Valuing Gene Therapies for Rare Diseases

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#AccessToHealthCare

LEADERSHIP & INNOVATION
ORLANDO SUMMIT
NOVEMBER 16–19, 2022
WOMEN IN GOVERNMENT

Women in Government Leadership & Innovation Summit November 17, 2022

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EVERYLIFE BACKGROUND

Mission

To empower the rare disease patient community to advocate for impactful, science-driven legislation and policy that advances the equitable development of and to access to lifesaving diagnoses, treatments, and cures.

What We Believe:

No disease is too rare to deserve treatment

Rare disease therapies should be safe and effective

We could do more with the science we already have

What We Do:

Advocate for evidence-based public policy and regulatory reform

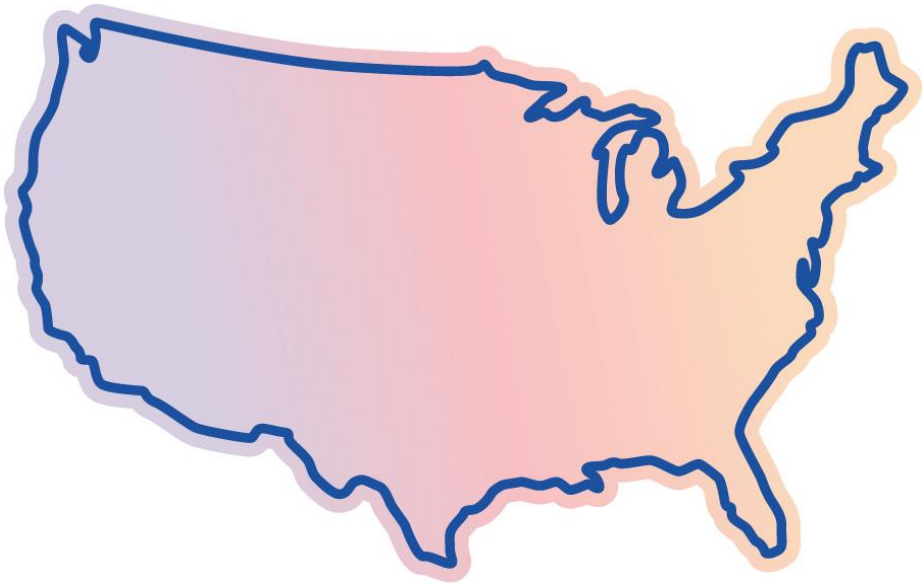
How We Get it Done:

Scientific and policy expertise

Grassroots action

U.S. Rare Disease Prevalence Estimates

10,000+
rare diseases



~30
million
affected

- In the U.S., a disease is considered rare when it affects fewer than 200,000 people
- Researchers estimate there are more than 10,000 RDs
- RDs affect an estimated 30 million Americans
- Actual RD prevalence could exceed this estimate

The National Economic Burden *of* Rare Disease Study

*"The **shortage of reliable information on the clinical, humanistic, and economic burden of RDs poses a challenge for accurate assessment of the value and impact of a new RD technology.** The frequently progressive and degenerative nature of RDs, paired with a poor understanding of the disease's natural history, is problematic for HTA modeling and projection of long-term treatment outcomes and associated costs."*

In general, we do not have the data we need to make good decisions

This is the problem EveryLife's Economic Burden of Rare Disease Study Addresses

Nestler-Parr S, Korchagina D, Toumi M, et al. Challenges in Research and Health Technology Assessment of Rare Disease Technologies: Report of the ISPOR Rare Disease Special Interest Group. Value Health. 2018;21(5):493–500. doi:10.1016/j.jval.2018.03.004

Study Results:
Economic Burden Measured by Three Costs Components

DIRECT MEDICAL COSTS

Examples

Inpatient or outpatient care

Physician visits

Rx medications and their administration

Durable medical equipment

Private and public insurance programs typically pay providers directly, and patients are responsible for co-pays

INDIRECT COSTS: PRODUCTIVITY LOSS

Examples

Forced retirement

Absenteeism

Presenteeism (when employees cannot fully function in the workplace)

Reduction in community participation and volunteer service

Reduces income for patients and caregivers, while reducing productivity for employers, communities, society

NON-MEDICAL & UNCOVERED HEALTHCARE COSTS

Examples

Necessary home or auto modifications

Transportation and education costs

Paid daily care

Healthcare services not covered by insurance: experimental treatments, medical foods, and more

Out-of-pocket costs absorbed directly by families living with RD

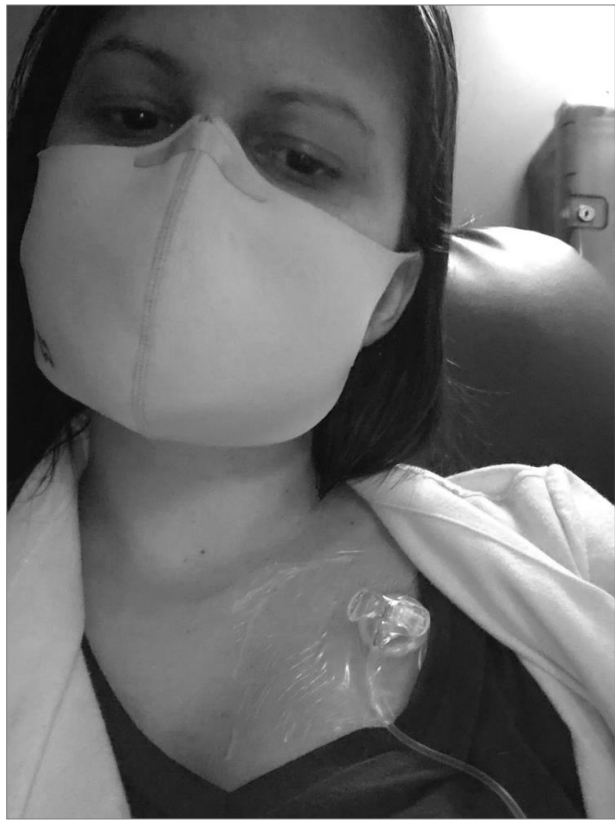
Study Results:
RD Impact Survey Captures Medical Burden, Long Diagnostic Odyssey

