Improving the Lives of People with Sickle Cell Disease
Using Data to Understand Gaps in Care and Outcomes

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Different types of hemoglobin (i.e., hemoglobin variants) affect how red blood cells (RBC) function

- The type of hemoglobin inherited through our genes determines whether a person has sickle cell disease and the type of sickle cell disease

Sickle hemoglobin (HbS) causes the red blood cells to stick inside narrow blood vessels, thus blocking blood flow and oxygen supply.

Normal hemoglobin (HbA) allows the red blood cells to flex and flow through narrow blood vessels without getting stuck.
“Sickle cell disease” has different combinations of hemoglobin variants
- Hemoglobin S/S or “sickle cell anemia”
- Hemoglobin S/β⁰ thalassemia
- Hemoglobin S/C
- Hemoglobin S/β⁺ thalassemia

“Sickle cell trait” is when one sickle gene is present
- Individuals with trait typically do not have any symptoms
- Two parents with trait may have a child with sickle cell disease
- Genetic counseling, including awareness of trait status, is important
Sickle Cell Disease (SCD) Throughout The World

- **Worldwide about 300,000 annual births**
  - 79% infants born with sickle cell occur in sub-Saharan Africa

- **Mortality is associated with access to prevention and health care**
  - In the U.S., over 95% of children with SCD live past the age of 18
  - In low-income and middle-income countries, about 90% of children die before the age of 5

- **Access to public health infrastructure, universal screening programs, and specific medical interventions could lower global mortality**

What Are Symptoms and Outcomes of Sickle Cell Disease?

- When blood flow is blocked, sudden and severe pain arises
  - Episodes are called “sickle cell crises” or “pain crises”

- Sickle cell crises can be life threatening
  - In the brain, can cause strokes
  - In the lungs, can cause acute chest syndrome

- Sickle cell disease can cause chronic organ damage
  - In the spleen, impairs immune function
  - In the bones, can result in avascular necrosis
  - In the kidneys, can result in chronic renal failure

- Severity and lifelong impact of sickle cell disease is difficult to predict
Increased Premature Mortality Related to Sickle Cell Disease


Death Rate per 1,000 Persons

Age at Death, in Years

5–14 15–24 25–34 35–44 45–54 55–64 65–74 ≥75

Sickle cell disease  
African American  
Total U.S. Population

Understanding Who Has Sickle Cell Disease (SCD) Is Important To Improving Outcomes

- Sickle cell disease can be life-threatening even at young ages
- Newborn screening for SCD in all 50 states
  - 1,500–2,000 babies are identified each year
- Approximately 100,000 Americans are affected
  - No national registries to understand how to improve outcomes

Understanding Sickle Cell Disease Through Surveillance

Registry and Surveillance System for Hemoglobinopathies (RuSH), 2010–2012
Public Health Research, Epidemiology, and Surveillance for Hemoglobinopathies (PHRESH) project was launched as next step

- Designed to evaluate and validate RuSH methods
- Conducted from 2012–2014

Disseminate findings from RuSH
- Families, healthcare providers, policymakers

Sites included California, Georgia and Mississippi
Moving Forward: Sickle Cell Data Collection (SCDC) Program

- Collect, synthesize and disseminate multi-source, population-based, longitudinal data for people with sickle cell disease (SCD)
  1. Establish a health profile of the SCD population
  2. Track changes in SCD outcomes over time
  3. Ensure credible, scientifically sound information to inform standards of care
  4. Inform policy and health care practices

- Improve quality of life, life expectancy, and health among those living with SCD

www.cdc.gov/ncbddd/hemoglobinopathies/scdc.html
SCDC Data Will Include Up to 10% of the U.S. SCD Population

- Newborn Screening Data 2004–2014
- Hospital Discharge Data 2004–2014
- Medicaid Claims Data 2004–2014
- Emergency Department Data 2004–2014
- Clinic Case Reports
- INDEX
- Case File
SCDC Next Steps

