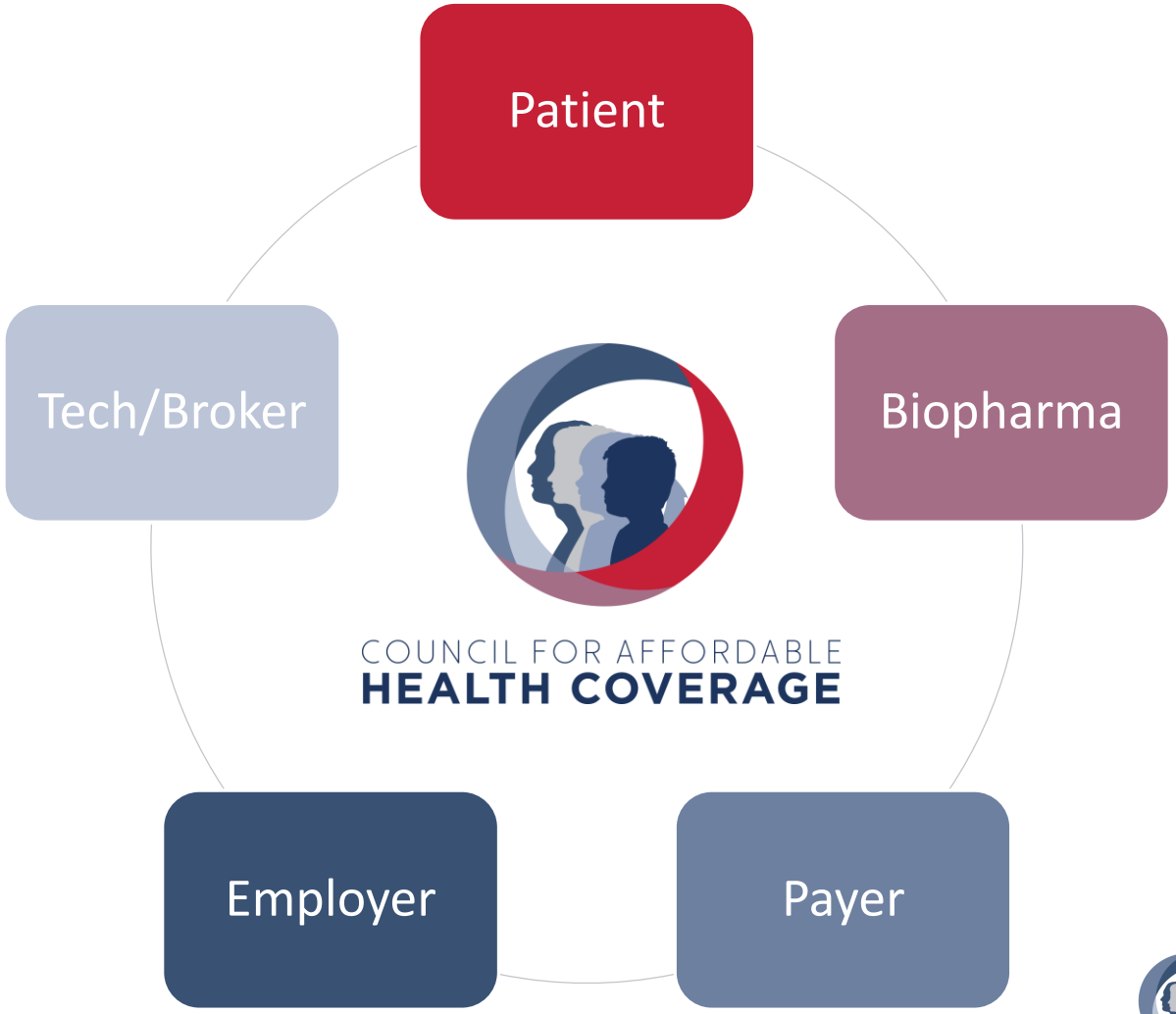
Unmet Medical Needs and How Gene Therapies Can Help

Sloane Salzburg
Council for Affordable Health Coverage
Campaign for Transformative Therapies

About CAHC and CTT

- The Council for Affordable Health Coverage (CAHC) members believe that the cost of health coverage is too high and growing too fast. CAHC promotes policies that lower health costs through increased competition, informed consumers, and more choices to help promote access to affordable coverage.

- CAHC Launched the Campaign for Transformative Therapies (CTT) to unite payers, manufacturers, and patients around policies that improve access to and lowers the cost of gene therapies.



A CAMPAIGN FOR Transformative Therapies

COUNCIL FOR AFFORDABLE HEALTH COVERAGE

A CAMPAIGN FOR Transformative Therapies

The Campaign for Transformative Therapies believes that encouraging value-based arrangements for gene therapies in federal health programs and the private sector is necessary to ensure patients can access affordable, innovative treatment.

Today's Speakers

Annie Kennedy, Chief of Policy & Advocacy, **EveryLife Foundation**

Will Hubbert, **Hemophilia Patient Advocate**

Glenn O'Neill, President & Co-Founder, **Cure Sanfilippo Foundation**

Steven Pipe, MD, Pediatric Medical Director Hemophilia and Coagulation Disorders Program, **University of Michigan**

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Measuring the Lived Experience of Rare Disease:

The National Economic Burden *of* Rare Disease Study

Annie Kennedy
Chief of Policy & Advocacy, EveryLife Foundation for Rare Diseases
July 2021

EVERYLIFE FOUNDATION FOR RARE DISEASES

LEWINGROUP® Part of OptumServe

Patient Experience Data Informing FDA Approval Decisions

To adequately assess benefits and risks, FDA must understand the context in which a potential therapy will be used

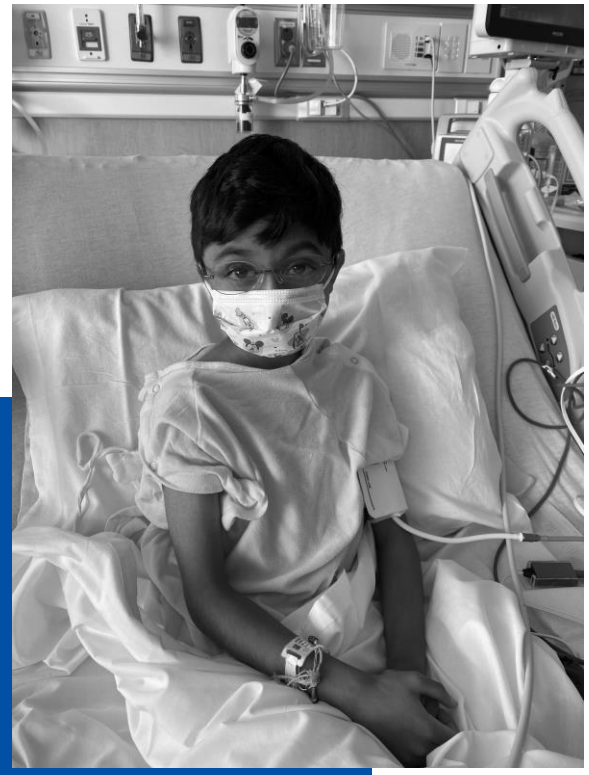
Two relevant categories of patient experience:

- ✓ **The burdens of disease and its impacts on patients' daily lives**
- ✓ **Patients perspectives about potential and current treatments**
- ✓ **Views on unmet medical needs & available medical interventions**
- ✓ **Enhanced understanding of the natural history of the disease of condition**

This helps FDA understand the types of benefit that matter most to patients

Beyond Approval to Access: Ensuring that Outcomes that Matter to Patients are Measured & Counted

Study Purpose:
Determine Economic Impact of Rare Disease (RD) in the U.S.



