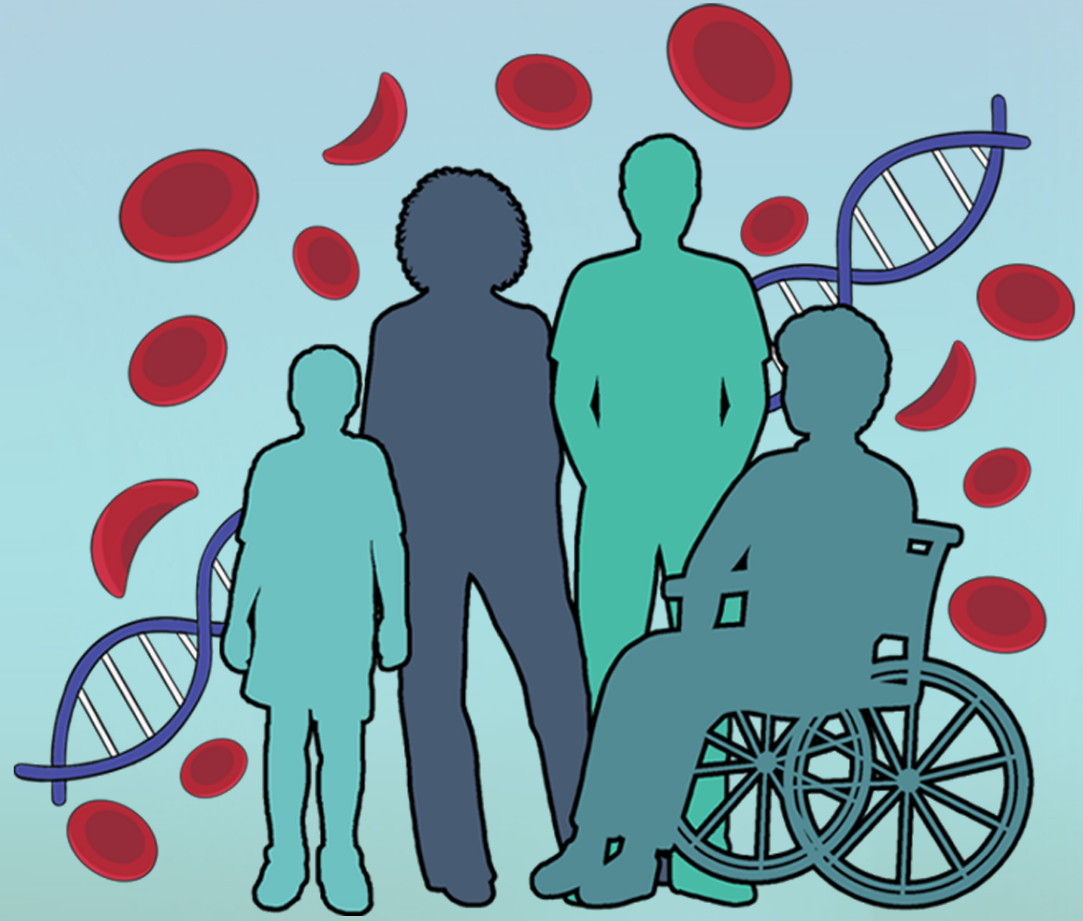
Part 1—Trust, Clinical Trials, and Transformative Therapies: Ethical Pathways in Gene Therapy and Sickle Cell Disease

Thursday, September 18, 2025
1:30-2:30 PM ET



OASH | Office for Human Research Protections

Welcome

Jonathan Green, MD, MBA

(Moderator)

Director, Office of Human Subjects Research Protections, National Institutes of Health (NIH)

Agenda

- Housekeeping
- Two Talks
  - Talk #1: *Parent/Caregiver Perspective on Gene Therapy*
  - Talk #2: *Responsibilities for the Ethical Conduct of SCD Research*
- Panel Discussion
- Audience Q&A
- Closing Remarks

Housekeeping

- Submit questions and comments using the Q&A box.
- Slides will be shared with all attendees afterwards.
- This event is being recorded and will be archived on the Sickle Cell Disease (SCD) playlist on the HHS YouTube site.

