Sickle Cell Disease:

Across the Lifespan

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American Academy of Physician Assistants
Annual Conference, 2020

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Sickle Cell Disease: Across the Lifespan

Financial Relationships

BioMarin – honoraria for non-branded speaking engagements on gene therapy

Off-Label/Investigational Uses

None

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Sickle Cell Disease: Across the Lifespan

Learning Objectives

1. Identify key improvements in the management of sickle cell disease for children
2. Express the challenges encountered in care of adult patients with sickle cell disease
3. Distinguish the unique features of pregnancy in women with sickle cell disease
4. Discuss the impact of appropriate medical management on health and quality of life in patients with sickle cell disease
5. Describe the current state of medical management of sickle cell disease
6. Describe future therapies that may impact the care of sickle cell disease

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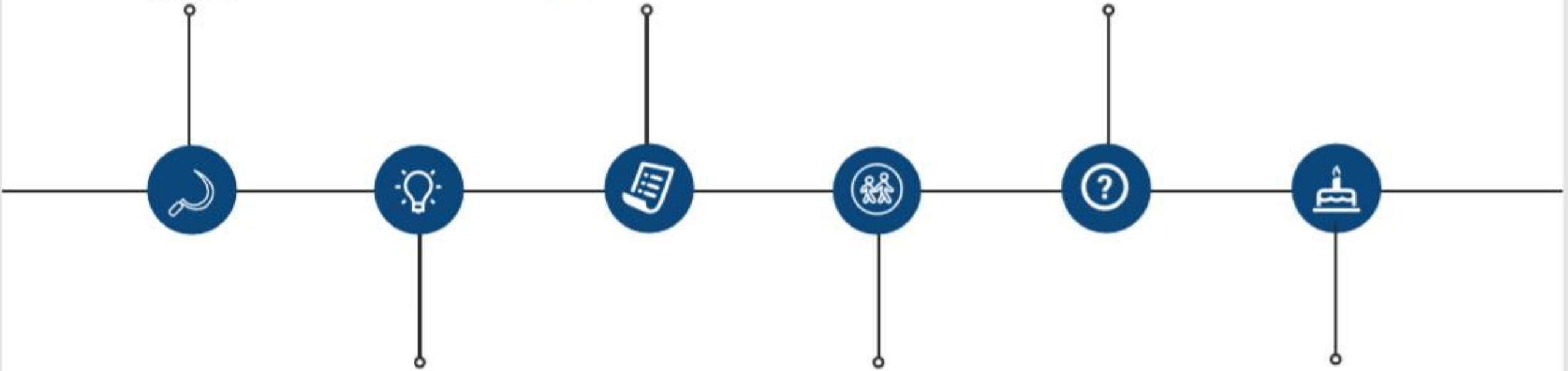
An Historical Perspective