- Conduct largest, most comprehensive assessment to date
  - Move from anecdotal cost estimates to high-quality evidence
  - Direct medical costs, indirect costs, non-medical costs
  - Research led by the community, for the community -representing hundreds of RDs
- Fill knowledge gap regarding less-examined costs
  - Costs absorbed by individuals, caregivers, and families
  - Economic impact of reduced ability to contribute in workplace and community
- Quantify the economic impact of RD in the U.S. in order to:
  - Evaluate the economic impact of living with a rare disease on individuals, families – and the public overall
  - Inform policy to better align the investment into RD to reflect the public health urgency
  - Work together to advocate for policy changes to improve lives of patients and families with RD

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 Methods:
Database Analysis and Community Survey Yield Comprehensive Data

The study estimated RD prevalence and analyzed per patient costs to determine the economic burden of 379 RDs in the U.S. in 2019

Direct Medical Costs

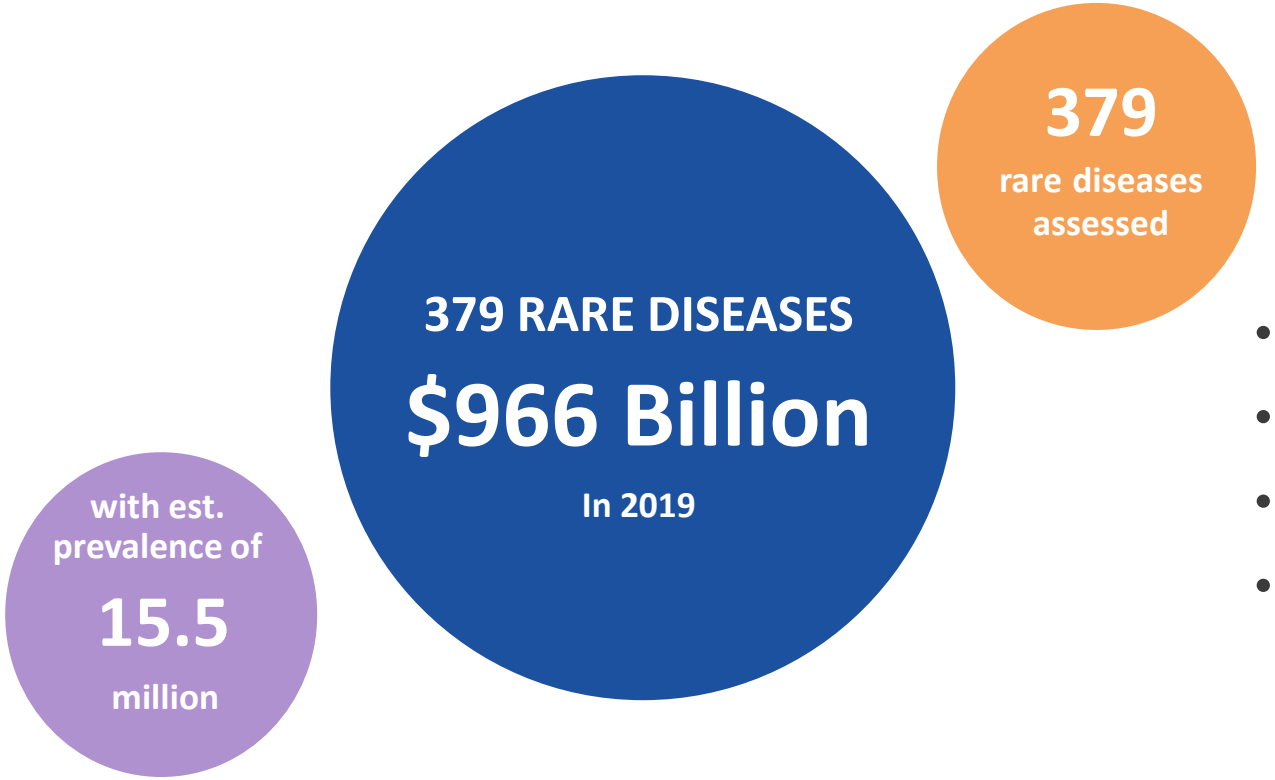
- Used diverse and best available medical claims data
  - Medicare
  - Medicaid
  - Privately insured
- Analyzed databases using ICD-10 codes
  - Assessed 379 RDs
  - With estimated prevalence of 15.5 million
- Categorized into RD groups
  - 16 for adults
  - 7 for children (<18 yrs.)

Indirect and Non-Medical Costs

- Fielded **RD Impact Survey** of patients, caregivers
- Worked with broad rare diseases patient advocacy community on survey development & dissemination
  - Disease history
  - Demographics, insurance coverage
  - Caregiver roles
  - Employment status, income
  - Non-medical costs
  - Disability benefits
- 1,409 households completed the survey
  - Final analysis sample = 1,360

Study Results:

Total Economic Burden of 379 RDs Was Nearly **$1 Trillion** in 2019



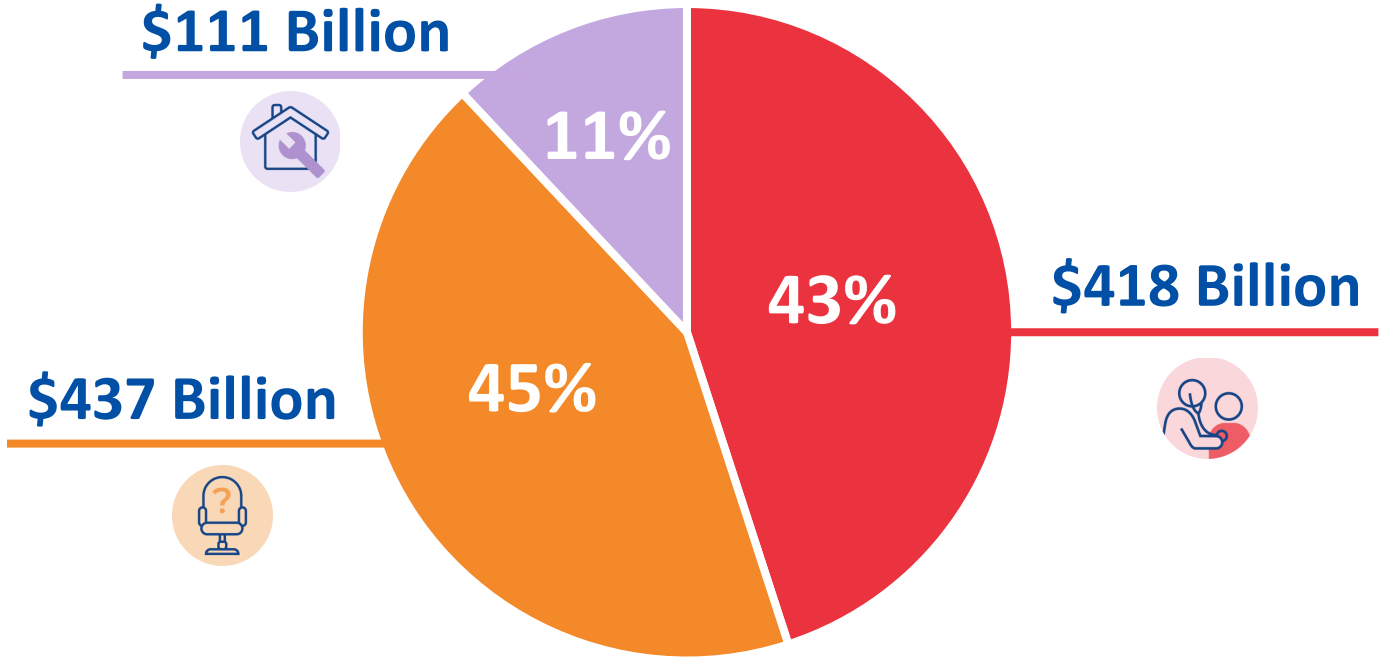
- The study assessed 379 out of 7,000 RDs
- Estimated prevalence of 379 RDs = 15.5 million
- Economic burden is not generalizable to all RDs
- Further research is needed to understand prevalence and economic burden of *all* RDs

Conservative Estimate of Economic Burden Based on 379 of 7,000 RDs

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

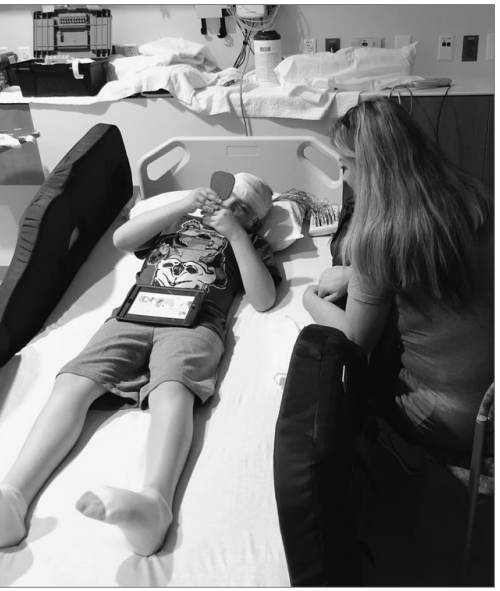
CATEGORY	COST IN BILLIONS	%
Inpatient	$143 B	34.2%
Outpatient	$62 B	14.8%
Other Ancillary	$49 B	11.7%
Prescription Medication	$48 B	11.5%
Outpatient Prescription Administration	$48 B	11.4%
Non-Acute Inpatient	$31 B	7.5%
Physician	$31 B	7.4%
Durable Medical Equipment	$4 B	1.1%
Caregiver	$2 B	0.5%

