Sickle Cell Disease: The Challenge of Healthcare Disparity

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Global Blood Therapeutics, Inc.
SICKLE CELL DISEASE (SCD): DISABLING INHERITED BLOOD DISORDER

• SCD is an uncommon (or orphan) disease in the U.S., affecting approximately 100,000 people.
• It disproportionately impacts African American and Hispanic Americans, occurring in 1 out of every 365 African American births and 1 out of every 16,300 Hispanic American births.
• Every system in the body is impacted due to a lack of oxygen.
• Symptoms vary from childhood (e.g., stroke, acute chest syndrome) to adulthood (e.g., osteonecrosis of bone).
• Clinical manifestations get worse over time in terms of the severity of particular episodes (e.g., pain) and the presence or absence of a particular problem (e.g., leg ulcers).


Sickle cell disease decreases median lifespan by decades

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James Herrick and Ernest E. Irons at Cook County Hospital in Chicago first described sickle cell disease in a student from Grenada, Walter Clement Noël. He had an anemia marked by red cells that looked like “crescents or sickles”. Noël returned to Grenada after training in dentistry.

Harvey Itano and Linus Pauling used the newly invented technique of protein electrophoresis to demonstrate that sickle hemoglobin (HbS) differed from normal hemoglobin (HbA).

Vernon Ingram at MRC in London used protein sequencing to demonstrate that HbS derived from a glutamic acid to valine amino acid change at position β-6. The recently elucidated genetic code allowed deduction of the nucleotide change (GAG → GTG).

*First demonstration of disease due to an abnormal protein

*First demonstration of disease due to a specific DNA mutation

90% of Children reach 18 years of age

Median life expectancy:
Males- 42 years
Females- 48 years

CLINICAL CARE CONTINUES TO LAG SCIENCE
CONCENTRATED POPULATION, MOSTLY INSURED BY MEDICAID & MEDICARE

Geographical Distribution

SCD is fairly concentrated in the US.
+ 80% of the population resides in 17 states
+ Most of the rural population lives in the south

Age Distribution

Older Adults
>30, 40%

Transitioning Adults
18 to 30, 27%

Pediatric Patients
<18, 33%

~100K Americans are living with SCD
+ ~90% of SCD are African American
+ ~10% are Hispanic American

Payer Mix

Medicaid: ~50% of the population
These individuals tend to be younger due to Medicaid eligibility criteria

Medicare: ~15% of the population

Commercial: ~30% of the population

Uninsured: <10% of the population
More likely to be adult patients
Most of the southern states did not participate in Medicaid expansion

A significant share of Medicare are dual eligible

Sources: Piel et al NEJM 2017. November 2017 Analysis of Administrative Claims Data For 72,573 patients sourced from Symphony Healthcare Solutions. On File at GBT

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# CURRENT THERAPIES FOR SCD ARE SUBOPTIMAL…

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Use</th>
<th>Duration</th>
<th>Consensus Recommendation</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin V</td>
<td>• Prevention of Infections</td>
<td>Daily until at least 5 years of age</td>
<td>• Strong</td>
<td>• Moderate</td>
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<tr>
<td>Pneumococcal vaccination</td>
<td>• Prevention of Infections</td>
<td>Every 5 years for life</td>
<td>• Strong</td>
<td>• Moderate</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Acute Blood Transfusion</td>
<td>• Treatment of Anemia</td>
<td>Limited</td>
<td>• Strong</td>
<td>• Low</td>
</tr>
<tr>
<td></td>
<td>• Pre-operative transfusion</td>
<td></td>
<td>• Strong</td>
<td>• Moderate</td>
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</tr>
<tr>
<td>Analgesics (Opioid and Nonopioid)</td>
<td>• Treatment of Acute Pain</td>
<td>Limited</td>
<td>• Strong</td>
<td>• High</td>
</tr>
<tr>
<td></td>
<td>• Treatment of Chronic Pain</td>
<td></td>
<td>• Moderate</td>
<td>• Low</td>
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<tr>
<td>Chronic Blood Transfusion</td>
<td>• Primary Stroke Prevention</td>
<td>Every 3-6 weeks indefinitely</td>
<td>• Strong</td>
<td>• High</td>
</tr>
<tr>
<td></td>
<td>• Secondary Stroke Prevention</td>
<td></td>
<td>• Moderate</td>
<td>• Low</td>
</tr>
<tr>
<td></td>
<td>• Prevention of additional Silent Cerebral Infarctions</td>
<td></td>
<td>• Moderate</td>
<td>• Moderate</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxyurea</td>
<td>• Universal Use</td>
<td>Daily indefinitely</td>
<td>• Moderate</td>
<td>• Moderate</td>
</tr>
<tr>
<td></td>
<td>• Prevention of Acute Complications</td>
<td></td>
<td>• Strong</td>
<td>• High</td>
</tr>
<tr>
<td></td>
<td>• Primary Stroke Prevention</td>
<td></td>
<td>• Strong</td>
<td>• Moderate</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endari</td>
<td>• Prevention of Acute Complications</td>
<td>Daily indefinitely</td>
<td>• Not yet assessed</td>
<td>• Not yet assessed</td>
</tr>
</tbody>
</table>

Sources:

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... LEADING TO SIGNIFICANT NUMBERS OF EMERGENCY DEPARTMENT VISITS...

**Average Number of Emergency Department Visits Per Year**

- In 2014, SCD was responsible for ~250,000 Emergency Department U.S. visits.
- About 20% of sickle cell disease patients receive most of their care in the emergency department setting.

