A Comprehensive Hemoglobinopathy Surveillance System as Statewide Long-term Follow-up across Life Span
Michigan Experience

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Outline

- Why focusing on Hemoglobinopathy/Sickle Cell Disease?
- Why using Surveillance?
- How we plan to improving the NBS program follow up through the use of surveillance?
Outline

- Why focusing on Hemoglobinopathy/Sickle Cell Disease?
Sickle Cell Disease

- Sickle-cell disease (SCD), or sickle-cell anaemia (or anemia; SCA) or drepanocytosis, is an \textit{autosomal} recessive genetic \textit{blood disorder} characterized by \textit{red blood cells} of abnormal, rigid, \textit{sickle} shape.

- Sickling decreases the cells' flexibility and results in a risk of various complications that lead to a short life expectancy.

- SCA is the specific form of sickle cell disease in which there is homozygosity for the mutation that causes HbS.
  - Referred to as "HbSS", "SS disease", "hemoglobin S" or permutations thereof.

- The prevalence of the disease in the United States is approximately 1 in 5,000, mostly affecting Americans of Sub-Saharan African descent.

- In the United States, about 1 in 500 births in Black women have sickle cell anemia.

* National Institute of Health
More about Sickle Cell Disease

- Other, rarer forms of sickle-cell disease that are compound heterozygous states include:
  - sickle-hemoglobin C disease (HbSC),
  - sickle beta-plus-Thalassemia (HbS/β+) and
  - sickle beta-zero-Thalassemia (HbS/β0)

- Sickle Cell Traits – Heterozygotes: Only one sickle gene and one normal adult hemoglobin gene
  - Referred to as "HbAS" or "sickle cell trait"
Sickle Cell Disease Complications

- Sickle-cell disease may lead to various acute and chronic complications, several of which being potentially lethal
- “Sickle cell crisis”: several independent acute conditions occurring in patients with sickle cell disease such as vaso-occlusive crisis, aplastic crisis, sequestration crisis, haemolytic crisis and others. Most episodes of sickle cell crises last between five and seven days.
- Complications:
  - Post-splenectomy infection, Decreased immune reactions due to splenectomy, Stroke, Cholelithiasis, Avascular necrosis, Osteomyelitis,
  - Acute papillary necrosis in the kidneys, Chronic renal failure and Sickle cell nephropathy,
  - Leg ulcer, Retinopathy, proliferative retinopathy, retinal detachments, blindness,
  - Pregnancy related: IUGR, spontaneous abortion, pre-eclampsia,
  - Chronic pain: Even in the absence of acute vaso-occlusive pain, many patients have chronic pain that is not reported
  - Pulmonary hypertension and risk of heart failure; typical symptoms are shortness of breath, decreased exercise tolerance and episodes of syncope
Pain—most severe and chronic complication of SCD

- Pain in adults with sickle cell disease is the rule rather than the exception
- It is mostly managed at home; therefore, its prevalence is probably underestimated by health care providers, resulting in misclassification
- More than two inpatient admissions per year is unusual, and most have no hospital or ED visits in a given year
- However, people with SCD are overrepresented among high utilizers of emergency departments and inpatient beds, even when compared to other serious hemoglobinopathies
- There is a small proportion of SCD patients who account for most health care utilization
- High utilization of resources may not be a stable pattern
- Determining the course of high utilization in sickle cell patients is a vital first step to either prevent or moderate it in favor of a more consistent – and probably more cost-effective – treatment strategy.

C. Patrick Carroll, M.D.,1 Carlton Haywood, Ph.D.,2,3 Peter Fagan, Ph.D.,1,4 and Sophie Lanzkron, M.D.2 The Course and Correlates of High Hospital Utilization in Sickle Cell Disease: Evidence from a large, urban Medicaid Managed Care Organization; Am J Hematol. 2009 October; 84(10): 666–670.
“Sickle cell disease-related pediatric medical expenditures in the U.S”


- MarketScan Medicaid and Commercial Claims databases for 2005 used to estimate total medical expenditures of children with and without SCD.
- Expenditures attributable to SCD were calculated as the difference in age-adjusted mean expenditures during 2005 for children with SCD relative to children without SCD in the two databases.
- Expenditures of children with SCD were found to be 6 and 11 times higher than of children without SCD enrolled in Medicaid and private insurance, respectively:
  - Children with SCD incurred medical expenditures that were $9,369 and $13,469 higher than those of children without SCD enrolled in Medicaid and private insurance
- SCD-attributable medical expenditures in children were conservatively and approximately estimated at $335 million in 2005.
Newborn Screening for Hemoglobinopathy/Sickle Cell Disease