16.5
YEARS
Since first RD symptom (mean)

10.2
YEARS
Years since RD diagnosis (mean)

6.3
YEARS
Navigating without RD diagnosis (mean)

16.9
Average number of specialists seen since first RD symptom

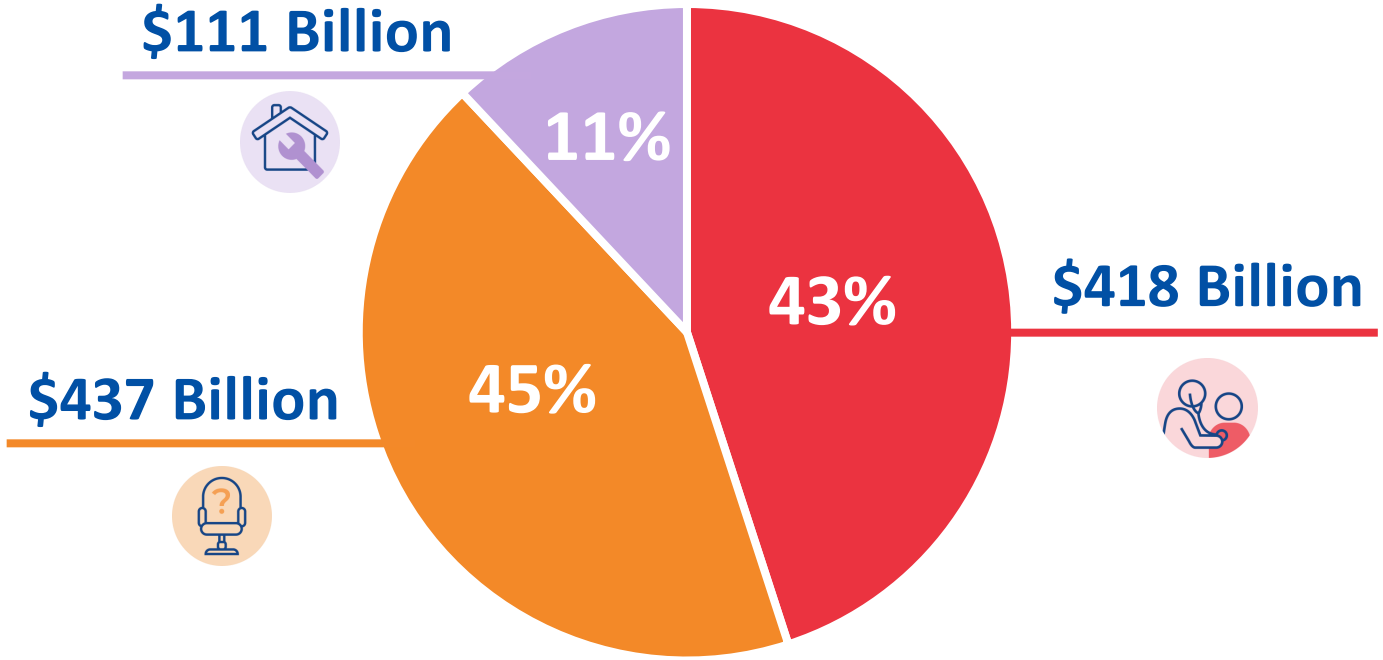


Based on final analysis sample of 1,360 completed responses

Study Results:
Indirect and Non-Medical Costs Drive Economic Burden of RD, Exceeding Direct Medical Costs

Total Economic Burden of 379 RDs in the U.S. in 2019:

$966 Billion



Source: The Lewin Group analyzed RD prevalence calculated from the 2018 dNHI claims, 2019 Medicare SAF 5% sample claims, and 2016 Medicaid claims combined with the census population projection for 2019. Direct medical cost estimates were obtained using 2018 dNHI claims, 2019 Medicare SAF 5% sample claims, and 2016 Medicaid claims. Indirect and non-medical costs were estimated using Lewin's analyses of the RD Impact Survey data.

Visit burdenstudy.org to learn more about the study's methods, results, conclusions, and limitations

The National Economic Burden of Rare Disease Study

Direct Medical Costs:
Inpatient and Outpatient Care Are Largest Cost Categories

Direct Medical Costs Due to RD by Type of Service

Caregiver costs were only covered by Medicaid
Also refer to productivity loss related to caregiving

$26,887
average per-person excess direct medical costs due to RD

CATEGORY	COST IN BILLIONS	%
Inpatient	$143 B	34.2%
Outpatient	$62 B	14.8%
Other Ancillary	$49 B	11.7%
Prescription Medication	$48 B	11.5%
Outpatient Prescription Administration	$48 B	11.4%
Non-Acute Inpatient	$31 B	7.5%
Physician	$31 B	7.4%
Durable Medical Equipment	$4 B	1.1%
Caregiver	$2 B	0.5%

Visit burdenstudy.org to learn more about the study's methods, results, conclusions, and limitations

The National Economic Burden of Rare Disease Study

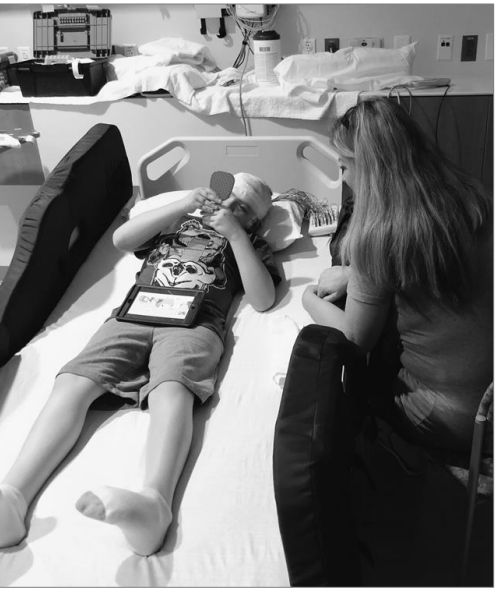
Direct Costs through the Community Lens

"The financial challenges are overwhelming and unrelenting. The search for a diagnosis or treatment requires navigating a complex medical system and battling with insurance companies all while trying to hold down a job."

Marissa Penrod
Mother of a son with a rare disease

Indirect Costs: Productivity Loss

Massive Economic Toll on Patients, Caregivers, Employers



CATEGORY	COST IN BILLIONS	%
Absenteeism	$149 B	34.2%
Presenteeism	$138 B	31.6%
Losses due to forced retirement	$136 B	31.1%
Social productivity loss	$14 B	3.2%

$34,074

Per-person cost of productivity loss in 2019 for adult caregiver(s) of child with RD (>18 yrs)

Combined productivity losses for absenteeism and presenteeism:

$135 billion for adults with RD and

$152 billion for their caregivers

Visit burdenstudy.org to learn more about the study's methods, results, conclusions, and limitations

Indirect Costs: Productivity Loss
$437 Billion

"Balancing a career with medical care is tough. You might not be able to complete everything your manager asks. You might not advance in your position quickly, if at all."

Allison Bones
Mother of a child who died of a rare disease

Non-Medical and Uncovered Healthcare Costs

Medical Food, Home Modifications, Transportation and More Total $111 B

CATEGORY	COST IN BILLIONS	%
Healthcare services not covered by insurance	$38 B	34.2%
Necessary auto modification	$24 B	21.6%
Transportation costs	$20 B	18.0%
Necessary home modification	$10 B	9.0%
Education costs: home schooling, missed schooling, special education	$10 B	9.0%
Paid daily care	$9 B	8.1%

Healthcare services not covered include experimental and alternative therapies, non-prescription medicine, dental surgeries, etc.

Visit burdenstudy.org to learn more about the study's methods, results, conclusions, and limitations

Non-Medical Costs through the Community Lens

"If a family cannot afford to repair an electric wheelchair, buy a hearing aid, fix teeth, or travel to specialists, then the person with a rare disease receives inadequate care.
These costs accumulate and limit educational and career opportunities, making it harder to contribute to society."