Talk #1

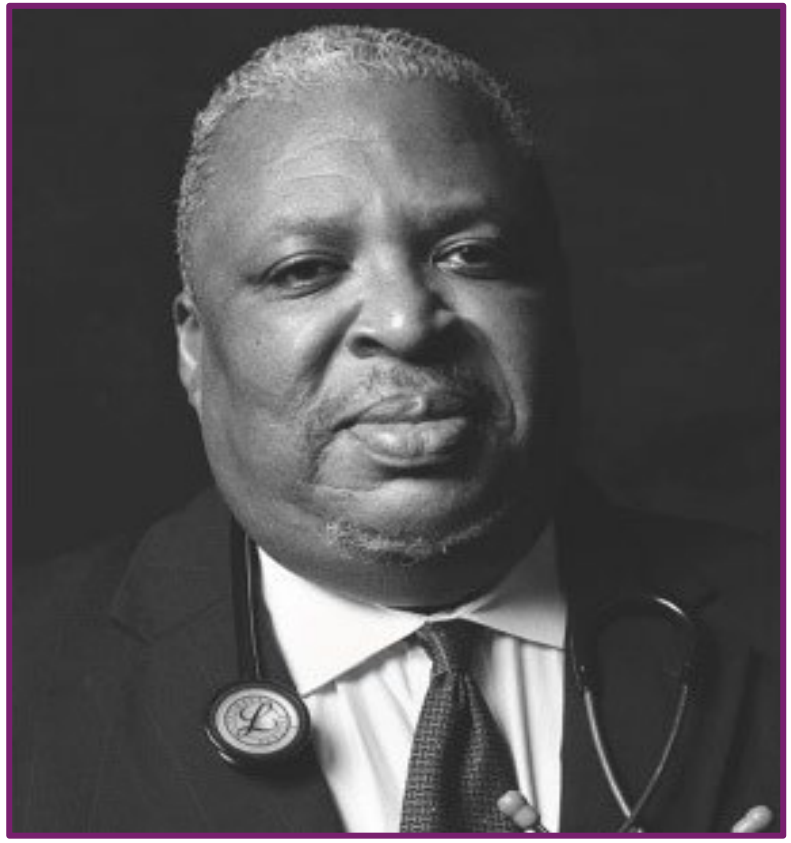
Parent/Caregiver Perspective on Gene Therapy