- **Disseminate findings**
  - Peer-reviewed publications, scientific presentations, social media, policy briefs

- **Include additional states**
  - Establish training institute to help other states develop population-based surveillance system for sickle cell disease

- **Secure additional sustained support and funding**
Thank You to SCDC Partners, Families, and Participants
The Sickle Cell Community and Pediatric Care for SCD

Kim Smith-Whitley, MD

Chief Medical Officer (Immediate Past)
Sickle Cell Disease Association of America, Inc.
Historical Perspective

- Sickle cell disease is an inherited hemoglobinopathy
- Characterized by hemolysis, vascular occlusion
- Unpredictable clinical complications such as acute pain, life-threatening infection, stroke and acute chest syndrome (i.e., pneumonia-like illness)
- In 1971, Sickle Cell Disease Association of America formed
- In 1972, the National Sickle Cell Anemia Control Act passed
Dramatic Improvement for Children Given Oral Penicillin Prophylaxis to Prevent Pneumococcal Infection

Cumulative Infection Rates for All Patients in the Prophylactic Penicillin Study

Study recommended penicillin prophylaxis start at age 4 months

Infection prophylaxis meant infants with SCD needed to be identified early

Newborn screening
- Universal screening recommended by NIH in 1987
- State-by-state adoption of screening
- By 2006, all states screening at birth

Specialized vaccine programs
- Pneumococcal vaccines developed
Who Is At Risk for Stroke?

Transcranial Doppler Ultrasonography (TCD) in 3 Siblings with SCD-SS

RMCA: Right middle cerebral artery
LMCA: Left middle cerebral artery

Transfusion Therapy for Primary Stroke Prevention in SCD STOP Trial

- **Background**
  - Chronic red blood cell transfusions reduce recurrent stroke rate in children with SCD
  - Transcranial Doppler ultrasonography (TCD) detects children at risk for stroke

- **Hypothesis:** Could children who have increased risk of stroke be helped by transfusions before a stroke occurs?

Transfusion Therapy Reduces Risk of Primary and Secondary Stroke in Sickle Cell Disease

- 92% reduction in stroke risk, (P < 0.001)
- Chronic transfusion therapy greatly reduces the risk of first stroke in children with SCD-SS who have repeatedly abnormal transcranial Doppler ultrasonography results

Painful crises occurred later in patients receiving hydroxyurea than in those receiving placebo, and the effect was evident in less than six months.
**Hydroxyurea Works for SCD-SS**

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<th>Adverse Event</th>
<th>Hydroxyurea</th>
<th>Placebo</th>
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<td>Sepsis</td>
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Hydroxyurea is not FDA approved for use in children.
Hydroxyurea Works for SCD-SS

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Kaplan–Meier Estimates of Survival and Event-free Survival after Bone Marrow Transplantation in 22 Patients with Sickle Cell Disease

As of 2016, over 1,000 individuals have received transplants.
Approach to Pediatric Treatment

- Prevent complications before they occur
  - Penicillin prophylaxis
  - Transcranial Doppler

- Prevent recurrence of complication
  - Hydroxyurea therapy
  - Chronic transfusion therapy
  - Bone marrow transplantation
Sickle Cell Disease: Milestones

- SCDAA established: 1971
- Sickle Cell Prevention Act: 1972
- NIH Newborn Screening Conference: 1987
- NIH Newborn Screening Conference: 1986
- TCD and High Risk Stroke: 1992
- Hydroxyurea Therapy: 1995
- Bone Marrow Transplantation: 1996
- Stroke Prevention and Transfusion Therapy: 1998
- Sickle Cell Disease Treatment Act: 2003
Sickle Cell Disease Association of America: Common Agenda and Goals

- Increased access to high-quality health care across the lifespan
- Drug development, therapies and programs
  - Improve quality of life
  - Decrease disease-related complications
- Research towards a cure accessible for all people with sickle cell disease
SCDAA’s Get Connected
Sickle Cell Disease Registry Initiative