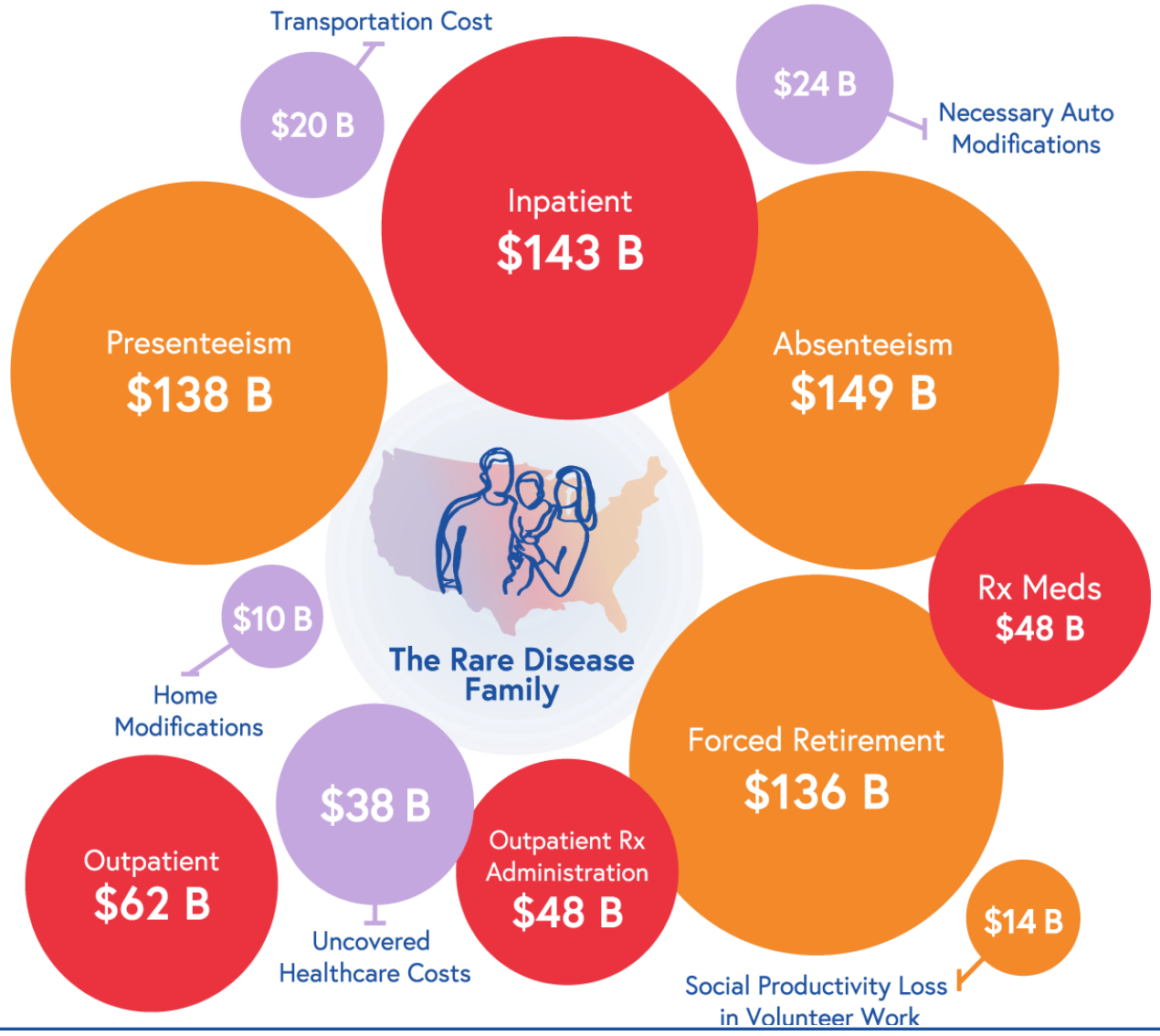
Steve Smith
Father of a son with a rare disease

What is the Impact on the Average Rare Disease Family?

$418 Billion
DIRECT MEDICAL COSTS

$437 Billion
INDIRECT COSTS: PRODUCTIVITY LOSS

$111 Billion
NON-MEDICAL & UNCOVERED HEALTHCARE COSTS



Total Economic Burden of Rare Disease in the U.S in 2019:

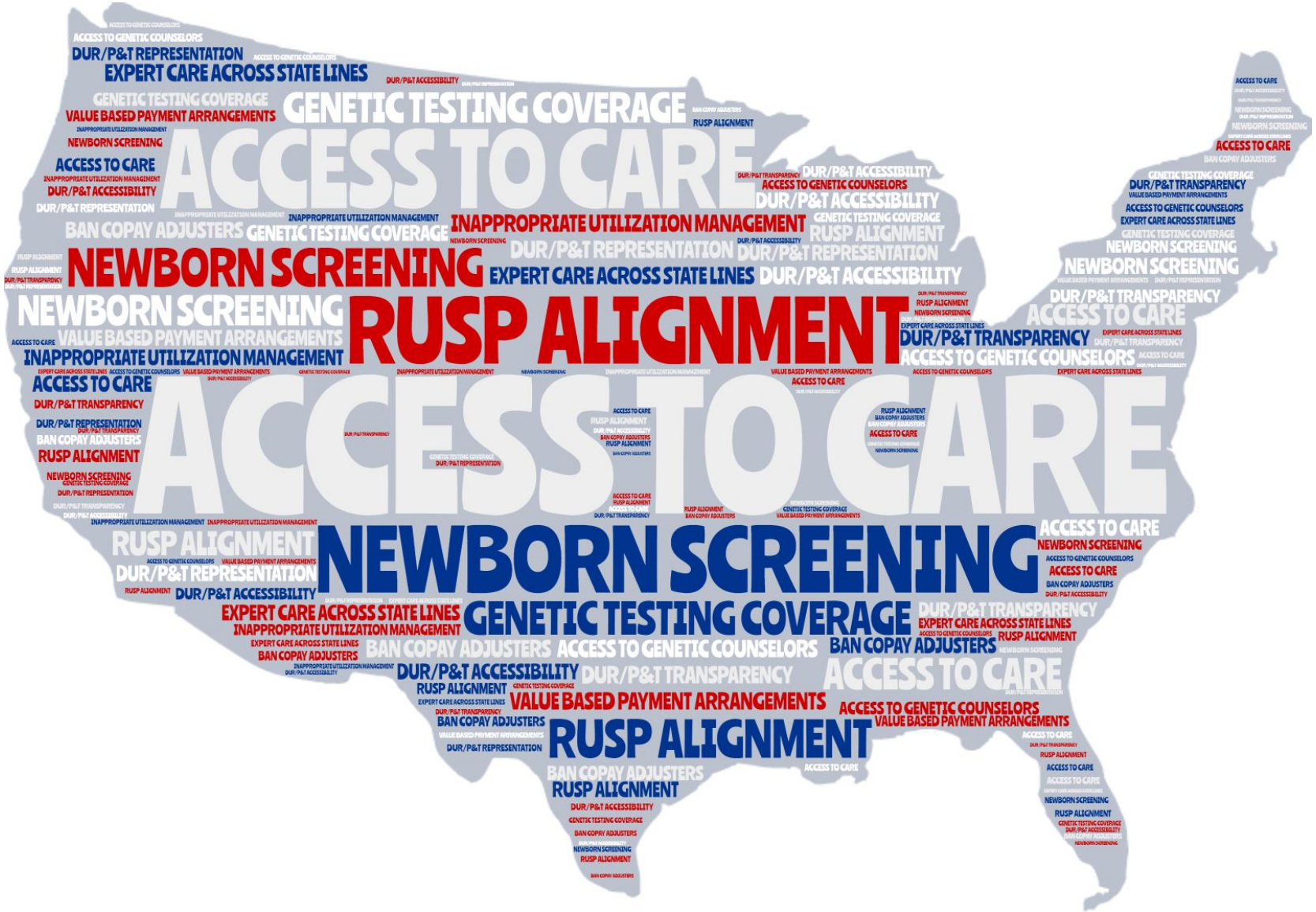
$966 Billion

Estimated prevalence of 379 RDs

15.5 million

The National Economic Burden of Rare Disease Study

RARE DISEASE ISSUES IN THE STATES



Study Contributors:
Special Thanks to the Rare Disease Community, Study Team, and Study Sponsors