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

The National Economic Burden of Rare Disease Study

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

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

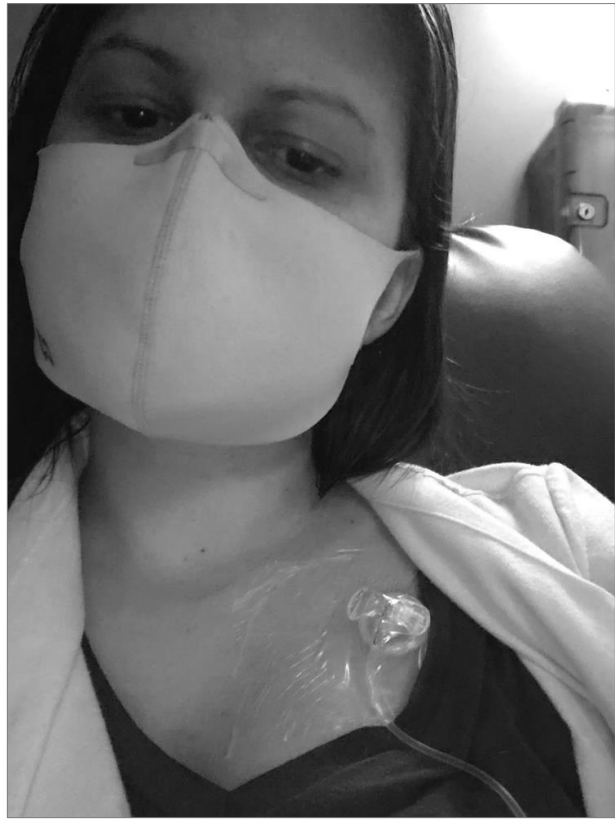
Study Results:
RD Impact Survey Captures Medical Burden, Long Diagnostic Odyssey

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

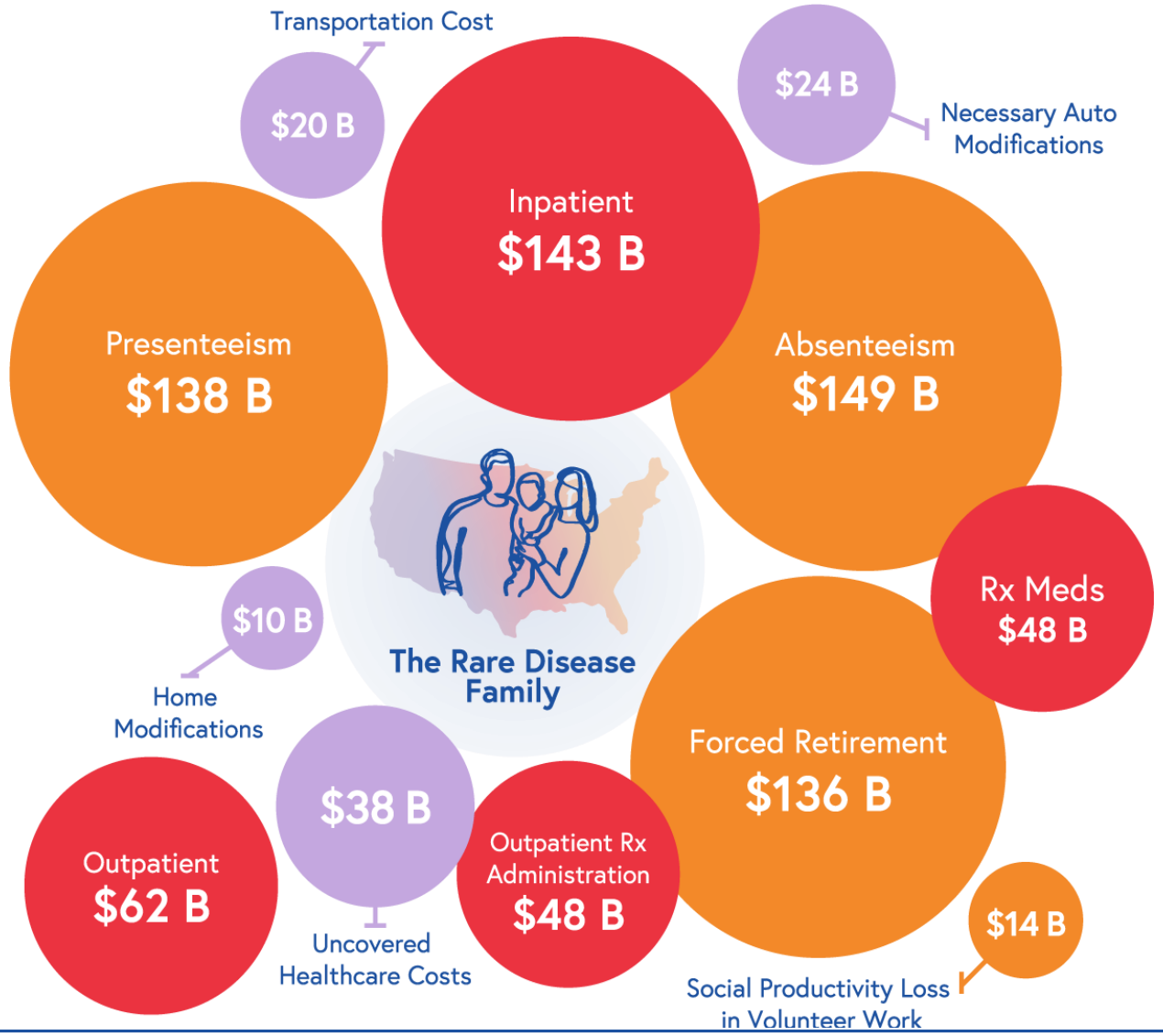
The National Economic Burden of Rare Disease Study

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

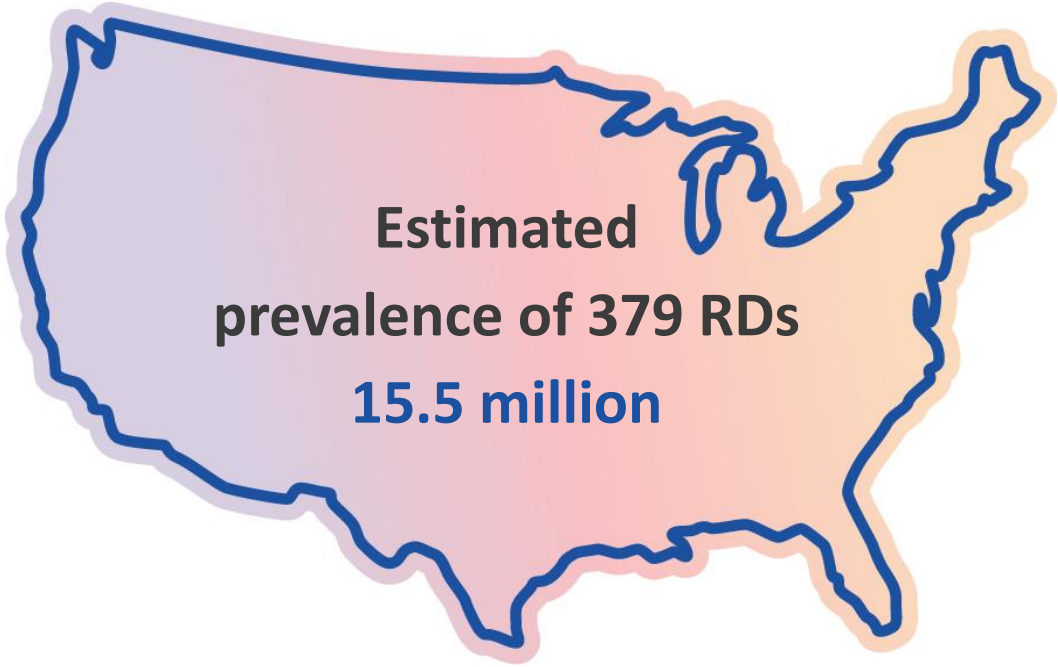
15.5 million

The National Economic Burden of Rare Disease Study

Rare Disease isn't so rare after all

7,000+
rare diseases

~30
million
affected



The National Economic Burden of Rare Disease Study

Study Contributors:

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

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PhRMA

Pfizer Inc.

REGENXBIO Inc.

Sanofi Genzyme

Sarepta Therapeutics

Spark Therapeutics

Travere Therapeutics

Rare Reflection, Dona Krystosek
2019 awardee in the adult category of Rare Artist.