- Establish a network to distribute information related to clinical care, research, health services, health policy, and advocacy
  - Children, adults, and families living with sickle cell disease and sickle cell trait
  - SCDAA member organizations, and other community-based organizations
  - Health care providers and other stakeholders

- Establish a mechanism to support care coordination

- Develop online communities for information sharing and psychosocial support
Get Connected: Activities and Early Results

- Identify, educate, and train community health workers
  - 35 community health workers trained
- Connect children and adults to services if not connected
- Enroll children and adults with sickle cell disease in Get Connected
  - 3,152 children and adults enrolled in 15 states

Funding Opportunity Announcement: HRSA-11-031
www.scdfc.org/what-is-get-connected.html
Sickle Cell Disease: Challenges and Opportunities

➢ Advances in pediatrics, but few across the lifespan
  ● Lack of data decreases ability to identify health care and policies to best support those with sickle cell disease

➢ Get Connected and Sickle Cell Data Collection project will identify, inform, and fill gaps

➢ Limited access to healthcare professionals with expertise in sickle cell disease
  ● Not just for children but for transition and adult care
  ● High mortality rate in young adult group
Working towards healthier lives for children and adults with sickle cell

SCDAA SCDNBS Program CBOs

National Institute for Healthcare Quality
  Dr. Suzette Oyeku
  Dr. Scott Berns

HRSA
  Dr. Donnell Ivy
  Andrea Williams

American College of Medical Genetics
  Dr. Amy Brower

National SCDAA HRSA Project
  Sonja L Banks
  Sonya Ross
  Meghan Ringgold
  Leroy Hughes, Jr.
Improving Outcomes for Adults with Sickle Cell Disease

Kathryn Hassell, MD
Professor of Medicine, Division of Hematology
University of Colorado Denver
Important Aspects of Adult Sickle Cell Disease

- Premature death and mortality
- Burden of chronic organ damage
- Health care access and utilization
Premature Death in Sickle Cell Disease

Age at Death of People with Sickle Cell Disease, By Type, Compared to People Without Sickle Cell Disease

- HbSS
- HbSC
- No sickle cell disease

Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Blood. 2010 Apr

Wierenga KJ, Hambleton IR, Lewis NA. Lancet. 2001 Mar
Surveillance Identifies Previously Missed Individuals

Number of Deaths of People with Sickle Cell Disease from Three Data Sources, Georgia and California, 2004–2008

Mean age at death: 42.2 years

NCHS: National Center for Health Statistics
MCOD: Multiple causes of death

Surveillance Can Assess Impact of Childhood Interventions

Limitations of the Sickle Cell Data Collection (SCDC) System

- Whole population data can provide important information, but results must be interpreted with caution.
- SCDC does not distinguish type of sickle cell disease for each person:
  - Type of hemoglobin can affect course of sickle cell disease
- Significant differences in premature death related to type of sickle cell disease:
  - Overestimates lifespan in more severe types
  - Underestimates lifespan in milder types
Limitations of the Sickle Cell Data Collection (SCDC) System

- Not all interventions are applied to all forms of sickle cell disease
  - Hydroxyurea is of proven benefit in HbSS and HbSβ⁰thalassemia
  - 40% of people have other types of sickle cell disease and thus would not be given this intervention

- May miss important gains in care and outcomes made within a given subset
Adult SCD: Chronic Organ Damage

- **Autopsy Study (1929–1996)**
  - Evidence of chronic organ injury in 74% of 306 cases
  - Chronic organ damage second most common cause of death after infection, in >18 year-olds
- **Cohort Study, N=1,056 patients with 40-year follow-up**
  - 73% with chronic organ damage

<table>
<thead>
<tr>
<th>Evidence of Injury at Autopsy</th>
<th>Chronic lung disease</th>
<th>56%</th>
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<tbody>
<tr>
<td>Chronic renal failure/atrophy</td>
<td>38%</td>
<td></td>
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<tr>
<td>Stroke</td>
<td>18%</td>
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</table>

