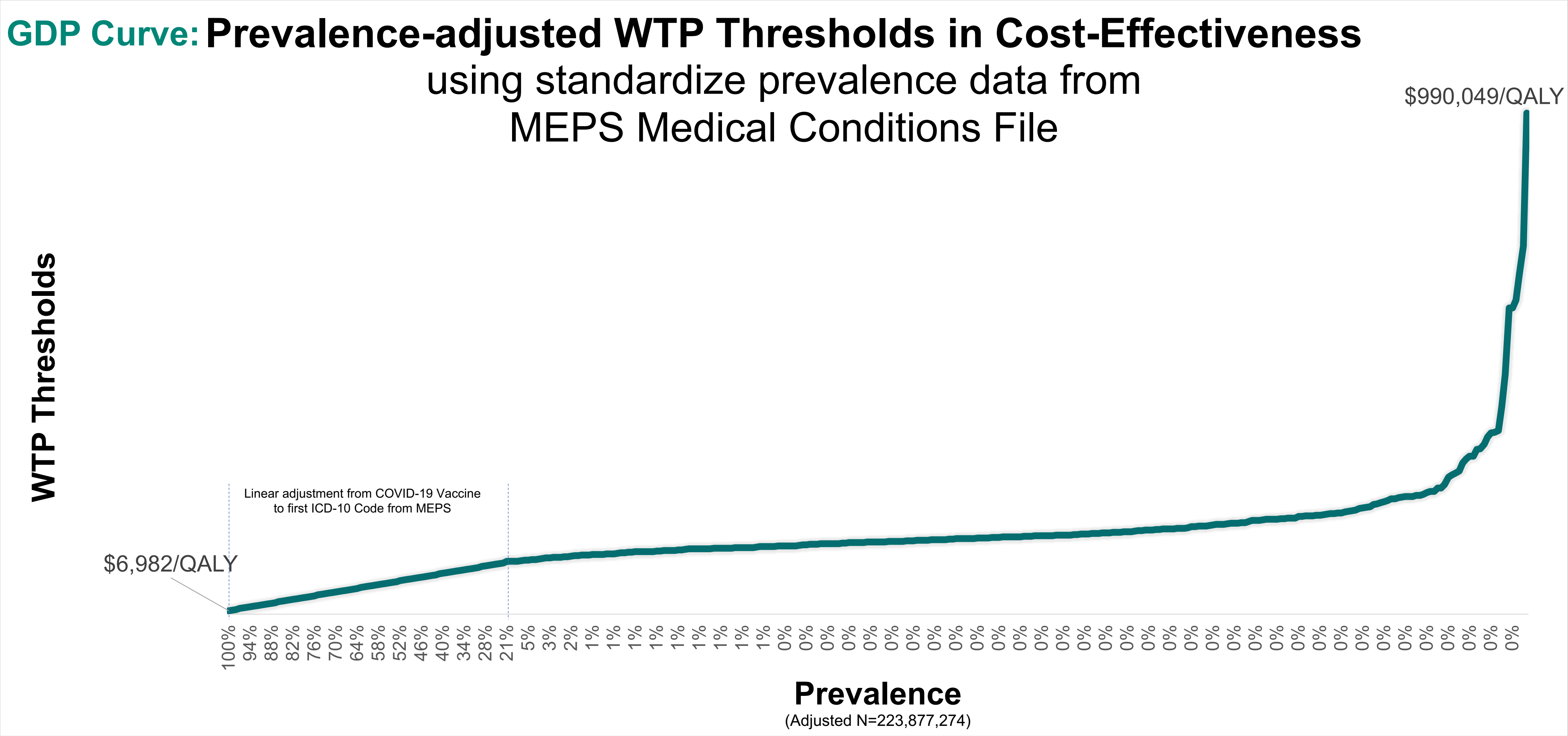
Box-Cox Transformation with $\lambda = 0$ exhibits the most normal distribution patterns (histogram and QQ plot)

The figure beside plots the $\alpha$ values by decreasing order of prevalence

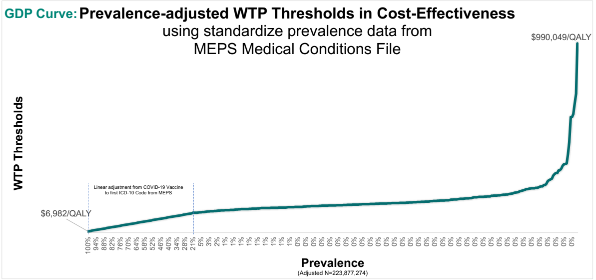
**Lower $\alpha$ value for most prevalent means the least adjustment needed to K (WTP)**



# **Results:** WTP Adjustments



# **GDP Curve:** Prevalence-Adjusted WTP Thresholds




WTP thresholds range between $6,892/QALY and $990,049/QALY

Most prevalent conditions yield similar currently used WTP thresholds

WTP threshold increases hold steady until **very** rare conditions (<0.01%)

K(WTP) thresholds >$200,000/QALY imply a prevalence smaller than 0.09%

**The approach is not apologetic about costly drugs, but a way to describe how opportunity costs are much higher for much rarer/severe conditions**

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# **GDP Curve:** Prevalence-Adjusted WTP Thresholds
*Real-world application*