RARE DISEASE LEGISLATIVE ADVOCATES ADVISORY GROUP

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Tonya Prince	President	Sickle Cell Assoc. of Houston	Mother of a daughter with a rare disease
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COMMUNICATIONS SUPPORT PROVIDED BY

SmithSolve

Valuing Gene Therapies for Rare Diseases

Carolyn Hickey
Executive Director, Government & Policy
November 17, 2022

ZYLER
Living with Duchenne muscular dystrophy

Duchenne muscular dystrophy is a rare, genetic, progressively debilitating disease resulting from a lack of dystrophin, a protein necessary for muscle function[1,2]

0-4 YEARS[2-6]

Inflammation soon after birth

Muscle fibrosis <1 year

Motor delays

Other delays, eg, speech

5-7 YEARS[2,7-10]

Progressive muscle weakness

Enlarged calves

Toe walking

Standing from supine difficult

Fat accumulation in muscle

8-11 YEARS[2,8,9]

Motor milestone delays

Decreased walking ability

Part-time wheelchair use

EARLY TEENS[2,8,9]

Decreased upper limb function

Loss of ambulation

TEENS[2,8,9,11]

Decreased respiratory function

Ventilatory support often required

Unable to perform ADL

TEENS/TWENTIES[8,9,11]

Increasing cardiac dysfunction

Heart failure

Life expectancy severely reduced

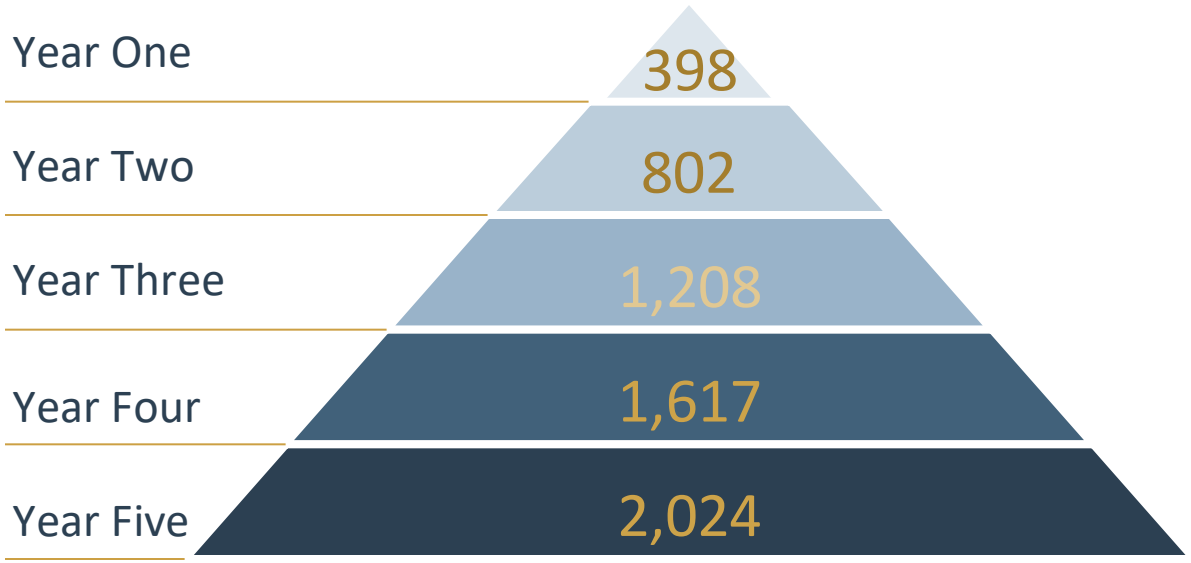
Current recommendations emphasize the importance of early diagnosis and treatment[8, 12]

ADL=activities of daily living; DMD=Duchenne muscular dystrophy.

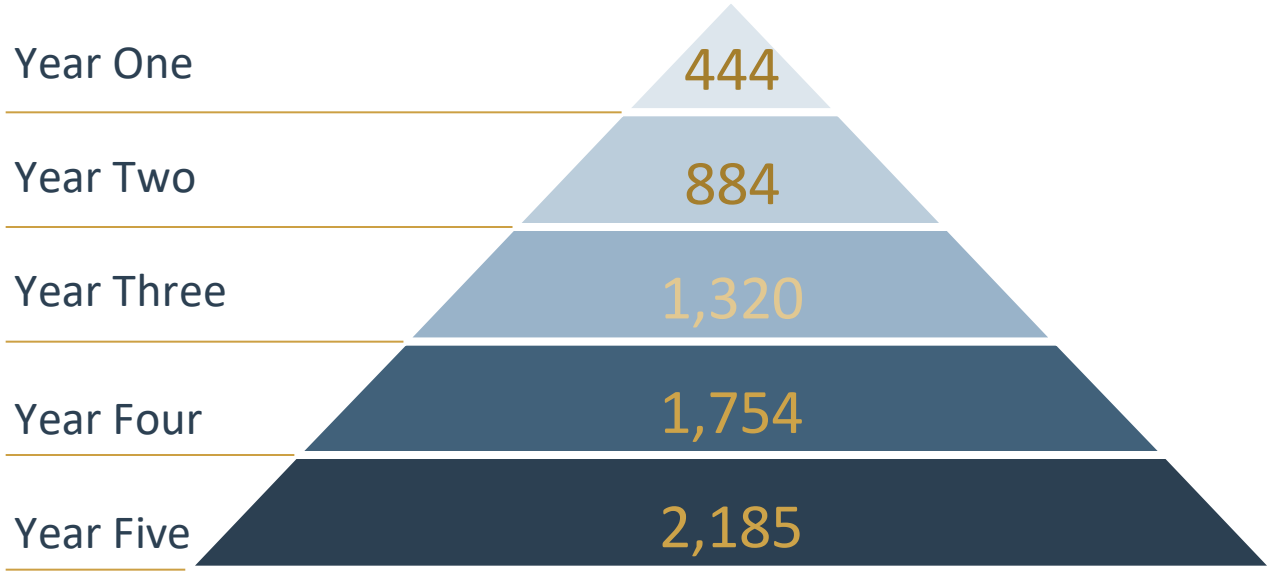
Aartsma-Rus A, et al. *J Med Genet*. 2016;53:145-151. 2. Birnkrant DJ, et al. *Lancet Neurol*. 2018;17(3):251-267. 3. Chen YW, et al. *Neurology*. 2005;65:826-834. 4. Peverelli L, et al. *Neurology*. 2015;85:1886-1893. 5. Lurio JG, et al. *Am Fam Physician*. 2015;91(1):38-44. 6. Cyrulnik SE, et al. *J Pediatr*. 2007;150:474-478. 7. Klingler W, et al. *Acta Myol*. 2012;31:184-195. 8. Emery AEH. *Lancet*. 2002;359:687-695. 9. Niks EH, Aartsma-Rus A. *Expert Opin Biol Ther*. 2017;17:225-236. 10. Willcocks RJ, et al. *Ann Neurol*. 2016;79:535-547. 11. Birnkrant DJ, et al. *Lancet Neurol*. 2018;17(4):347-361. 12. Rivera SR, Jhamb SK, Abdel-Hamid HZ, Acsadi G, Brandsema J, Ciafaloni E, et al. (2020) Medical management of muscle weakness in Duchenne muscular dystrophy. PLoS ONE 15(10): e0240687. https://doi.org/10.1371/journal.pone.024068