Everylifefoundation.org @EveryLifeOrg

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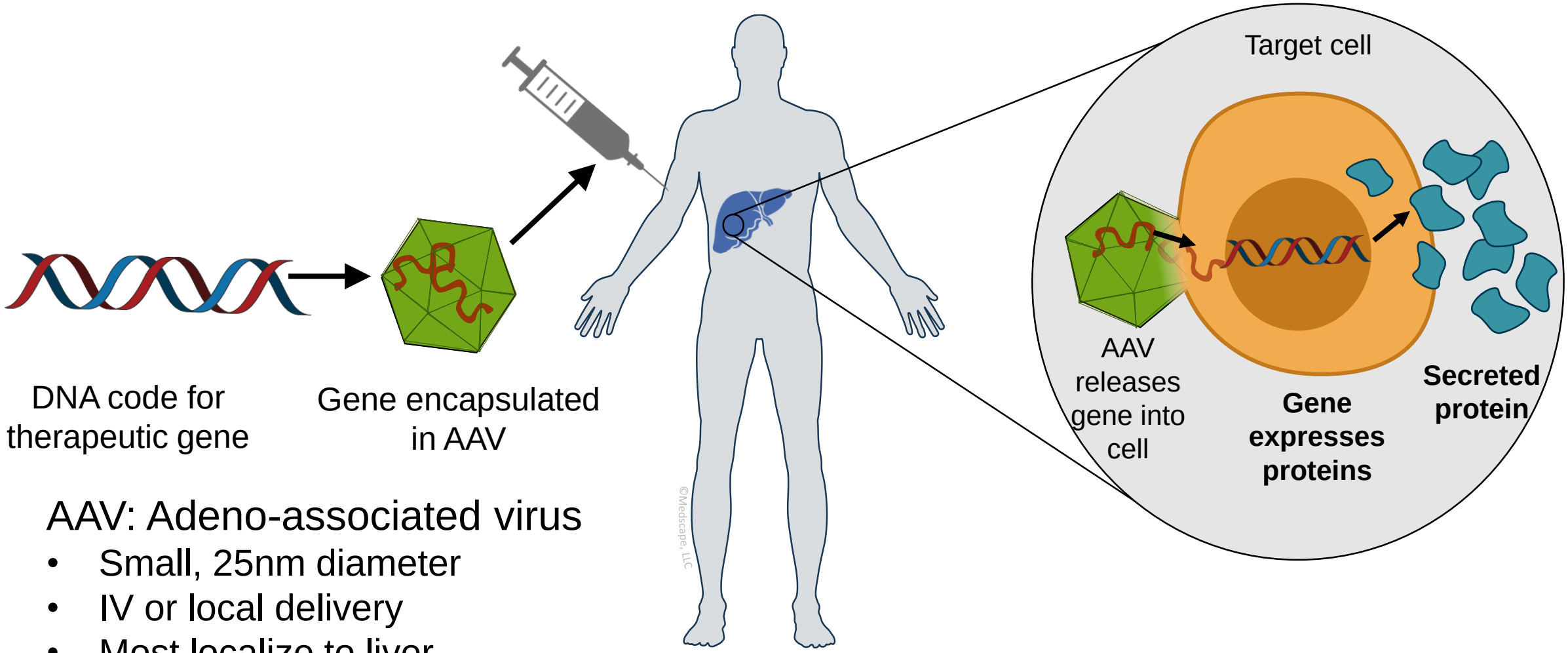
The O’Neill Family

Glenn, Cara,
Beckham & Eliza

Hemophilia Treatment Goals

- To treat bleeds
- To avoid bleeds
- To avoid joint disease
- To avoid bleeding complications
- To achieve the life they choose

The goal of gene therapy is to replace the dysfunctional gene with an exogenous functional gene to cure the disease



AAV: Adeno-associated virus

- Small, 25nm diameter
- IV or local delivery
- Most localize to liver

Wang D, et al. *Nat Rev Drug Discov*. 2019;18:358-378.

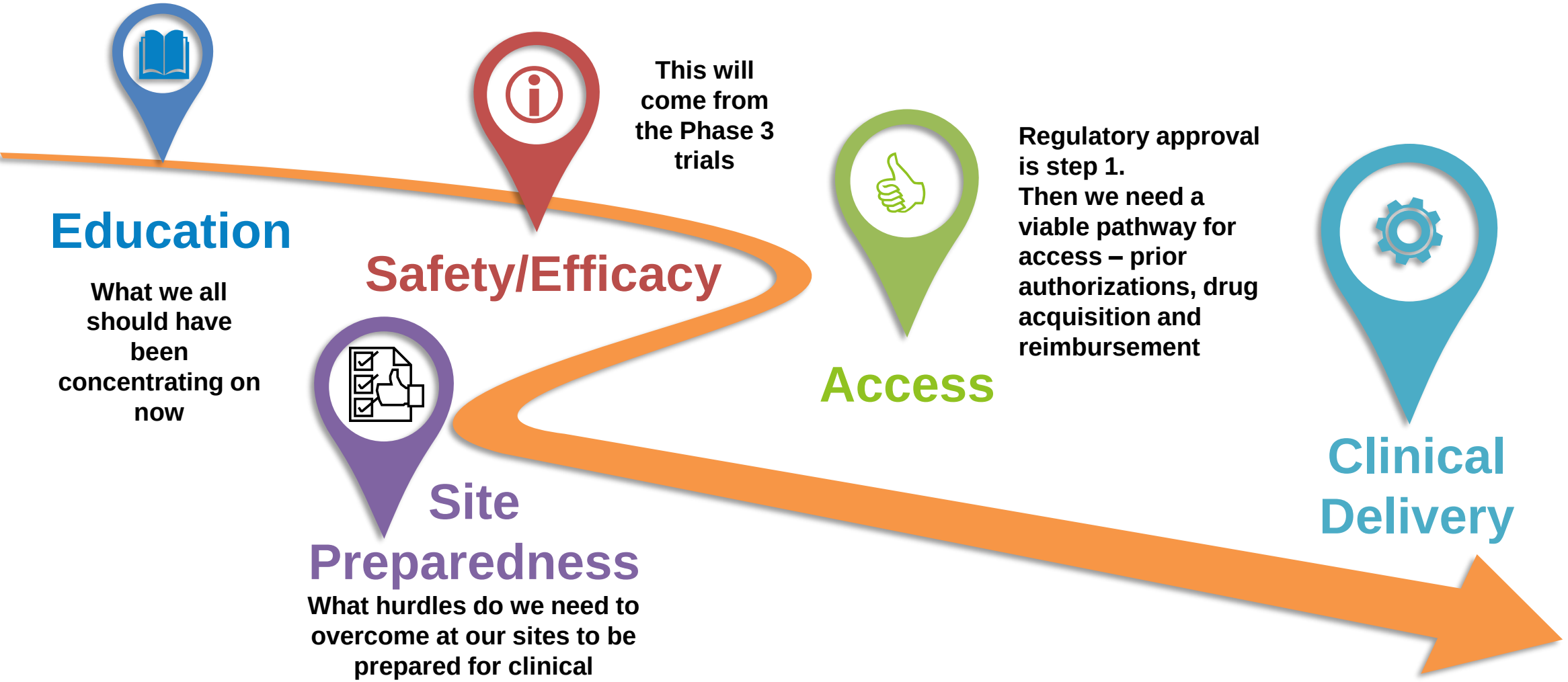
Conclusions

Gene therapy will become a powerful approach in the management of hemophilia and could offer a definitive cure

- Clinical trials have demonstrated that **one single intravenous infusion** of adeno-associated virus **(AAV) vector** containing *F8* or *F9* cDNA can achieve:
  - High protein expression levels
  - Long-term durable factor expression
  - Absence of spontaneous or traumatic bleeds
  - Cessation of prophylaxis regimens
- **Elevation** in **liver transaminase** is the main toxicity observed
  - The majority of events have been managed with **corticosteroids**
  - Some cases have been associated with partial or complete loss of transgene expression

Pathway to Preparedness

Gene Therapy for Haemophilia through our HTCs



Education

What we all should have been concentrating on now

Safety/Efficacy

This will come from the Phase 3 trials

Site Preparedness

What hurdles do we need to overcome at our sites to be prepared for clinical delivery?