Antuan Sartin

Louisville, KY

Sickle Cell Disease Advocate

Talk #2
Responsibilities for the Ethical Conductof SCD Research

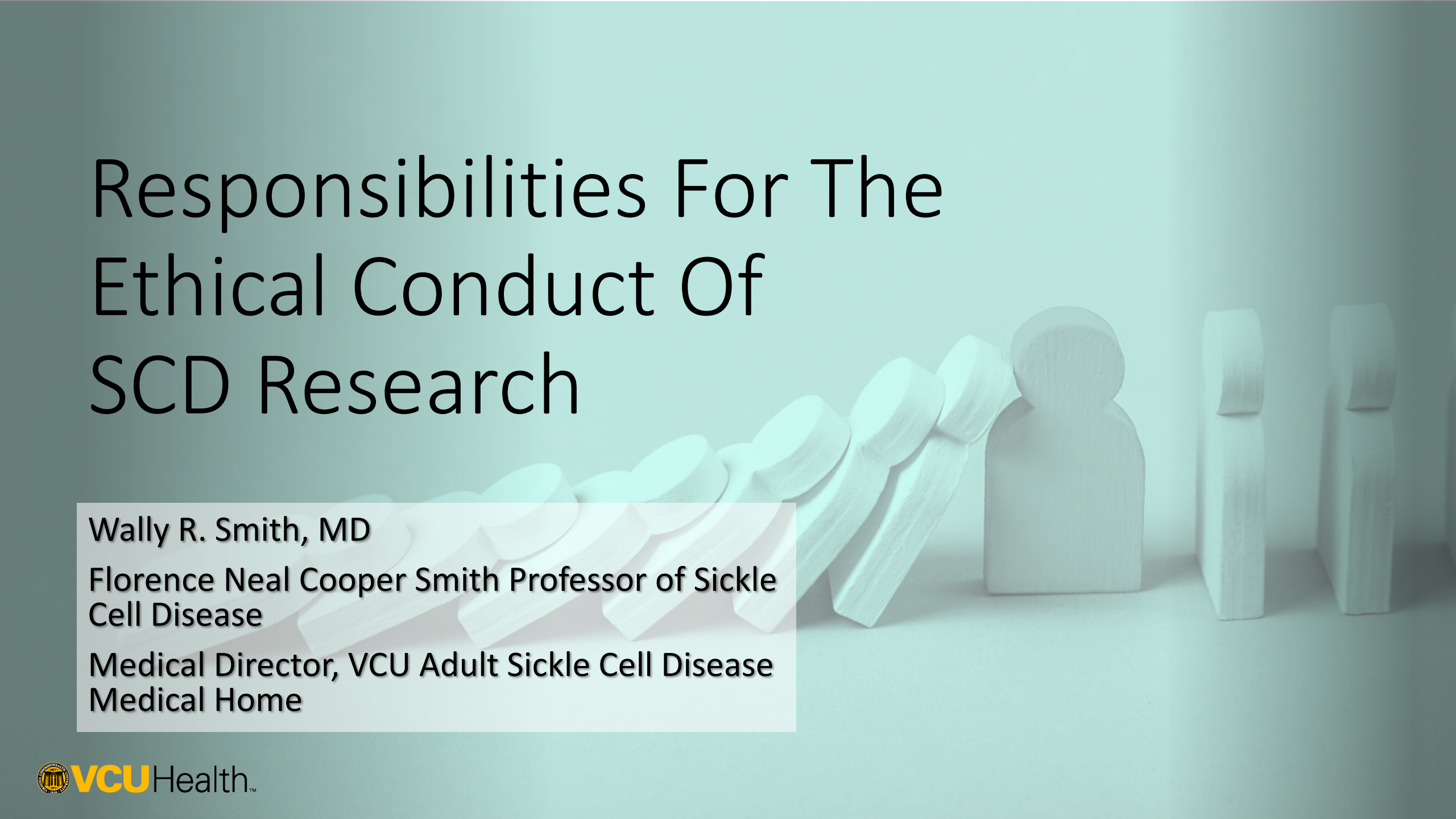


Wally Smith, MD

Richmond, VA

Florence Neal Cooper Smith Professor of Sickle Cell Disease, Vice-Chair for Research, Division of General Internal Medicine, VCU Health

Responsibilities For The Ethical Conduct Of SCD Research



Wally R. Smith, MD

Florence Neal Cooper Smith Professor of Sickle Cell Disease

Medical Director, VCU Adult Sickle Cell Disease Medical Home

VCU Health

Disclosures

- Agios –consultant, investigator
- Alexion-consultant, Investigator
- Bluebird Bio-consultant
- Emmaus Pharmaceuticals—consultant
- Health Resources and Services Administration--investigator
- National Heart Lung and Blood institute, National Institutes of Health-investigator
- Novo-Nordisk-Data Safety Monitoring Board
- Novartis Pharmaceuticals- consultant
- Patient-Centered Outcomes Research Institute-investigator
- Pfizer-consultant, investigator
- Vertex-consultant
- Fulcrum pharmaceuticals-consultant, investigator
- No off-label drug use will be mentioned in this presentation

Learning Objectives

VCU Health

Human Research Protection Program

Protect human subjects' rights, welfare, and safety

- Support scientifically sound research
- Minimize potential risks to participants
- Convey clear information to participants and their communities on the risks and benefits of research.

VCU Health

The Balance

VCU Health

Potential Benefit: SCD Mortality

Overall SCD mortality rate ↑ by 0.7% each year (p<0.001).

SCD mortality ↓ by 3% each year for children (1-19 years, p<0.001)

SCD mortality ↑ by 1% each year for adults (>19 years, p<0.001)

Mean age at death ↑ by 0.36 years each year, controlling for gender

- Median age at death = 42 years females
- Median age at death = 38 years males

From 1979 to 2005, adult SCD mortality rates actually worsened, while pediatric mortality rates improved, resulting in worsened overall mortality.