- Initiated in Michigan in 1987
  - Four hemoglobinopathies:
    - Sickle cell anemia (Hb SS)
    - Hb S/Beta-thalassemia (Hb S/Beta-Th)
    - Hb S/C Disease (Hb S/C)
    - Variant hemoglobinopathies

- SCD one of the four most prevalent conditions identified by NBS
# Disorders Identified via Newborn Screening, Michigan Residents, 1965-2009

<table>
<thead>
<tr>
<th>Type of Disorder Classification (Year Screening Began)</th>
<th>Cases in 2009 (N)</th>
<th>Cases Through 2009 (N)</th>
<th>Cumulative Detection Rate*</th>
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<tbody>
<tr>
<td>Galactosemia (1985)</td>
<td>22</td>
<td>159</td>
<td>1:21,118</td>
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<tr>
<td>Biotinidase Deficiencies (1987)</td>
<td>15</td>
<td>183</td>
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<td>Amino Acid Disorders (1965)</td>
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<td>Organic Acid Disorders (2005)</td>
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<td>Fatty Acid Oxidation Disorders (2003)</td>
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<td>90</td>
<td>1:9,716</td>
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<td>Congenital Hypothyroidism (1977)</td>
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<td>1,619</td>
<td>1:1,911</td>
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<tr>
<td>Congenital Adrenal Hyperplasia (1993)</td>
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<td>1:19,989</td>
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<td>Hemoglobinopathies (1987)</td>
<td>57</td>
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<td>1:2,057</td>
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<td>Cystic Fibrosis (October 2007)</td>
<td>33</td>
<td>79</td>
<td>1:3,363</td>
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<tr>
<td>Total</td>
<td>234</td>
<td>4,411</td>
<td>-</td>
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</table>
NBS Follow Up Program

Follow-up of positive, unsatisfactory and early specimens

Education – Primarily Hospital staff, Pediatrician and Family Practice Physicians

Monitoring Hospitals and Midwives

Assuring and Monitoring Medical Management contracts with University of Michigan, Children’s Hospital of Michigan and Sickle Cell Association of Michigan

Medical Home in collaboration with other programs

Other New Initiatives: Hospital Coordinators Network, Parents Network
Collaboration: Sickle Cell Disease Association of America (SCDAA), Michigan Chapter

- Coordinating center - located in Detroit and directed by Dr. Wanda Whitten-Shurney
  - Offices for social workers (patient advocates) in Grand Rapids, Benton Harbor, Kalamazoo, Lansing, and Saginaw.

- Primary responsibilities are to assure that:
  1. all newborns referred with positive sickle cell screening results are appropriately diagnosed,
  2. penicillin prophylaxis is initiated,
  3. sickle cell counseling and social work services are available, and
  4. each newborn has a medical home

- Focus on short term follow up and children
- Increasing needs for expanding the short term follow up to other hemoglobinopathies and for developing long term follow up strategies
Partnership and collaboration with hematologists

Michigan Hemoglobinopathy Advisory Committee
Outline

- Why focusing on Hemoglobinopathy/Sickle Cell Disease?
- Why using Surveillance?
Surveillance

- In recent years, surveillance constitutes a critical part of public health practice.

- The Centers for Disease Control and Prevention (CDC) officially describes public health surveillance as:
  “the ongoing and systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice” (Thacker, Berkelman 1988).

- By definition, surveillance systems include:
  - capacity for data collection and analysis,
  - timely dissemination of information
  - effective prevention and control interventions related to specific health outcomes
Goals of surveillance

1. To recognize cases or cluster of cases to trigger interventions to prevent transmission or to reduce morbidity and mortality
2. To assess the public health impact of a health event or determinant and measure trends
3. To demonstrate the need for public health intervention programs and resources, and allocate resources
4. To monitor effectiveness of prevention and control measures and intervention strategies
5. To identify high-risk population groups or geographic areas to target interventions and guide analytic studies, and
6. To develop hypotheses leading to analytic studies about risk factors for disease causation, propagation, or progression

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Michigan Hemoglobinopathy Surveillance and Quality Improvement Program (MiHemSQIP)

- National name of the project: Registry and Surveillance System in Hemoglobinopathies (RuSH)

- MiHemSQIP=MI RuSH

- Funded by NHLBI/NIH through a cooperative agreement with CDC

- Seven states funded to implement a surveillance process for hemoglobinopathies (sickle cell and thalassemia)
MiHemSQIP Goals

**Goal 1:** Develop cross sectional and longitudinal data collection methods

**Goal 2.** Develop a model comprehensive surveillance system

**Goal 3.** Utilize the surveillance system to inform public health planning, services implementation, evaluation and policy development related to hemoglobinopathies across the life span
How do we define “life span”?  