Sources:
1. Dampier et al. Access To Care For Medicaid And Commercially-Insured United States Patients With Sickle Cell Disease. GBT Sponsored ASH 2017 poster
3. November 2017 Analysis of Administrative Claims. Data For 63,256 patients sourced from Symphony Healthcare Solutions
... AND INPATIENT HOSPITAL STAYS, PARTICULARLY FOR ADULTS LIVING WITH SCD

Average Number of Inpatient Stays Per Year

- In 2014, SCD was responsible for ~90,000 Inpatient stays in the United States
- Average length of stay was 4-7 days

Sources:
1. Dampier et al. Access To Care For Medicaid And Commercially-Insured United States Patients With Sickle Cell Disease. GBT Sponsored ASH 2017 poster
SCD DRIVES HIGHEST ALL-CAUSE 30-DAY READMISSION RATES

Table 2. All-cause 30-day readmissions ranked by conditions with the highest readmission rates,*
U.S. hospitals, 2010

<table>
<thead>
<tr>
<th>Rank</th>
<th>Principal diagnosis for index hospital stay **</th>
<th>Number of index stays</th>
<th>30-day all-cause readmissions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Number of readmissions</td>
</tr>
<tr>
<td>1</td>
<td>Sickle cell anemia</td>
<td>87,326</td>
<td>27,837</td>
</tr>
<tr>
<td>2</td>
<td>Gangrene</td>
<td>33,786</td>
<td>10,693</td>
</tr>
<tr>
<td>3</td>
<td>Hepatitis</td>
<td>37,480</td>
<td>11,593</td>
</tr>
<tr>
<td>4</td>
<td>Disease of white blood cells</td>
<td>54,861</td>
<td>16,771</td>
</tr>
<tr>
<td>5</td>
<td>Chronic renal failure</td>
<td>17,394</td>
<td>4,766</td>
</tr>
<tr>
<td>6</td>
<td>Systemic lupus erythematosus and connective tissue disorders</td>
<td>18,950</td>
<td>5,123</td>
</tr>
<tr>
<td>7</td>
<td>Mycoses</td>
<td>23,026</td>
<td>6,222</td>
</tr>
<tr>
<td>8</td>
<td>HIV infection</td>
<td>34,958</td>
<td>9,230</td>
</tr>
<tr>
<td>9</td>
<td>Screening and history of mental health and substance abuse</td>
<td>60,417</td>
<td>15,695</td>
</tr>
<tr>
<td>10</td>
<td>Peritonitis and intestinal abscess</td>
<td>25,219</td>
<td>6,315</td>
</tr>
</tbody>
</table>

- Studies in the US indicate that about a third of patients are rehospitalized within 30 days of initial discharge due to SCD-related complications. 2,3

Sources:
1. Elixhauser A and Steiner C, HCUP Strategical Briefs, 201
SCD RESULTS IN ~$10 MM IN LIFETIME HEALTHCARE EXPENSES & LOST PRODUCTIVITY PER INDIVIDUAL

- **Average annual fee** for the care of an adult with SCD (SS genotype) is $231,000*

- **Lifetime healthcare fees** are ~$9 MILLION per individual*

Sources:
1. Ballas, American Jour of Hematology, 2009. Assumptions based on HbSS patients
2. SCD Societal Cost Model In Development by GBT for Journal Submission. All SCD Patients

* in 2009 dollars, cost does not include future inflation rates; fee is defined as the price charged by providers; cost is usually about 60-65% of fee

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Expected Lifetime Income Per Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCD (all genotypes)</td>
<td>$1.2M</td>
</tr>
<tr>
<td>Non-SCD (Matched Controls)</td>
<td>$1.9M</td>
</tr>
<tr>
<td>General US Population</td>
<td>$2.1M</td>
</tr>
</tbody>
</table>

SCD significantly also limits quality adjusted life expectancy & **costs the US economy over $800M in lifetime productivity**

This estimate does not include lost educational potential, caregiver productivity or patient time spent in the hospital.
CURRENT ECONOMICS ARE CHALLENGING FOR SCD CLINICS TO PROVIDE INTEGRATED CARE

Medicaid payments can be significantly lower than other payers…

Charges vs Payment Analysis for Routine Outpatient Visit (Established Adult Patient)

Benioff Children’s Hospital Oakland (BCHO)

- Charge: $148
- Commercial: $92
- Medicare: $89
- Medicaid: $28

62% (payment to charges ratio)

Commonly Needed Resources for SCD Quality Care Delivery

- SCD specialist (e.g. Hematologist)
- Nurse Practitioners / Physician Assistants
- Primary Care Physician
- Community Health Workers (CHW)
- Nurse Educators
- Social Workers
- Patient Navigators
- Mental Health Professional

Source: BCHO 2017 Practice Analysis for CPT Code 99214 - 25 minute office visit (most commonly billed code)

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LESS THAN 10% OF CMS PATIENTS SEE A SPECIALIST ANNUALLY

Proportion of SCD Population with at Least 1 Hematologist* Visit Per Year

Source: Dampier et al. Access To Care For Medicaid And Commercially-Insured United States Patients With Sickle Cell Disease; ASH 2017
* Includes Board certified Hematologist or Oncologist.

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Medical Care Experience Among Children with SCD

Elements of a Patient-centered Medical Home (PCMH)

Regular Provider
Comprehensive
Family-centered
Coordinated

% of Patients

Raphael- Pediatr Blood Cancer. 2013 60: 275
KEY TAKEAWAYS

• Sickle cell disease is an uncommon debilitating illness affecting primarily African Americans and Hispanic Americans

• Patients lack access to quality chronic care which increases expensive hospital and ED usage and driving up costs to our healthcare system and to our society

• Current treatment options are sub-optimal and therefore limited in use

• Integrated, comprehensive care program with effective and preventative interventions are essential to reverse healthcare disparity in sickle cell disease