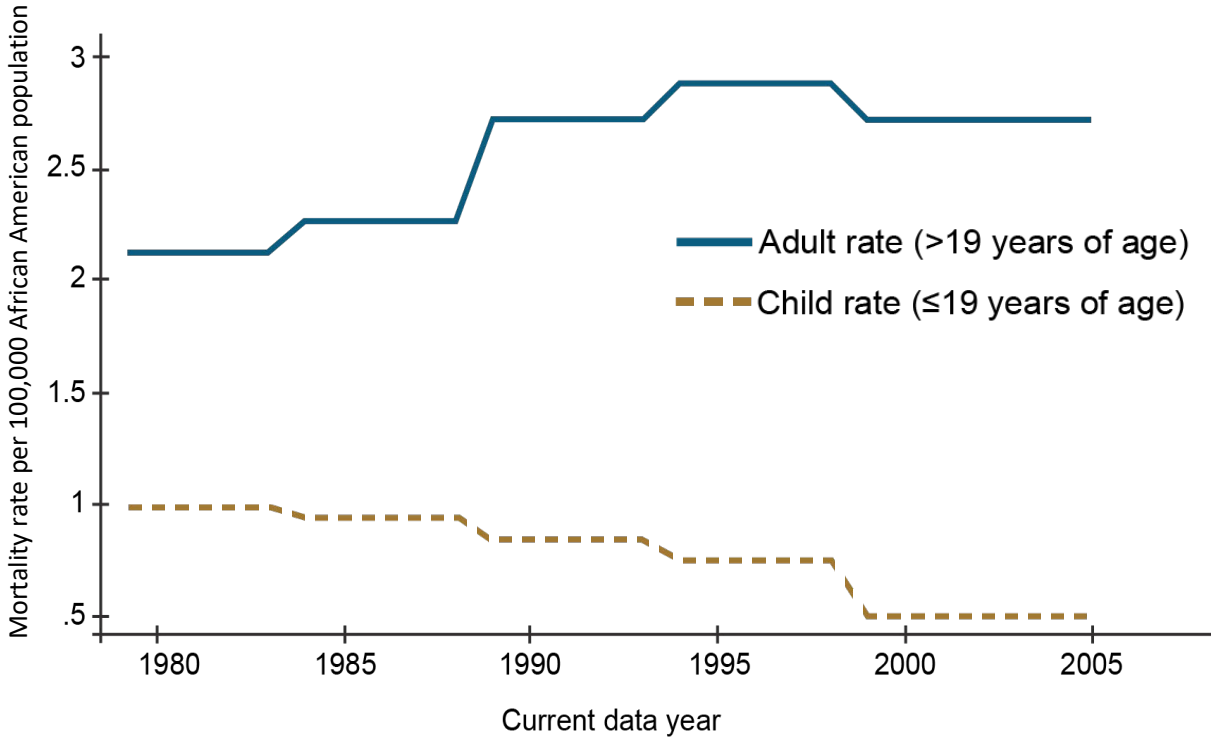
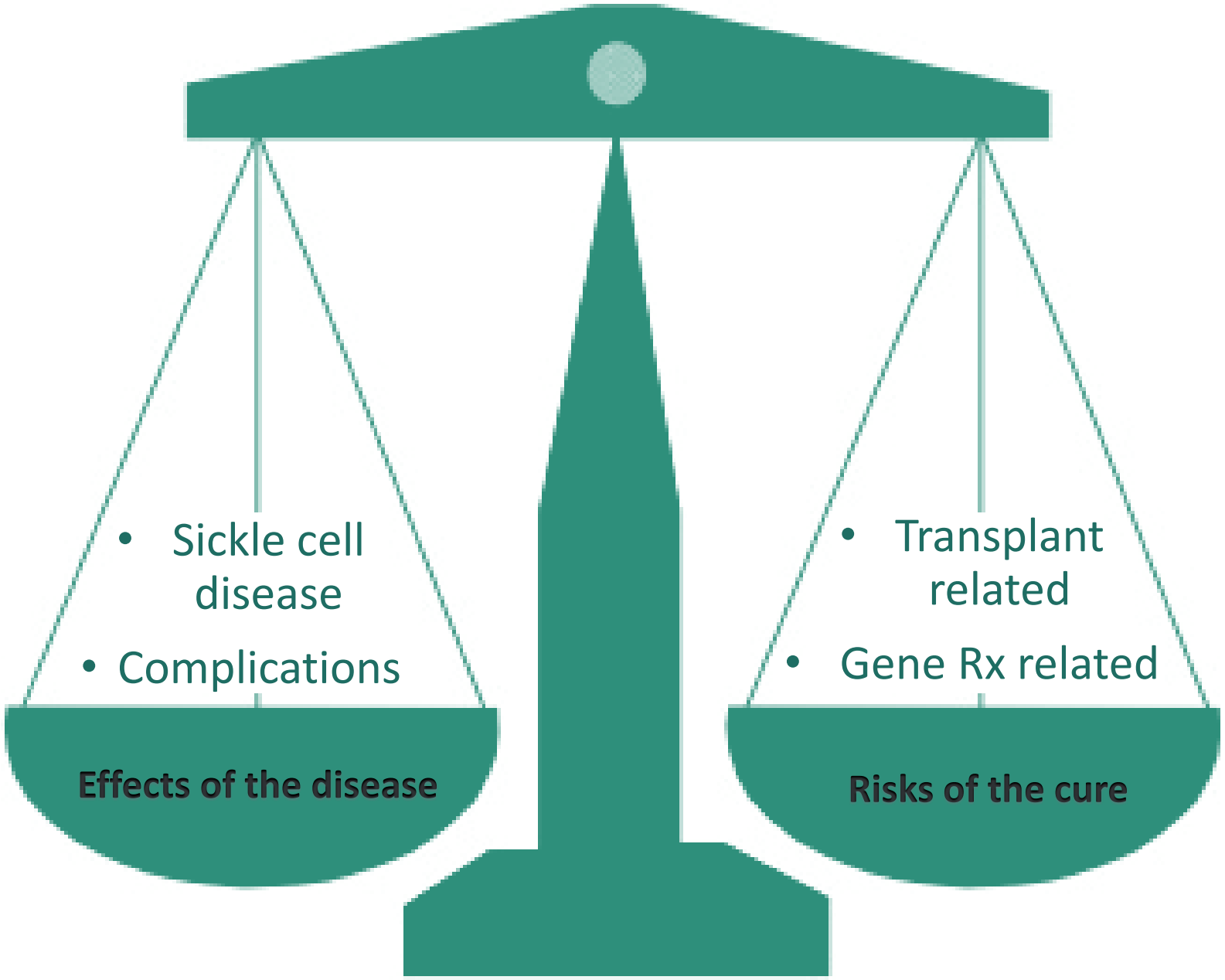