Access

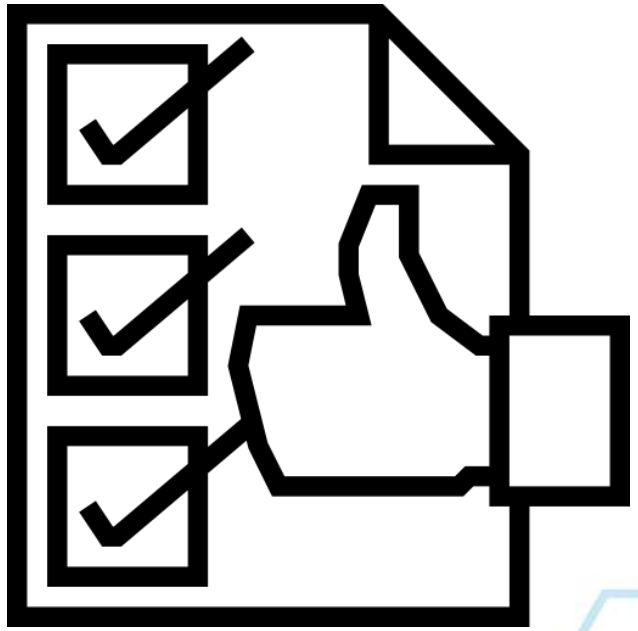
Regulatory approval is step 1.
Then we need a viable pathway for access – prior authorizations, drug acquisition and reimbursement

Clinical Delivery

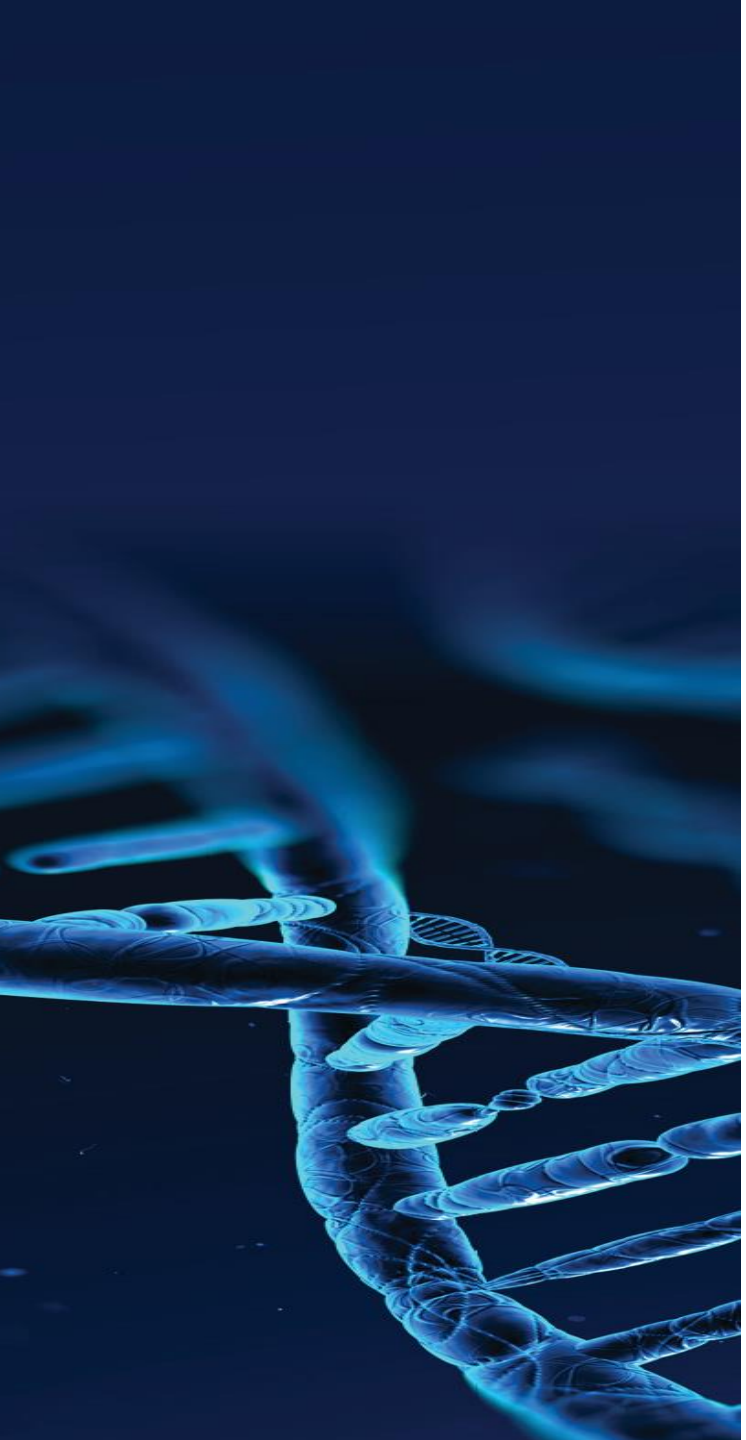
Striving for excellence in delivery and outcomes

Clinical Delivery: Site Preparedness

- Institution preparedness for product handling and administration
  - Infection control committees, nursing handling and infusion, patient and staff precautions
- Pharmacy preparedness
  - Receipt, handling, storage
  - Thaw time
  - Containment
  - Clinical pharmacy is NOT the same as research pharmacy



- Where will you administer? Observe after administration?
- Subject selection and follow up
- Familiarity, practice, will lead to improved outcomes



Four universal principles for the introduction of gene therapy to people with haemophilia[1]

The PWH should be at the centre of decision-making
All PWH should have an equal opportunity to access gene therapy
The safe introduction of commercial gene therapy with lifelong follow-up is paramount to ensuring long-term success
The integrated comprehensive care model currently employed for the treatment of haemophilia improves outcomes and is best placed to support the introduction and long-term follow-up of gene therapy

1. Miesbach et al, Haemophilia, 2021 Apr 23. doi: 10.1111/hae.14309

WFH GENE THERAPY ROUND TABLE

WFH
WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA

Regional Hemophilia Network

149

MCHB Maternal and Child Health Bureau → athn™ american thrombosis & hemostasis network

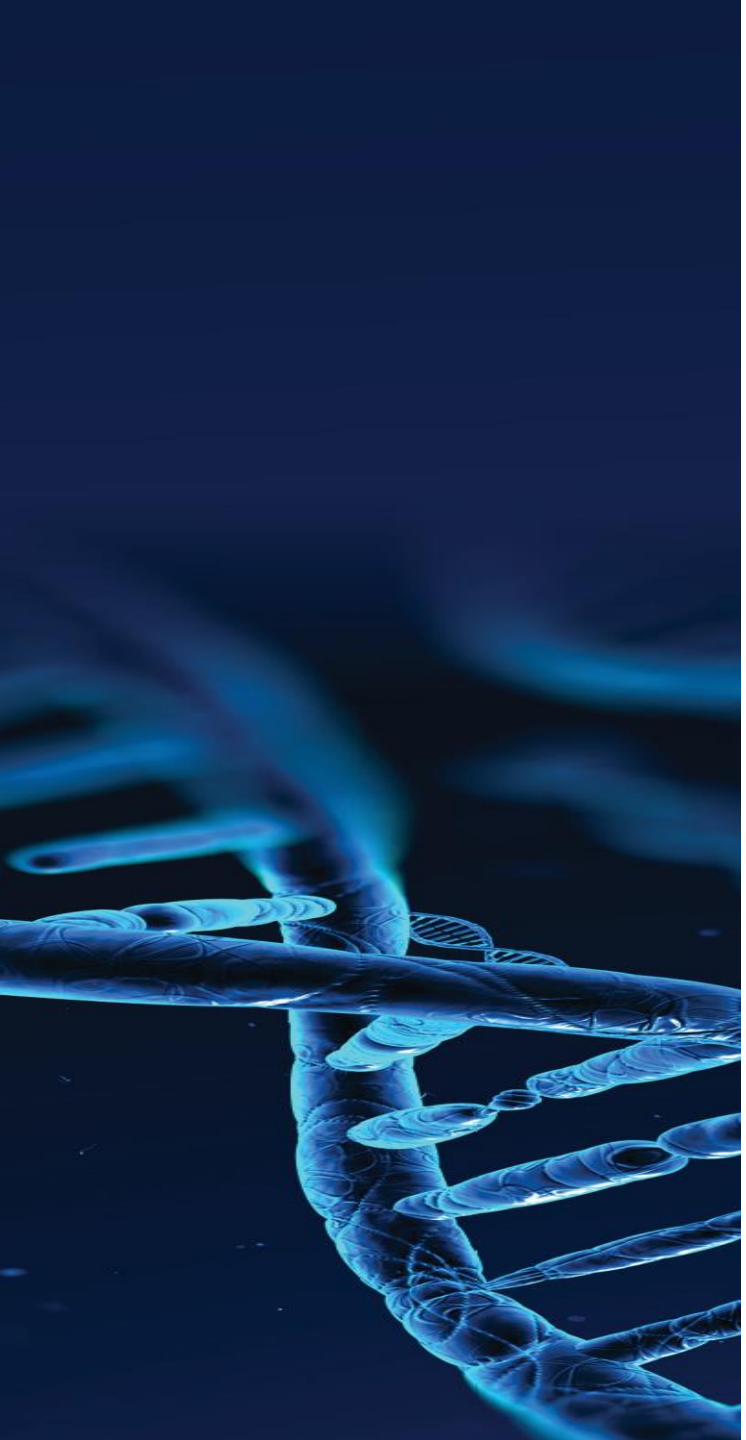
ATHN Affiliates
ATHNdataset
Research
- ATHN 1 – ATHN 5