## High blood cholesterol (HBC)

Number of patients with HBC

**89,451,000**

Prevalence

**27 in every 100**

**26.988%**

## Sickle cell disease (SCD)

Number of patients with SCD

**100,000**

Prevalence

**1 in every 3,000**

**0.030%**

## Duchenne muscular dystrophy (DMD)

Number of patients with DMD

**≤50,000**

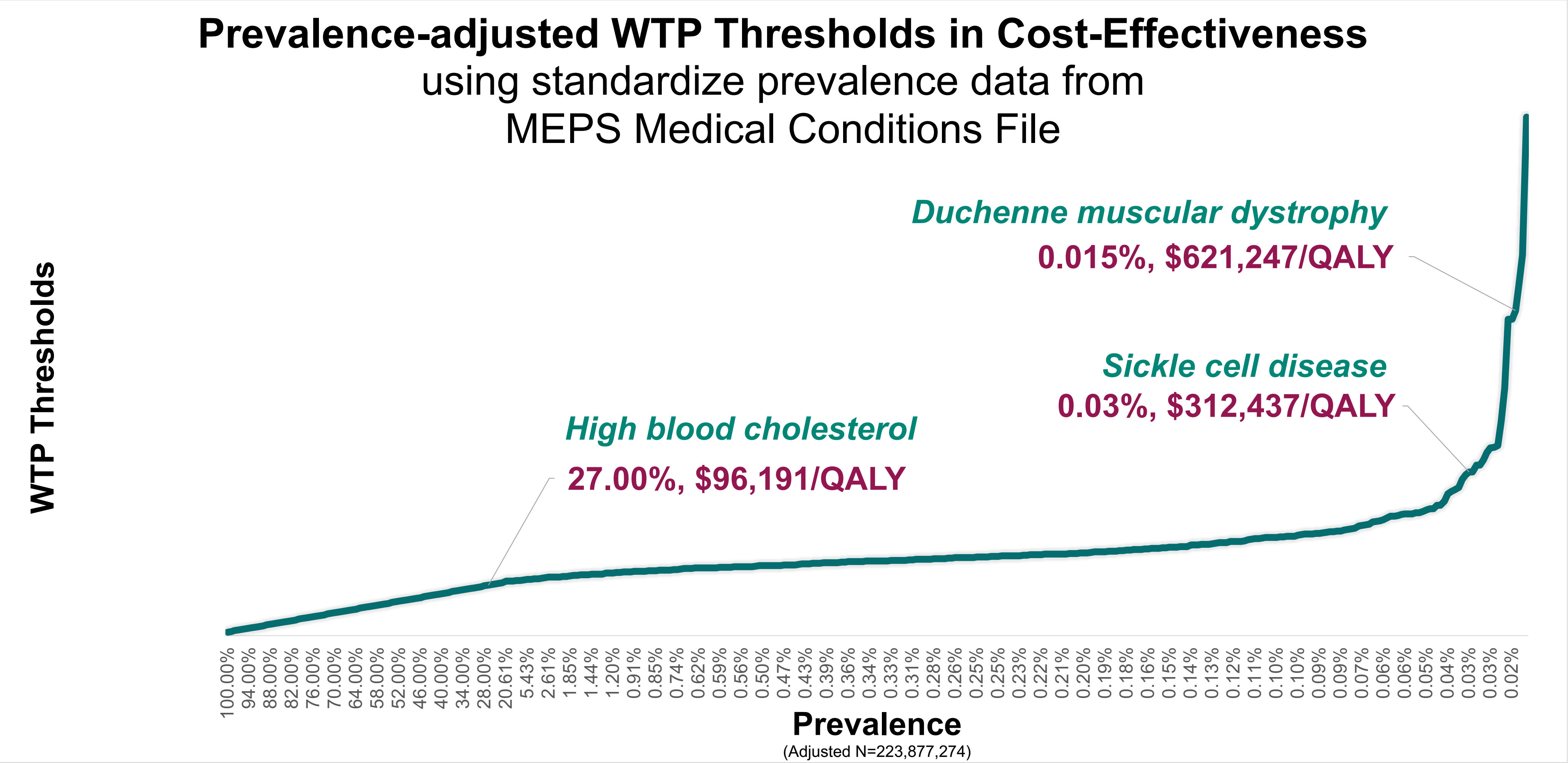
Prevalence

**1 in every 6,500**

**0.016%**

2020 US Census Population: 331,449,281

# **Real-world application:** WTP Adjustments



# Prevalence-adjustment of WTP Thresholds

## Why use GDP WTP Adjustment?

Demand-based (prevalence) approach to determining opportunity costs of healthcare technologies

**GDP**

$$Adjusted\ K = K' \times \frac{1}{1 - \alpha^2}, where\ \alpha\ [0, 1]$$

- Explicit theoretical foundation for adjusting WTP thresholds for diseases that are rare with limited therapeutical alternatives
- Approach is measure-agnostic and easy to translate to other utility measures (QALY, HYT, LYG, evLY)
  c.f. CMS drug price negotiation
- Addresses another petal of the ISPOR Value Flower related to dynamic prevalence

# Study/Approach Limitations

- Assumption that ICD-10 codes imply one different disease
- MEPS likely does not include diagnoses for which patients are not obtaining treatment
- Linearization between WTP at 100% prevalence and WTP at the highest observed condition, addressed by future fitting of a gamma distribution function.

# Authorship & Acknowledgments

## GDP Curve Authors

Vasco Miguel Pontinha,
PhD, MPharm, MBA

William Vincent Padula,
PhD, MSc, MS

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# Thank you!

Q&A