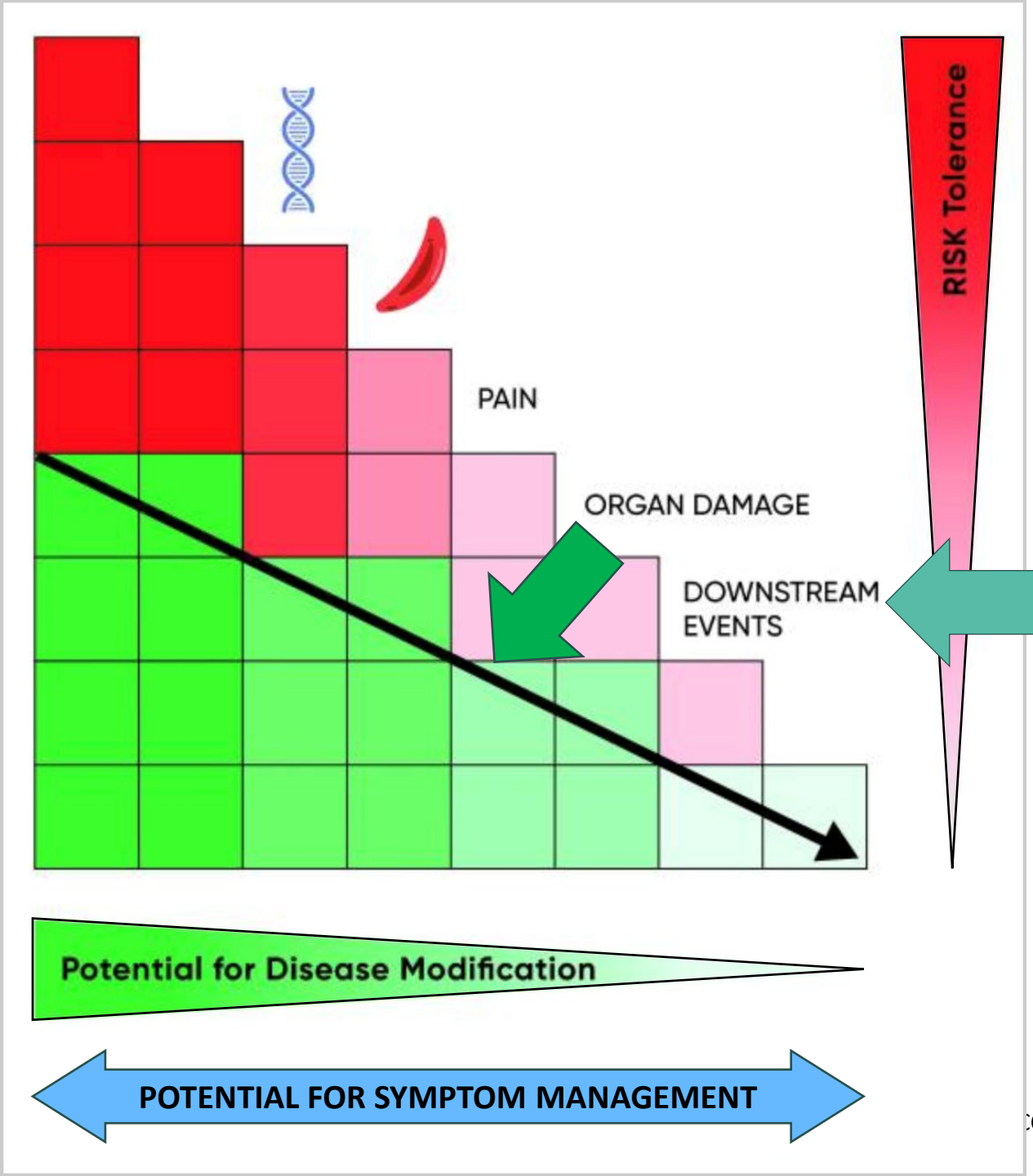