Over 400 children or young adults die each year from Duchenne

Milestone:
Losing ambulation

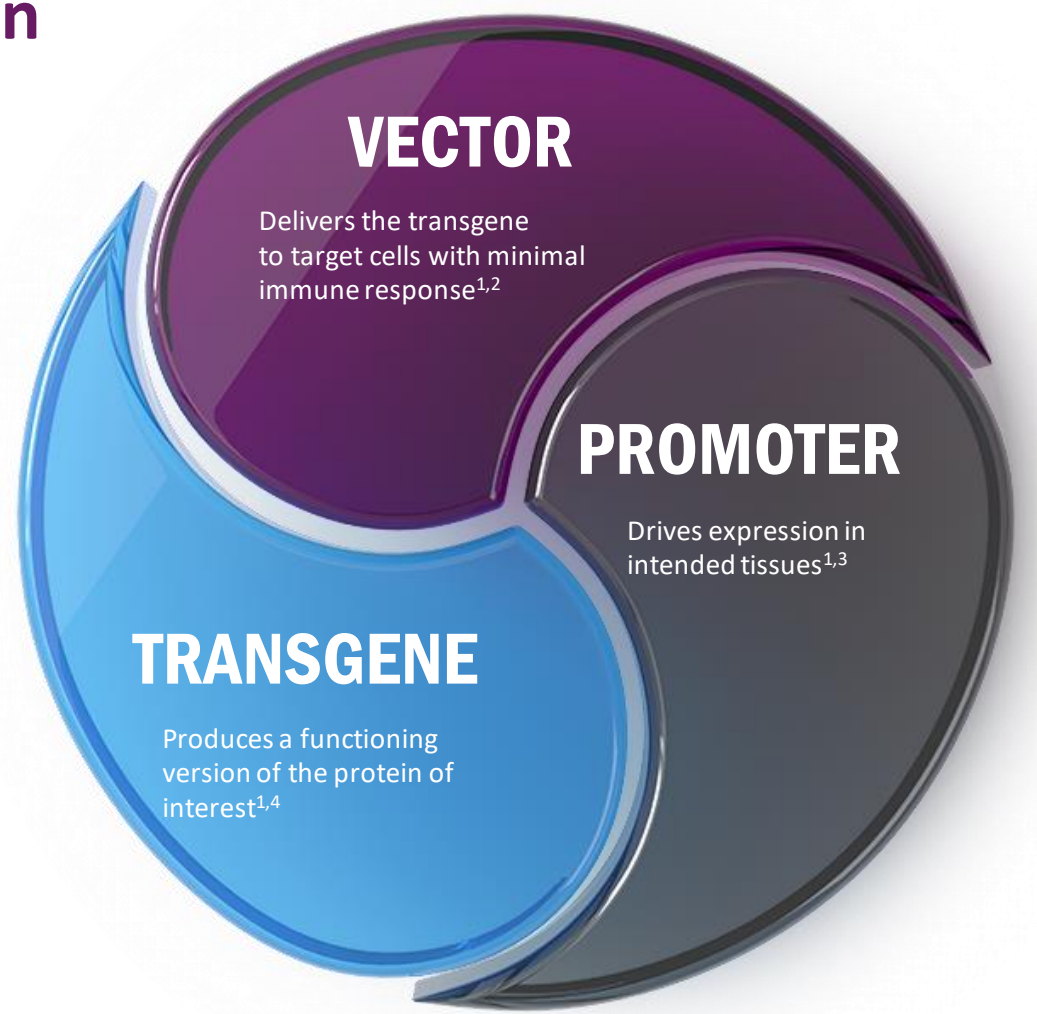


Milestone:
Passing away



Assuming a birth incidence of 1:5,050 live male births and mortality per Philips et al

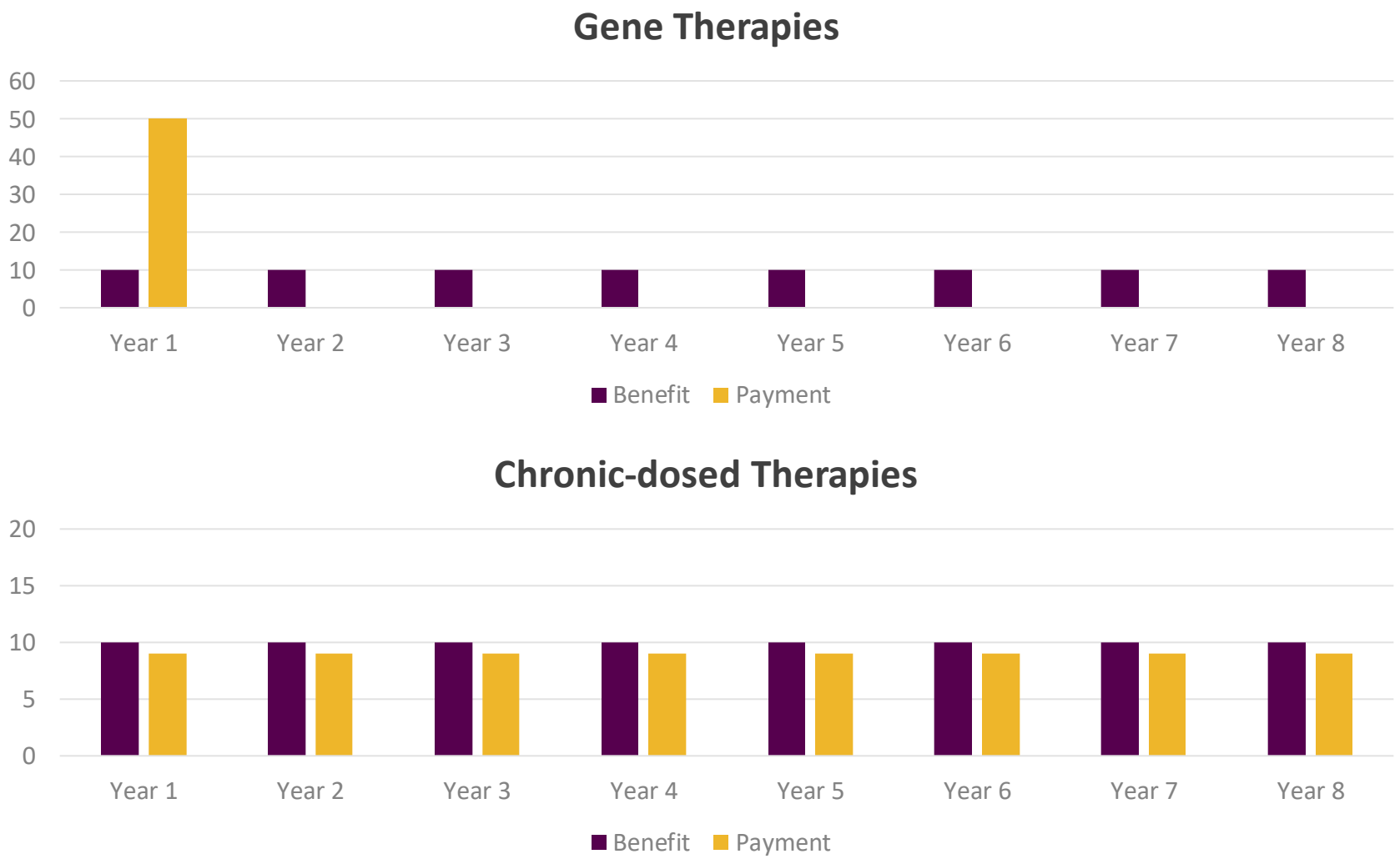
Gene therapy delivers a functional gene to affected cells throughout the body so tissue can produce a functional version of the missing or malfunctioning protein



1. Asher DR, et al. Clinical development on the frontier: gene therapy for Duchenne muscular dystrophy. *Expert Opin Biol Ther*. 2020;20(3):263-274.
2. US National Library of Medicine. Help Me Understand Genetics: Gene Therapy. https://ghr.nlm.nih.gov/primer/therapy/genetherapy. Accessed Nov. 22, 2021.
3. Zheng C, Baum BJ. Evaluation of promoters for use in tissue-specific gene delivery. *Methods Mol Biol*. 2008;434:205-219.
4. Chandler RJ, Venditti CP. Gene Therapy for Metabolic Diseases. *Transl Sci Rare Dis*. 2016;1(1):73-89.