CDC Surveillance
- Community Counts

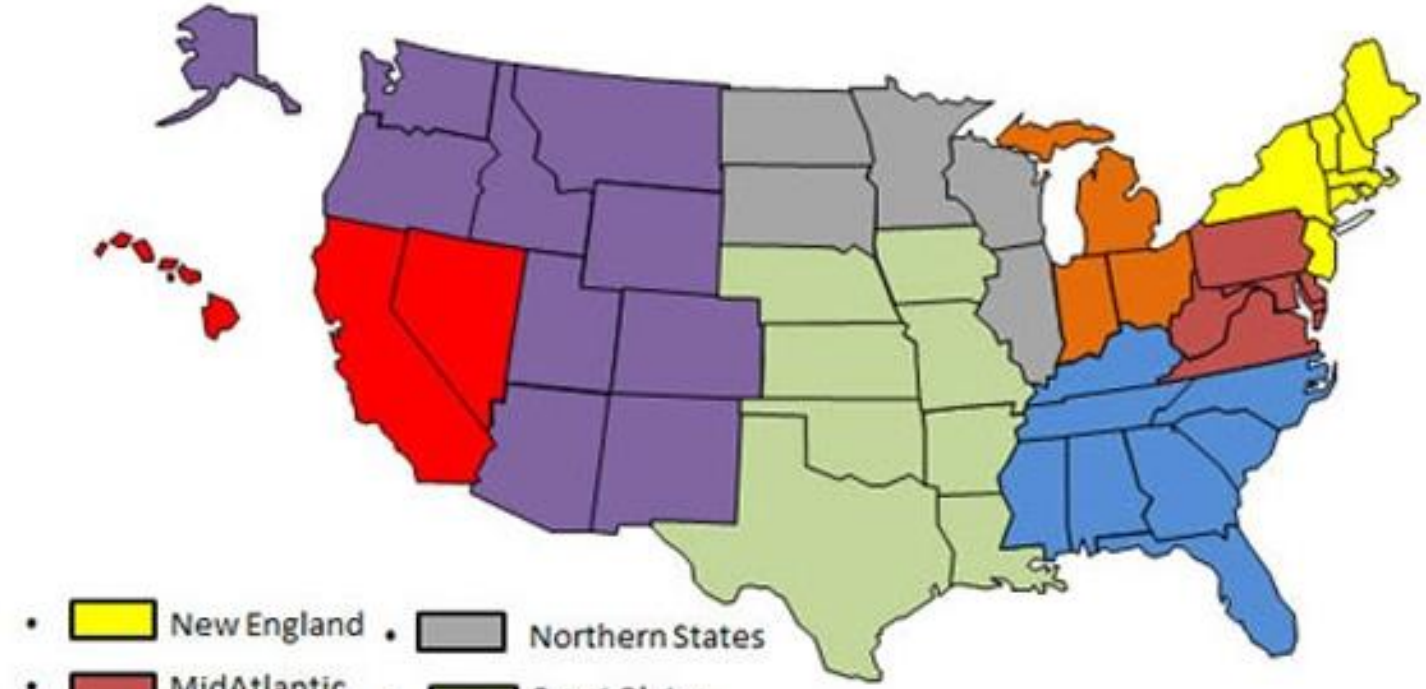
8 Regional Networks ↔ National Hemophilia Coordinating Center

135 HTCs

Committees
Work Groups



HRSA/MCHB Regional Structure



- New England
- MidAtlantic
- Southeast
- Great Lakes
- Northern States
- Great Plains
- Mountain States
- Western States

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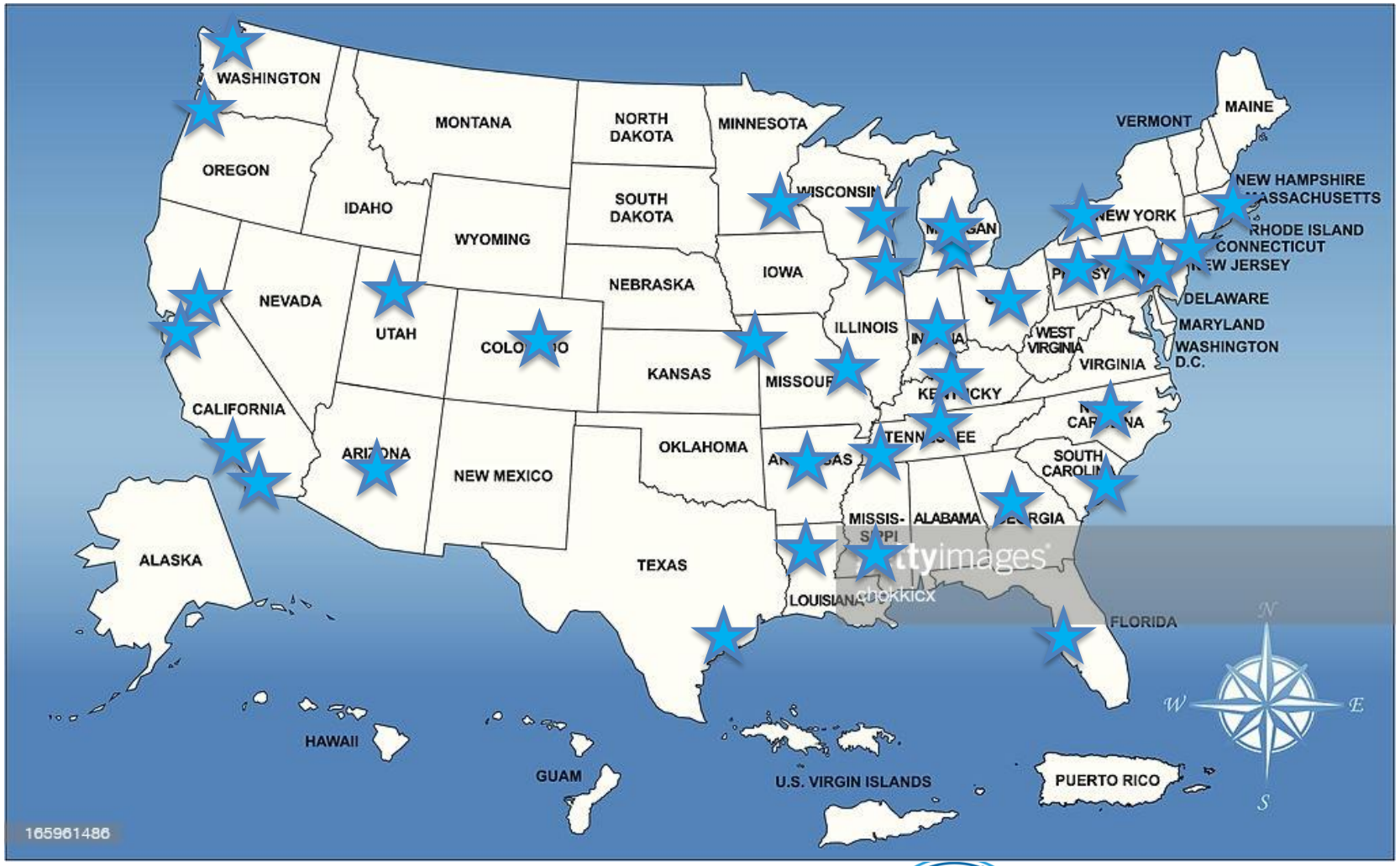
Gene Therapy Clinical Trial Experience (USA)