Image created by Symbiotix, LLC

Lanzkron S et al. *Public Health Rep*. 2013;128(2):110-6.



Curative Therapy Risk vs Benefit



Risk-Benefit of Points of Interventon

Downstream targets= palliation, lengthen life

- but primarily management tools
- may not warrant as great a risk

Shift level of risk tolerance

- based on projected Rx impact.

Carden MA, Little J. Emerging disease-modifying therapies for sickle cell disease. Haematologica. 2019 Sep;104(9):1710-1719. doi: 10.3324/haematol.2018.207357. Epub 2019 Aug 14. PMID: 31413089; PMCID: PMC6717563.

Human Subjects Research Approval Requires…

Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design
b. Study Procedures, Materials, and Potential Risks

Adequacy of Protection Against Risks

a. Informed Consent and Assent
b. Protections Against Risk
c. Vulnerable Subjects, if relevant to your study

Benefits to Participants & Others

Benefits to participants and others.

Why risks are reasonable in relation to anticipated benefits

Importance of Knowledge to be gained

Why risks reasonable in relation to knowledge to be gained

Which Therapy to Offer?

Remittive Rx

- Transfusion
- Hydroxyurea
- Crizanlizumab
- L-glutamine

Transplant

- **Haploidentical Match**
- **Matched Sibling Donor**

Gene Therapy

- Two approved Rxs
- Only available on clinical trial if <12 yrs of age
- significant pain/complication burden
- government agency and insurance support

FDA Indication for Gene Therapy for Sickle cell Disease

-SCD

->12 yrs

-Recurrent VOCs

- **Pain Crisis**
- **Splenic Sequestration**
- **Acute Chest Syndrome**
- **Priapism**

Beware of Health Care Corruption

Political/ Governmental

Large organizations

- Pharma, device, biotech, hospitals/ hospital systems, managed care/ health care insurers, health care information technology vendors, consultants, lobbying/ marketing/ public relations firms, contract research organizations, medical education and communication companies, academic medical institutions, health care foundations, accrediting organizations, professional societies, patient advocacy groups, etc

Health care professionals

New Panelists

Lakshmana Krishnamurti, MD

Professor of Pediatrics, Chief of the Section of Pediatric Hematology/Oncology/Bone Marrow Transplantation, Yale School of Medicine, New Haven, CT

Megha Kaushal, MD, MSc

Branch Chief, Division of Clinical Evaluation, Hematology Office of Therapeutic Products, Center for Biologics Evaluation and Research, FDA

PANEL DISCUSSION

Q&A

Closing Remarks

Natalie Klein, PhD

Acting Director, Office for Human Research Protections

U.S. Department of Health and Human Services

Be sure to Join the HHS Office of Minority Health

for

"PART 2—INNOVATIONS AND ADVANCES IN SICKLE CELL DISEASE GENE THERAPIES"

Thursday, September 25, 2025, 2:00-3:30 PM ET

Scan here to register!

THANK YOU!

Have feedback about today's webinar?

Email us at **ohrp-edu@hhs.gov**
with comments, questions, or suggestions.