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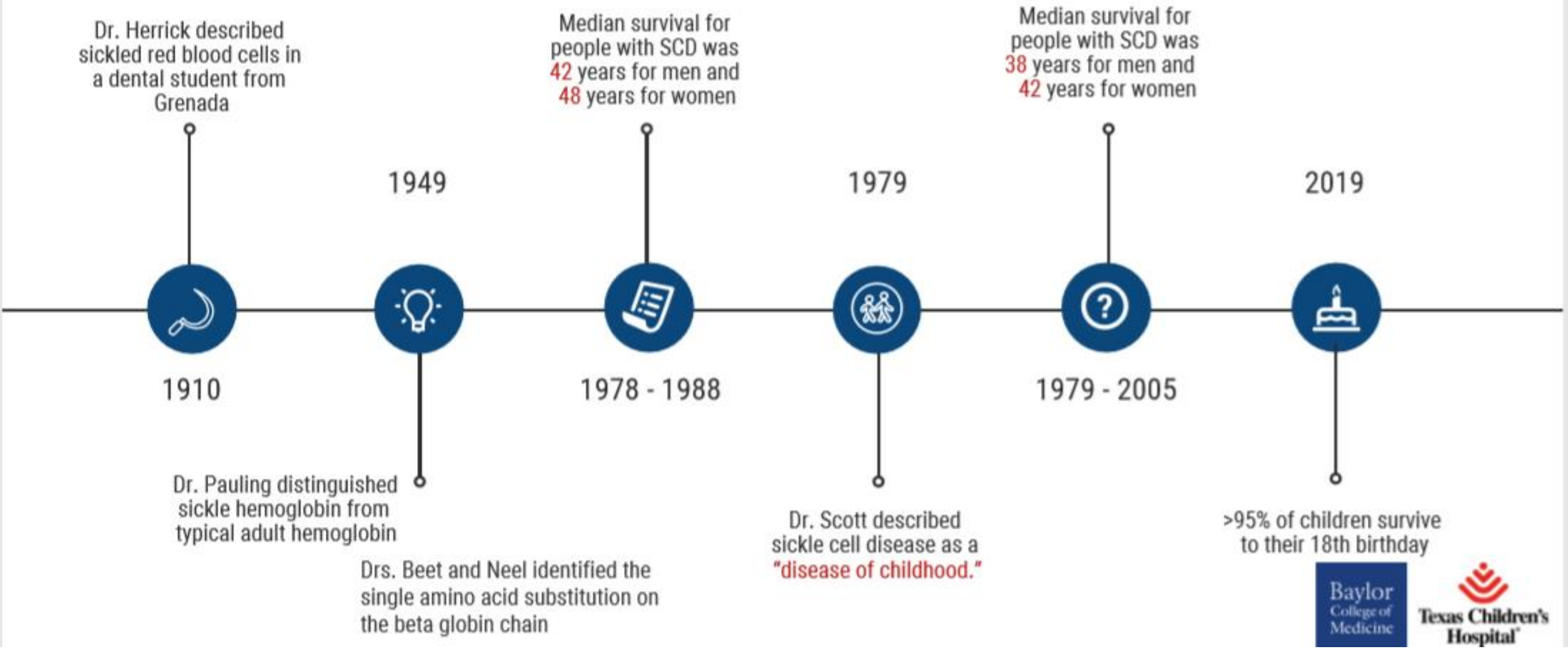
An Historical Perspective



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What changed for children?

1975-1985: Newborns screening positive for sickle cell disease were incorporated into a comprehensive sickle cell center

PARENTS WERE TAUGHT:

- Fever management
- Spleen palpation
- When to seek medical attention

OVERALL MORTALITY DROPPED FROM 8% TO 1.8%

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Contributions to child health

PROPS Trial (1988)

Penicillin prophylaxis is effective in preventing pneumococcal sepsis

Vaccines against encapsulated bacteria

STOP Trial (1998)

Transcranial doppler ultrasound screening for stroke and chronic transfusions to prevent primary stroke

BABY HUG Trial (2011)

Hydroxyurea safe and effective in children

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Let's all think back...
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Living to Adulthood

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Sickle Cell Trait and Disease: The Numbers

Babies with SCD born in the US each year

1:12

Black Americans have S trait

1:150

Hispanic Americans have S trait

Babies born each year with sickle cell disease globally

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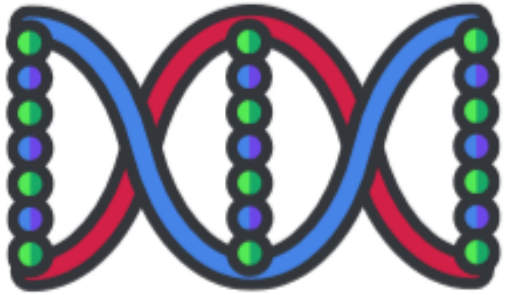
Genetics of SCD

Chromosome 11



Valine → Glutamine

Autosomal Recessive

Must have two abnormal copies to result in disease

Genotypes

AA: "Normal" hemoglobin

AS: Sickle cell trait

SS: Sickle cell disease

Other beta globin traits:

C trait (AC)

β^0 trait ($A\beta^0$)

β^+ trait ($A\beta^+$)