~36 sites with GT experience

9 sites have never dosed a patient in Ph3

- institutional/infrastructure barriers

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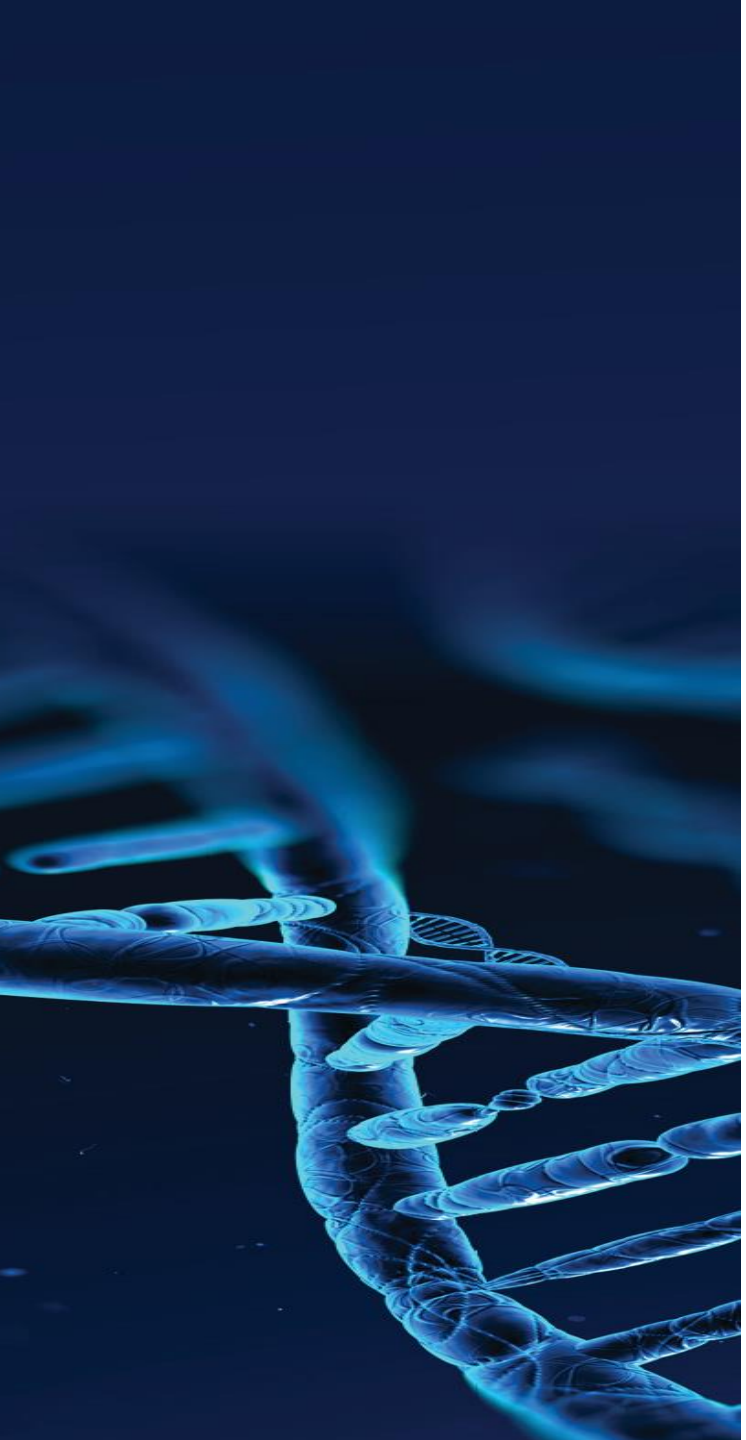

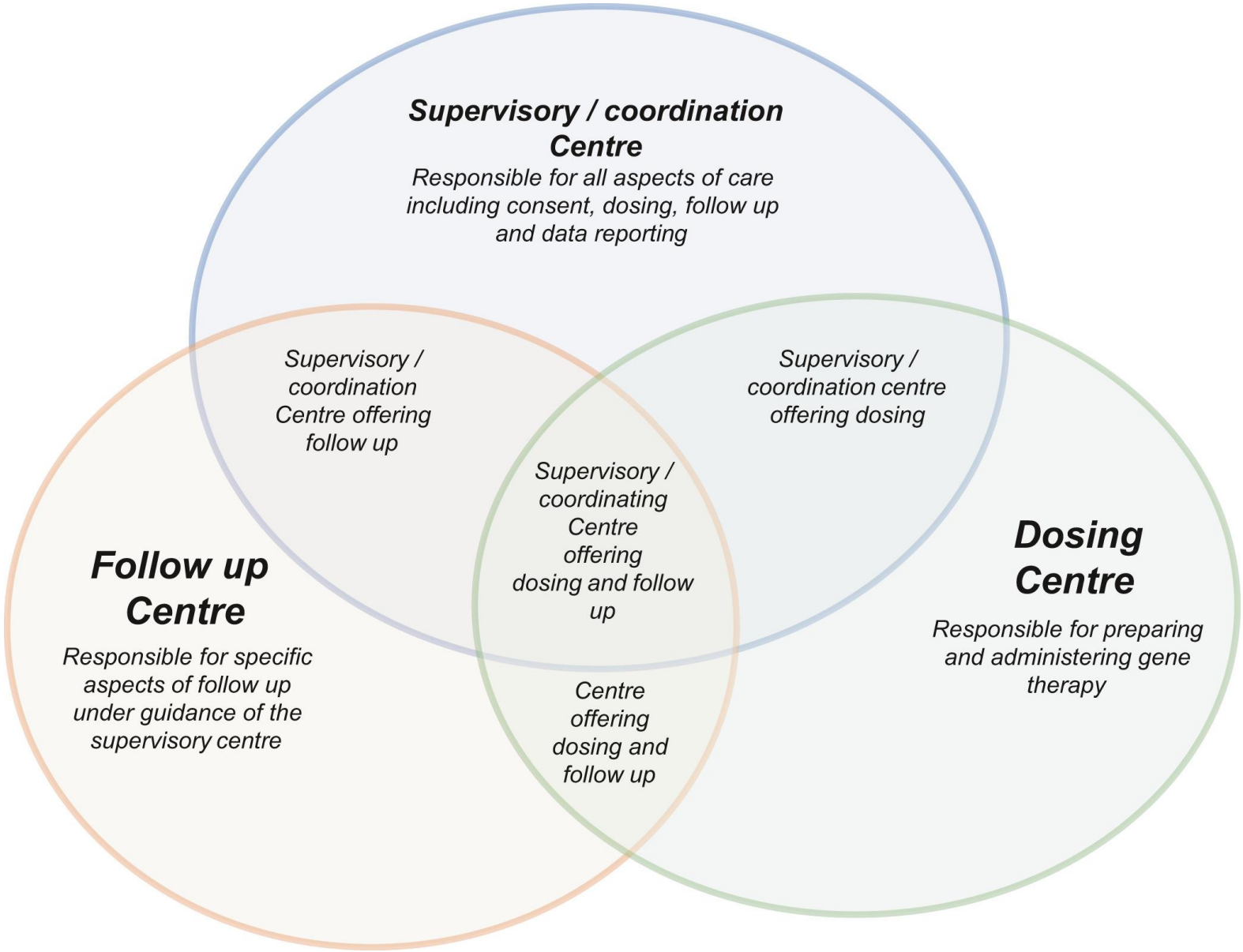

Miesbach et al, Haemophilia, 2021

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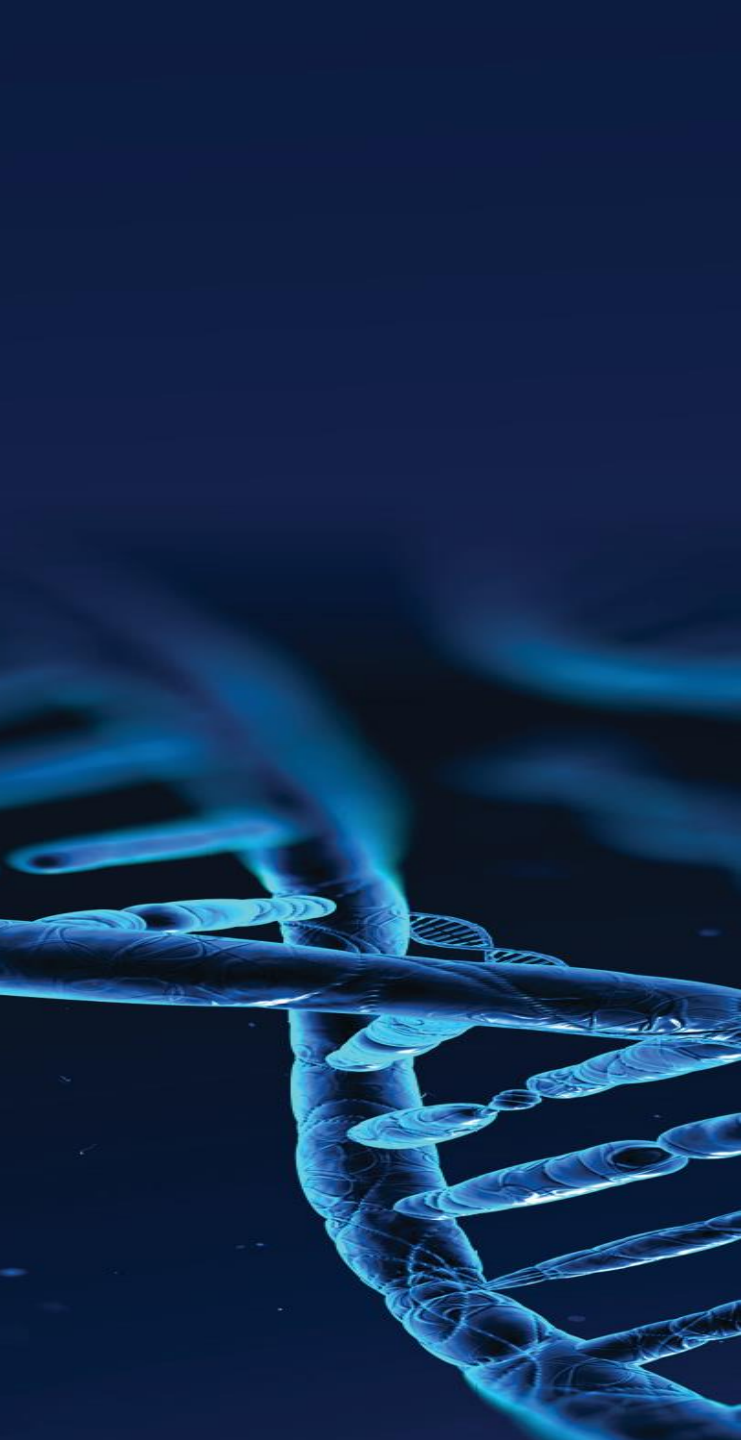
Delivering Access to Gene Therapy

Drug access and reimbursement

- Likely to require innovative payment approaches
- Linked to specific outcome measures:

e.g. persistence of factor activity
continued bleed control
reduced/eliminated need for factor replacement

J Manag Care Spec Pharm. 2019;25(2):156-162.