Valuing a Gene Therapy

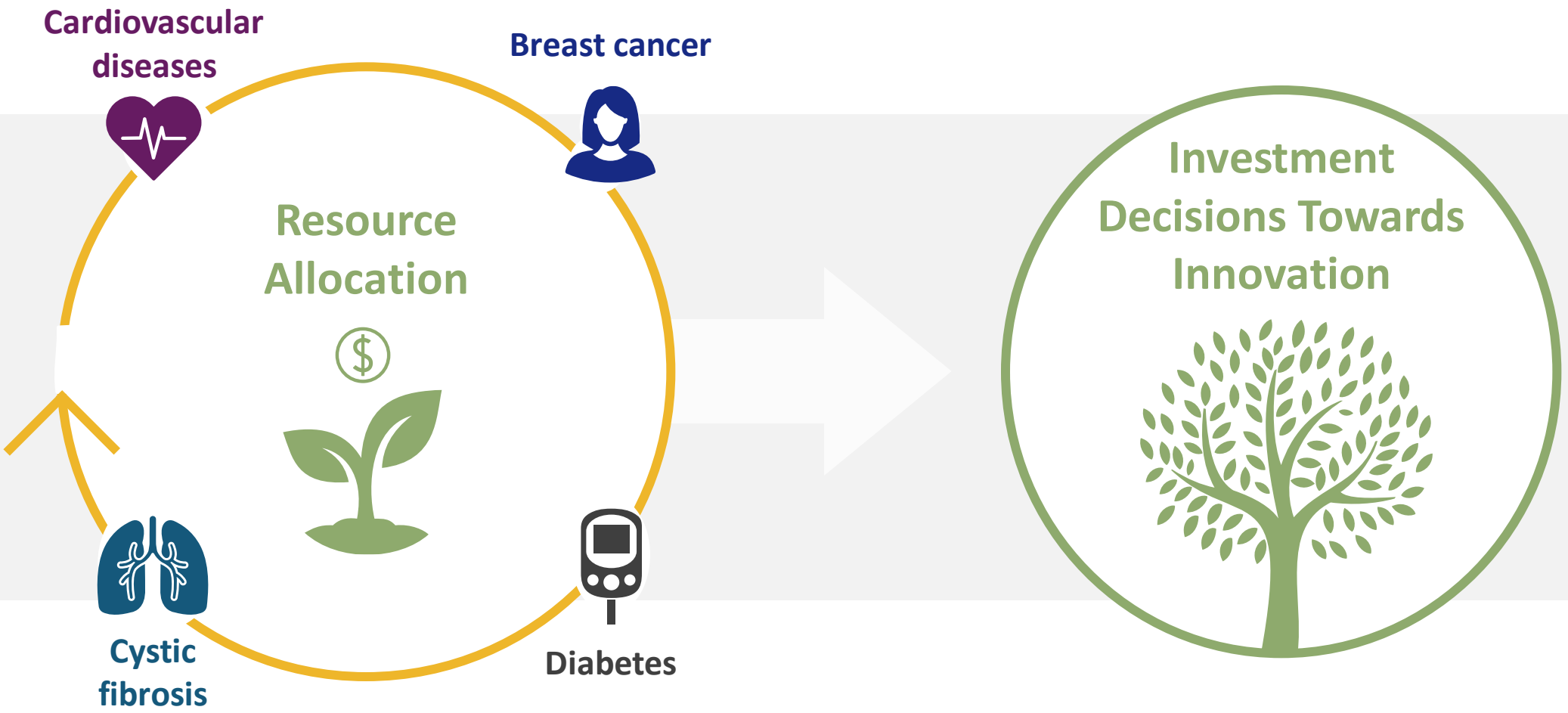
One-time gene therapies challenge our health care system by requiring payment upfront, but value accrues over time



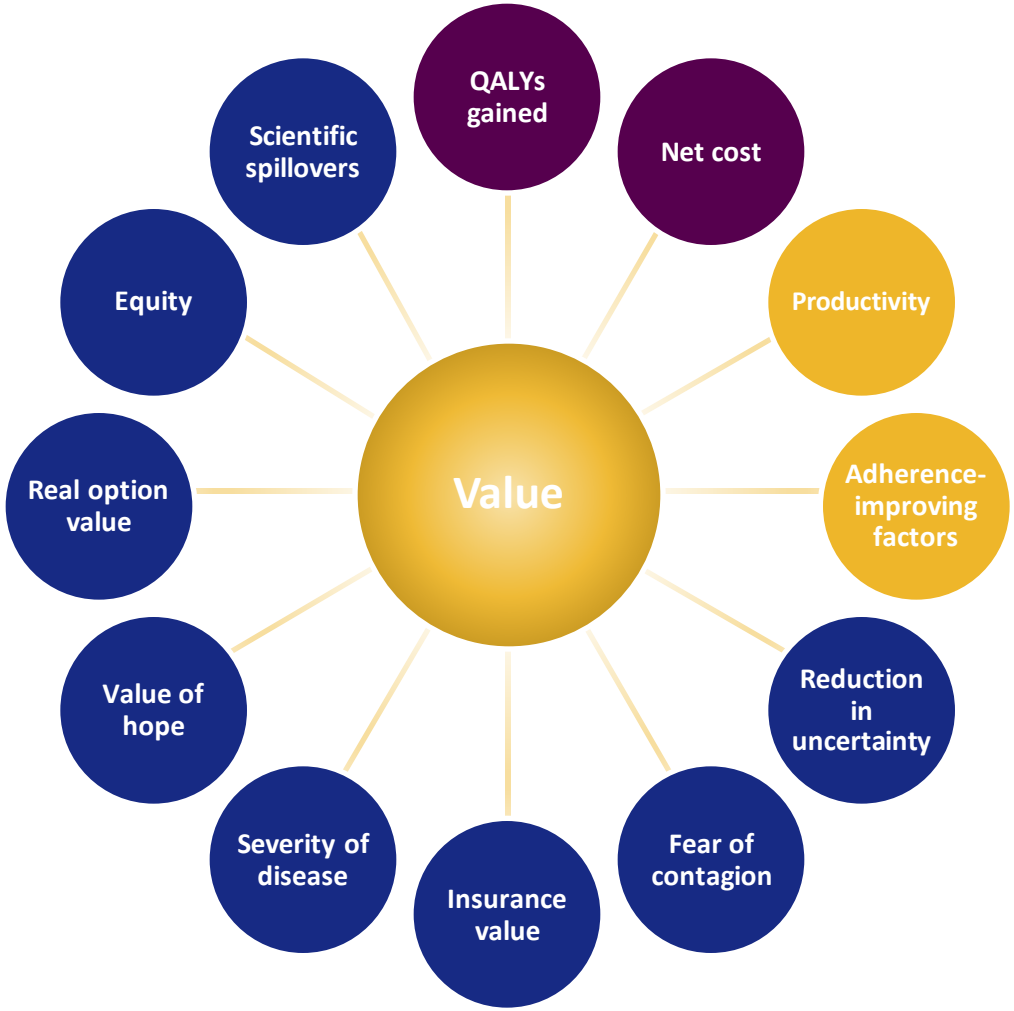
*For illustrative purposes

Source: MIT NEWDIGS FoCUS: Paying for Cures Toolkit. Accessed March 2, 2020. Available at: https://www.payingforcures.org/toolkit/

Value assessments influence resource allocation and inform investment decisions in future innovations



Many factors determine value, although most are not traditionally included in value assessments



THE IMPACT

Value assessments may influence whether a health intervention will be covered by an insurer and therefore accessible to patients…

… As innovative therapies become more prevalent, a broader view is needed to capture the true value to patients, caregivers, and society

Key: QALY – quality-adjusted life-year.
Source: Lakdawalla DN, et al. Defining elements of value in health care-a health economics approach: an ISPOR Special Task Force report [3]. *Value Health*. 2018;21(2):131-139.