<table>
<thead>
<tr>
<th>Secondary Organ Damage</th>
<th>Liver failure/hepatitis</th>
<th>10%</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cardiomegaly</td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td>Congestive Heart Failure</td>
<td>10%</td>
</tr>
</tbody>
</table>
Chronic Organ Damage Likely Now Leading Cause of Death

- CDC multiple causes death certificate data, 1999–2009
- Only 20% died during acute crisis
- Common premorbid conditions are often seen in sickle cell disease (SCD)
  - Congestive heart failure
  - Hypertension
  - Pneumonia/Acute chest syndrome

Adapted from Hamideh D and Alvarez O. Pediatr Blood Cancer. 2013 Sep;60(9):1482-6
Population Surveillance Reveals Course of Disease


Increase in complications occurs at 15–16 years of age

Any complication

Pain

Pulmonary

Age, in years

Mean Number of Days with ≥1 Diagnosis Per Patient Per Quarter

Mean Number of Transfusion Events and Prescriptions Per Patient Per Quarter
Population Surveillance Reveals Use of Interventions

Decrease in use of interventions occurs at 15–16 years of age

- Transfusion
- Hydroxyurea

Increased Use of the Emergency Department Begins in Adolescence

EDR: Emergency department reliance = total emergency department visits/total ambulatory [outpatient + ED] visits
Sickle Cell Data Collection (SCDC): Clarifying the Course of Disease

- **Longitudinal tracking**
  - Onset and progression of complications
  - Use and impact of complication-specific and overall disease-modifying therapy

- **Limitation**: SCDC does not distinguish type of sickle cell disease
  - Rate and severity of complications varies between types of sickle cell disease
  - Some disease-modifying therapies (e.g., hydroxyurea) are used only for some types of sickle cell disease (HbSS and HbSβthalassemia)
Adult Healthcare Access and Utilization

- Oft-stated assumption is that all children with sickle cell disease receive comprehensive sickle cell care from sickle cell providers
  - Maryland Medicaid data: 38% of children had not seen a hematologist by age 2
- Adult health care is often characterized as nonexistent, inaccessible, or rendered by providers without knowledge or interest
  - Mostly based on anecdote, not data
  - Increase in complications, ED utilization, mortality in early adulthood said to be evidence for this, but data suggest change actually occurs in adolescence
Quality Adult Sickle Cell Health Care Exists

5-Canada
1-India
1-Tobago (Caribbean)
1-Brazil
1-Puerto Rico

Find a Hematologist
www.scapn.net and www.hematology.org
Insurance Is Not the Same as Access

- Few adults with sickle cell disease are truly uninsured (<5%), but:
  - May not cover necessary services
  - Limited or no access to expert providers
  - High-deductible plans may preclude use

- Intermittent loss of coverage
  - Loss of employment – lose employer-based plans
  - Gain of employment – no longer eligible for Medicaid, Medicare, or disability coverage

hcupnet.ahrq.gov/HCUPnet.jsp, National Inpatient Sample report, run 21 May 2016
Role of Self-Determination

- **Evaluation in adult sickle cell program, 1993–2009**
  - 22 patients with history of overt stroke on chronic transfusion
  - Mean age at transition (transfer): 22 years old
  - Mortality: 36% (8/22) within 5 years
    - All who died actively refused transfusion or stopped coming
Opportunities and Limitations of Sickle Cell Data Collection

- Identify sites of care and use during the critical period of adolescence and young adulthood
  - Observe disease course while still in pediatric care, without change in provider
- However, lack of use may not mean lack of access
  - Data regarding referrals, arranged transfers and scheduled appointments that were not kept are not captured
Important Aspects of the Sickle Cell Data Collection Program

- Population-level data regarding
  - Premature death
  - Disease course
  - Impact of interventions
  - Healthcare utilization

- Identify providers and sites of care

- Data can be used to develop strategies to prevent and reduce the burden of sickle cell disease and its complications
Jean L. Raphael, MD, MPH