Unresolved Challenges

- **Reimbursement/funds flow models**
  - What does this look like with a hub and spoke delivery structure and a private pay model?
- **Coordination of care between HTCs**
  - Limited experience with patients moving fluidly for services between HTCs
- **Institutional approvals and local infrastructure needs**
  - ¼ of approved US clinical trial sites were never able to get to the place of dosing a patient
- **Personnel/staffing**
  - Leaving the supports of clinical trial infrastructure and shifting to the heavy demands of the clinical care infrastructure
- **Standardization of Practice**
  - Development of SOPs
  - Sharing of best practices

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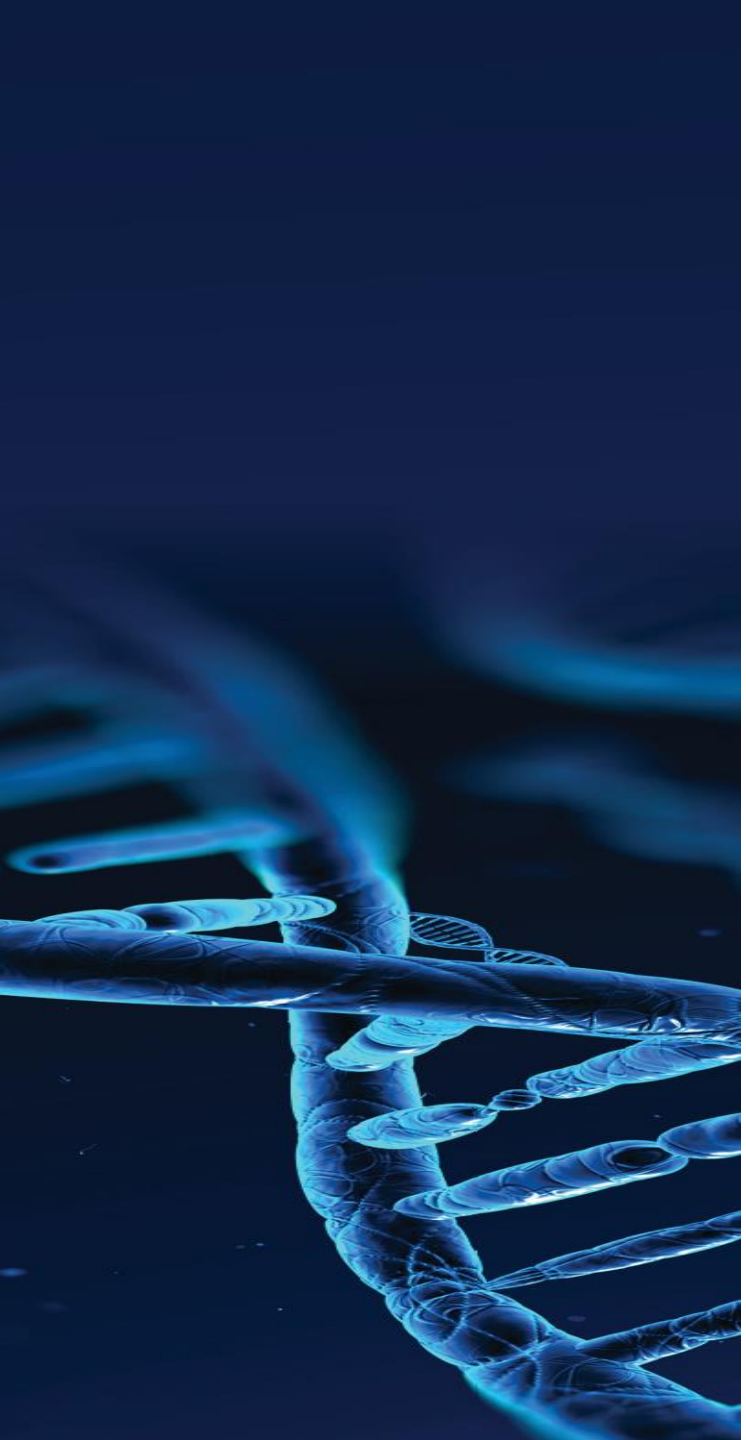

Conclusions

- US HTCs have a collaborative and integrated national infrastructure of 8 regional hemophilia networks
- ~25% of HTCs have clinical trial experience in gene therapy from Phase 1 to 3
  - Institutional/infrastructure barriers still a challenge for dosing
  - “hub and spoke” model has already been operational within clinical trial programs
- HTC preparedness currently focused on educational priorities
- Reimbursement/funds flow may be the most critical hurdle
  - Pharma bears significant responsibility to ensure that HTCs will be compensated adequately for their contribution to GT delivery whether serving as referral, dosing/coordinating and/or follow up centers

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Innovative Payment Arrangements

Gene Therapies

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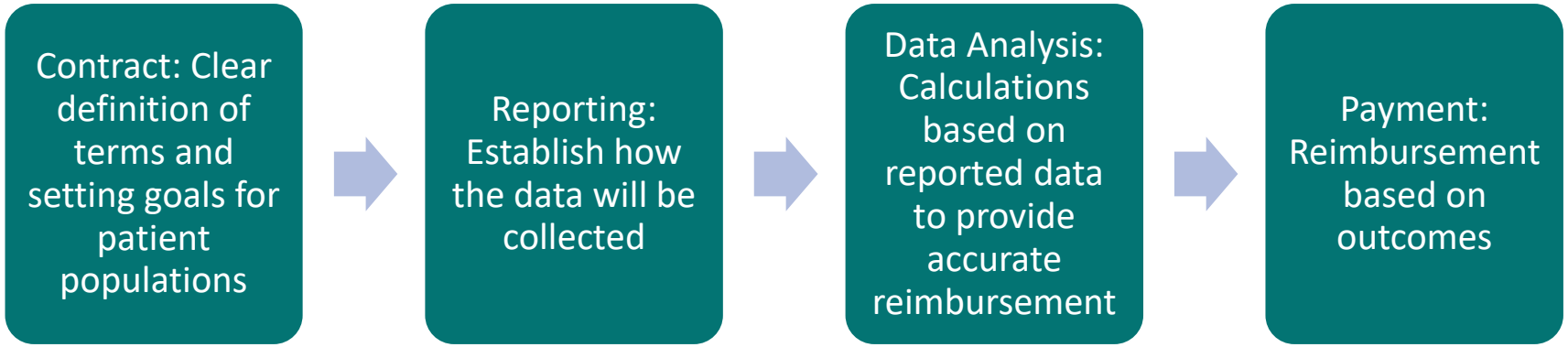
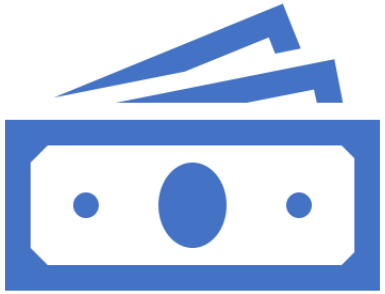
Value-Based Arrangements 101

- **AKA: Outcomes-based, results-based, indication-based, pay-for-performance, innovative payment arrangements**
- VBAs tie reimbursement to outcomes (i.e. did the drug do what it was supposed to?)
- VBAs can base outcomes on: clinical circumstances, patient outcomes, or other measures
- The reimbursement structure can vary:
  - Rebates/refunds, paying directly for a service, etc.
- How do they (generally) work:



Current Policy Barriers



Federal Health Program Drug Price Regulations:
Medicaid Best Price & AMP

The Anti-Kickback Statute & Stark: Under current statute, some "pay for results" discounts negotiated under a value-based contract might be construed as an unlawful inducement to use a manufacturer's drug.

Policy Solutions

REGULATION

- December 2020 CMS Final Rule on Medicaid VBPs
  - Multiple Best Price solution
  - *Update*: Biden Admin extended reporting deadline

LEGISLATION

- **House**: Schrader/Guthrie/Mullin DRAFT language
- **Senate**: Crapo/Burr- Lower Costs More Cures Act (S.2164)

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COUNCIL FOR AFFORDABLE HEALTH COVERAGE

Questions?

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Council for Affordable Health Coverage

Campaign for Transformative Therapies

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