Life is defined by numbers in value frameworks

QALYs capture both improvements in quality of life and increases in survival

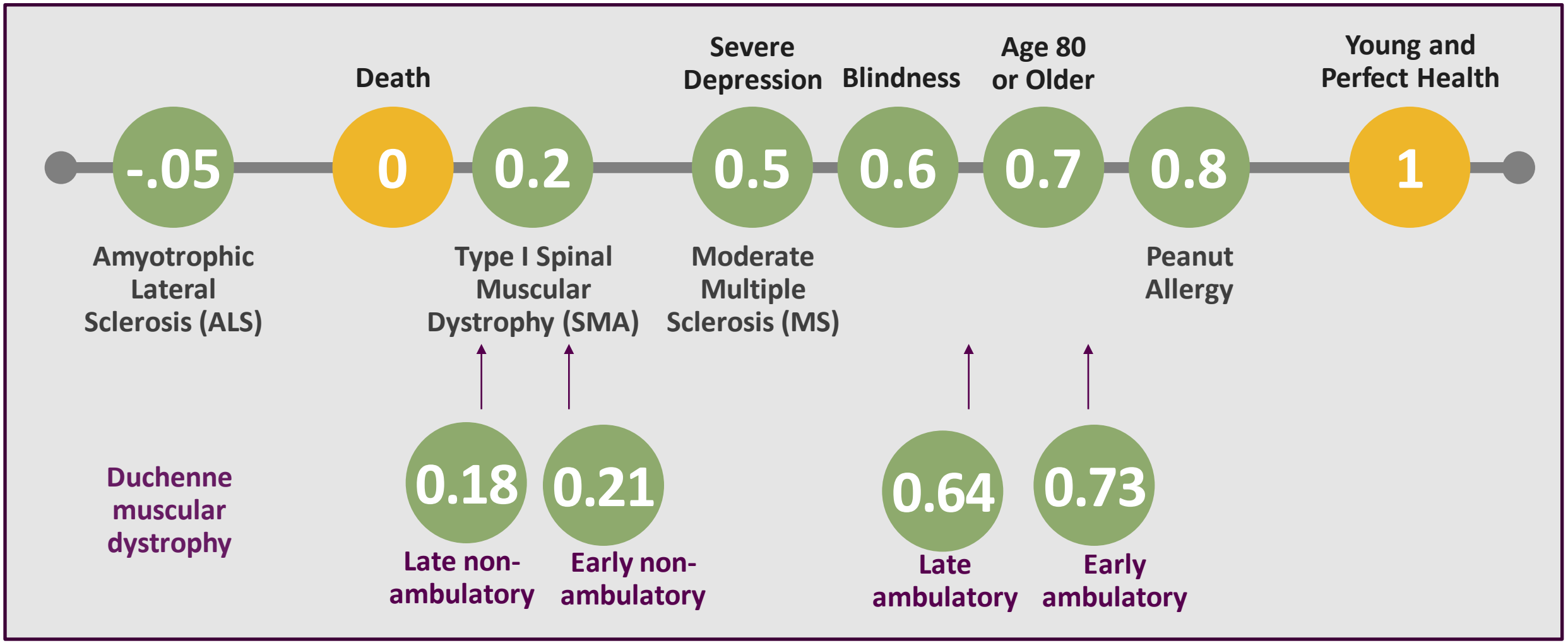
QALYs are based on the number of years spent at a given quality of life

It assumes that a year of life lived in perfect health is worth 1 QALY (1 Year of Life × 1 Quality-of-Life = 1 QALY) and that a year of life lived in a state of less than this perfect health is worth less than 1.

Key: QALY – quality-adjusted life-year.

Traditional HTA frameworks mainly rely on the QALY, devaluing the disabled suffering from genetic-causing diseases

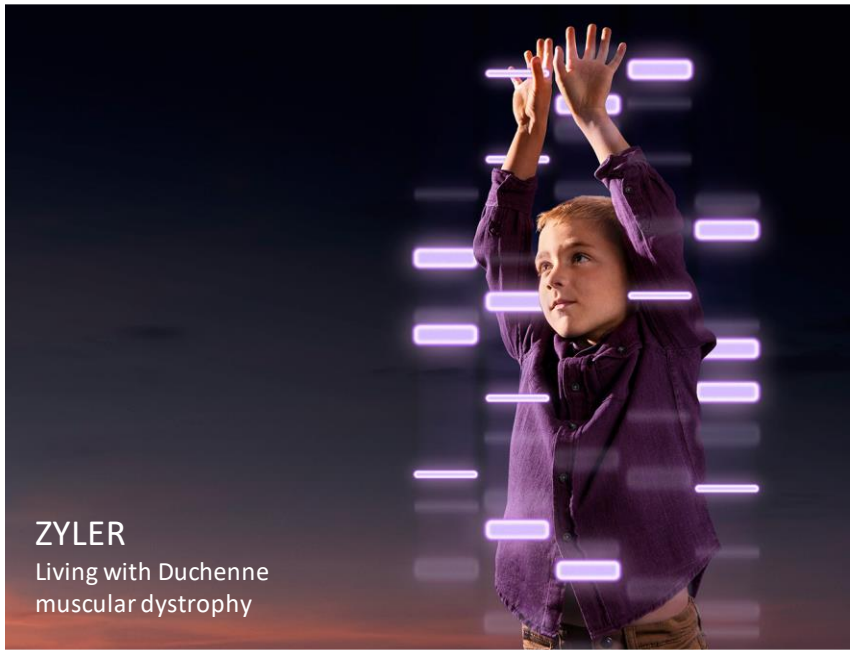
QALY Rating Relative to Various Genetic-Causing Diseases



Source: Value Our Health: https://valueourhealth.org/wp-content/uploads/2020/08/PIPC_QALY_Graphic.pdf
Source: Institute for Clinical and Economic Review: http://icerorg.wpengine.com/wp-content/uploads/2020/10/ICER_DMD-Final-Report_081519-2.pdf

Why are patients valued differently?

Maximum value of extending survival via the traditional framework:



$50,000 per year

vs

–$12,000 per year

A therapy extending survival for non-ambulatory patients is *not* cost-effective in a traditional framework *even if it were free*

Willingness to pay of $100,000.
Estimated potential value of treatment based on direct medical cost and utility value per health state per year; inputs from 2019 ICER DMD report.
Does not consider impact of discounting costs or benefits.