Associate Professor of Pediatrics
Baylor College of Medicine

Director, Center for Child Health Policy and Advocacy
Texas Children’s Hospital
Objectives

- Describe current guiding principles in health care policy
- Identify policy challenges in sickle cell disease
- Outline a policy agenda for sickle cell disease
## Triple Aim for Population Health

1. **Reduce costs**
   - Eliminate overuse or misuse of diagnostic tests or therapies

2. **Improve population health**
   - Identify systematic variations in care or outcomes
   - Apply knowledge to develop policies for improvement

3. **Enhance patient experience**
   - Actively survey patient experience
   - Involve patients and families in system redesign

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*Berwick DM, Nolan TW, Whittington J. *Health Affairs*. 2008 May-June;27(3):759-769*
Road Map of High-Quality Care Leads to Improved Outcomes

Basic Biomedical Science  T1  Clinical Efficacy Knowledge  T2  Clinical Effectiveness Knowledge  T3

Key T1 Activity: Test what care works
1. Clinical Efficacy Research

Key T2 Activity: Test who benefits from promising care
1. Outcomes Research
2. Comparative Effectiveness Research
3. Health Services Research

Key T3 Activity: Test how to deliver high-quality care reliably and in all settings
1. Measurement and accountability of health care quality and cost
2. Implementation of interventions and health care system design
3. Scaling and spread of effective interventions
4. Research in above domains

Improved health care quality, and value, and population health

Healthy People 2020

- Hemoglobinopathies were previously well represented
- Focus on treatment
  - Screening for complications, and disease-modifying therapies
- Focus on access to medical home, community resources, and educational support

These objectives were retired because existing data systems could not assess them!

Advances in Care Are Opportunities to Improve Outcomes

- **Advances in care**
  - Hydroxyurea
  - TCD screening for stroke risk
  - Chronic transfusions

- **Extended life expectancy**
  - In 1973, life expectancy was 14 years
  - In 2008, life expectancy was 42 years

TCD: Transcranial Doppler ultrasonography
Challenges Remain to Improve Outcomes

- Persistently high resource use
  - Especially for acute care
- High risk of mortality at early adulthood
  - Transition to adult care
- Poorly studied population
- Poor funding and organizing relative to other conditions
Challenges for Further Research in SCD

- Lack of data sources with adequate numbers of people with SCD or sufficient clinical detail
- Limited evidence base for management guidelines
- Limited number of dedicated clinical providers

Agenda for Sickle Cell Disease: Research and Policy

- Population health and big data
- Comparative effectiveness research of treatments
- Technology-based interventions
  - Outreach through technology that patients are already using (e.g., health apps)
- Development of new funding strategies
Agenda for Sickle Cell Disease: Healthcare Delivery

- Building medical neighborhoods
  - Primary care providers and specialists collaborate to manage patients

- Supporting adult providers with expertise (e.g., ECHO Model)

- Modifying existing reimbursement models
  - Reimbursement for care coordination

- Addressing social determinants of health

ECHO: Extension for Community Healthcare Outcomes, echo.unm.edu
What Do We Need Now?

- Health care policy strategies are needed to fully realize benefits of basic and clinical science advancements for sickle cell disease (SCD).

- Strategies must align with current priorities in reforming health care system.

- Policy solutions in SCD should be patient-centered, provider-centered, and health system-oriented.
Improving the Lives of People with Sickle Cell Disease

- **Continue progress in advancing care**
  - Translating research into treatment and practice

- **Use data to identify gaps in care**
  - Variability in disease course and management
  - Availability, use, and access to care
  - Transitions from pediatric to adult care, and for adult care

- **Need more support to meet healthcare needs**
  - Connect people to care
  - Understand better which care is best for each individual
  - Better systems to provide patient-centered care
CDC PUBLIC HEALTH GRAND ROUNDS

Improving the Lives of People with Sickle Cell Disease

November 15, 2016