Two-dimensional concept that involves recognizing that health and well-being along with other exposures and risks occur over a continuum from conception to death (horizontal dimension) but have also an impact on offspring (vertical dimension)  

- **Horizontal dimension:**  
  - (1) longitudinal follow-up of the same cohort diagnosed at birth by newborn screening, which can be very challenging and requires resources and time; and  
  - (2) cross-sectional long term follow-up in order to assess and monitor sickle cell disease prevalence, mortality, co-morbidities, service utilization and costs at different stages across the lifespan, which entails the cross-sectional use of data from multiple sources.  

- **Vertical dimension:** applies to those of reproductive age and reflects the impact of disease on offspring.  

What do we need for implementation?

- Identify a process and develop a plan:
  - Surveillance process and plan

- Identify the existing data sources that could be useful:
  - Multiple data sources for different issues and age groups,
  - Standard schedule for existing linkages and plan for new ones as needed

- Develop new data collection tools if need be:
  - Sickle cell module in MCIR;
  - New question in BRFSS for estimating the prevalence

- Find partners and engage them:
  - Michigan Hemoglobinopathy Advisory Group
  - CBOs
  - Other programs and surveillance processes

- Evaluate the plan to identify gaps and improve:
  - CDC guidelines for surveillance evaluation
Multiple data sources - Data linkages

Newborn Screening

MCIR → Live birth records → PRAMS

Birth Defects → Hospital discharge → Medicaid → Infant Death linked files → WIC

Data in Blue boxes are all linked through the use of Live births as intermediate files
MiHemSQIP New data collection tools

- New question in BRFSS* for cross sectional prevalence estimate

- Sickle cell module in MCIR: longitudinal data collection for NBS cohort plus/minus cases identified in providers’ offices
  - Patient level data
  - Annual health status assessment

* Behavioral Risk Factor Surveillance System
Michigan Care Improvement Registry (MCIR)

- Web-based system established in 1998 to track immunizations
- Expanded in 2006 to include adults
- Healthcare providers are required to report childhood immunizations to MCIR within 72 hours of administration
- New “Follow-up” tab
  - Hemoglobinopathies
  - Early Hearing Detection and Intervention
  - Perinatal HIV
- [http://www.mcir.org](http://www.mcir.org)
Results - snapshot

- Percent of children age 19-35 month with SCD who completed DTaP + IP+ MMR vaccinations: 72% (MICR)

- Percent of children age 19-35 month with SCD who completed Haemophilus Influenzae Type b (Hib) Vaccine: 68% (MICR)

- Percent of children age 3-6 years with SCD who completed pneumococcal (PCV) vaccination: 66% (MCIR)

- Percent of mothers with SCD babies also enrolled in Medicaid: 68% (Medicaid)

- 4,570 hospital stays occurred where sickle cell disease was recorded as a diagnosis (2007 hospital discharge)

- Sickle cell disease or trait found as primary or contributing cause of death for 21 individuals (1 - 89 years old) (2007 death certificates)
New emerging topics

- Immunization in children with SCD and SCT
  - Poster at the National MCH Epi Conference and National Immunization Conference
  - Another study in progress
- Birth defects in SCD
  - Validation study in progress
  - Preliminary findings presented at the MCH Epi National Conference
- ED visits - collaboration with Medicaid, CON and MHA
- Maternal Mortality in women with SCD and SCT – chart review of maternal deaths in progress
- Sudden cardiac deaths of the young and SCD and/or SCT: adopt and expand the process of MI SDCY
Conclusion and implications for public health practice

- Surveillance may be used as NBS long term follow up strategy

- A surveillance system across the lifespan can:
  1. further public health knowledge and
  2. inform policy makers by consolidating the use of multiple data sources and record linkage with epidemiological skills and strong partnership with a statewide network of providers.
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“The future belongs to those who believe in the beauty of their dreams.”

Eleanor Roosevelt
Thank you!

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