Despite the good intentions of the QALY, there are drawbacks

Prominent organizations have found many limitations when using QALY[1]

QALYs do not truly capture the burden a disease places on patients and their families

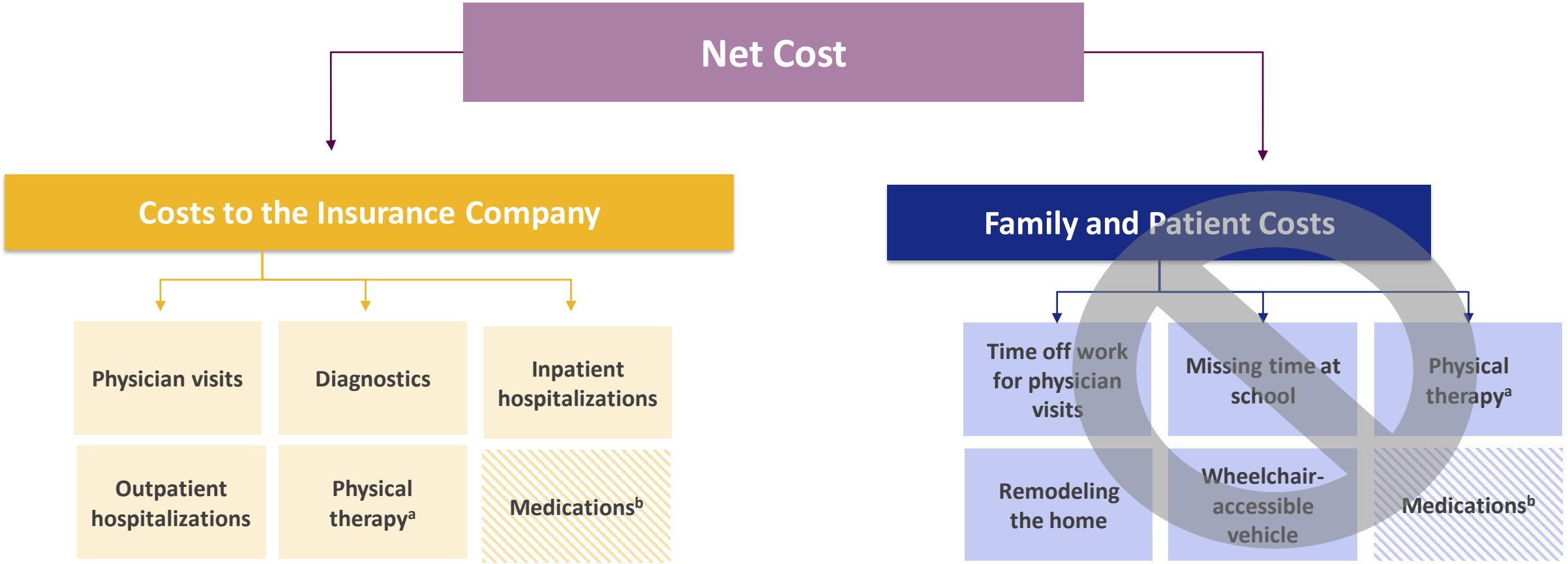
QALYs effectively place a different dollar value for a year of life for different patients

QALYs do not prioritize the most severe patients, despite society's preference

Key: QALY – quality-adjusted life-year.
Additional considerations to highlight QALY drawbacks.

1. National Disability Council. Quality-adjusted life years and the devaluation of life with disability. November 6, 2019. Accessed August 2, 2021. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

Traditional value frameworks focus on costs to the insurer, not costs borne by the family and society



Examples of costs typically incurred by family/patient.
[a] If not covered by insurance.
[b] Only included if determined to be cost-effective.

The progressive nature of Duchenne will inevitably lead to the need for full-time caregiving, which is most often provided by families

Patients with DMD are unable to live an independent life…

29%	do not leave the house in a typical week[1]
84%	are unemployed[2]
92%	are unable to live independently[1,2]
87%	are not in a relationship[2]

Caring for a child with DMD impacts every aspect of caregivers' lives

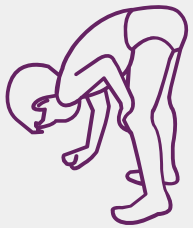
74%	are **worried** for the **future** of other **children**†,[5]
50%	are moderately or extremely **anxious** or **depressed**[4]
69%	**neglect** hobbies and **things they enjoy** doing in their free time†,[5]
84%	have experienced a **feeling of loss**†,[5]
44%	feel they **neglect** other **family members**†,[5]
56%	find it difficult to carry out usual **work or household activities**†,[5]

1.Pangalila RF, et al. Arch Phys Med Rehabil. 2015;96(7):1242-1247. 2.Rodger S, et al. J Neurol. 2015;262(3):629-41.

1.Schreiber-Katz O, et al. Orphanet J Rare Dis. 2014;9(1):210. 2.Landfeldt E, et al. Dev Med Child Neurol. 2018;60(10):987-996. 3.de Moura MCDS, et al. Arq Neuropsiquiatr. 2015;73(1):52-57. 4.Landfeldt E, et al. J Neurol. 2016;263(5):906-915. 5.de Oliveira LC, et al. Journal of Health Sciences. 2020;22(1):56-60. 6.Gocheva V, et al. Eur J Paediatr Neurol. 2019;23(6):832-841. 7.Jackson JL, et al. J Child Neurol. 2021;36(3):177-185. 8. Schwartz et al. JPRO. 2022:6:22. 9..Magliano L, et al. Acta Myol. 2014;33(3):136. 10.Podolska K, et al. Parent Project Muscular Dystrophy Annual Conference 2020 (LINK).

Disease management costs for Duchenne are relatively very low compared to other rare diseases

Annual Disease Management Costs with Current Standard of Care



Duchenne

$31,000/year

Beta thalassemia

$102,000/year

SMA type 1

$325,000/year

Hemophilia A

$706,000/year

Under traditional value assessment models, the current cost of treating a disease can have a big impact on the value assessment of a new therapy and whether that therapy can save the health plan money

Key: ICER – Institute for Clinical and Economic Review; SMA – spinal muscular atrophy.
Costs listed are only the average direct medical costs borne by the payer, not the cost of any therapies. Cost values are rounded.
Duchenne: Landfeldt E, et al. *Neurology*. 2014;83(6):529-536. Beta thalassemia: ICER. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value. Final evidence report. July 19 , 2022. SMA type 1: ICER. Spinraza and Zolgensma for spinal muscular atrophy: effectiveness and value. Final report. April 3, 2019. Hemophilia A: ICER. Valoctocogene roxaparvovec and emicizumab for hemophilia A without inhibitors: effectiveness and value. Final report. November 20, 2020.

A paradoxical situation: Traditional assessments place less value on treatments for patients with the greatest unmet need

Demonstrating value for gene therapies for patients who currently have no/limited treatment options is more difficult than if patients have existing treatment options because the latter offers the insurer an opportunity to save money

We need to change this narrow view of value and define value through the lens of the patient

How can you advance patient-centered policy solutions and ensure patient access to treatments while advancing innovation?

- ✓ Adopt newborn screening for Duchenne to reduce the diagnostic odyssey
- ✓ Ban the use of the QALY metric in your state as it devalues and discriminates against patients with genetic diseases (Oklahoma HB 2587 and Massachusetts Bill HB 201)
- ✓ Ensure the rare disease patient perspective and an expert treating physician is incorporated into medical and pharmacy benefit covered prescription drug reviews by Medicaid Pharmacy & Therapeutics Committees and Drug Utilization Review Boards or similar state bodies (Illinois HB 2259 and Arkansas SB 143)
- ✓ Avoid pricing and reimbursement policies that will disincentive innovation, particularly for rare, pediatric genetic diseases
- ✓ Advance policies that recognize the holistic value of a rare disease treatment

Thank you