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Genetics of Sickle Cell

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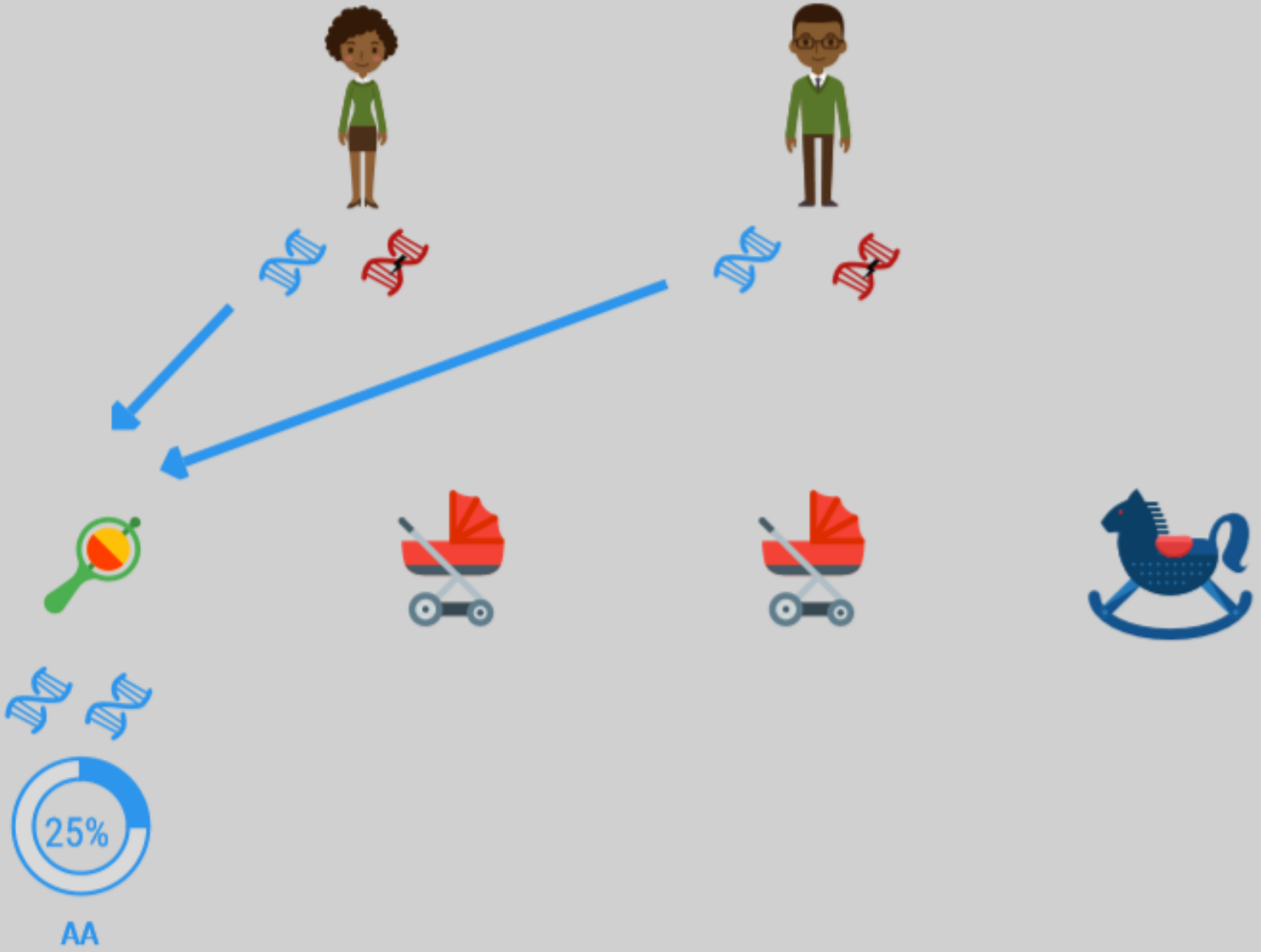

Genetics of Sickle Cell

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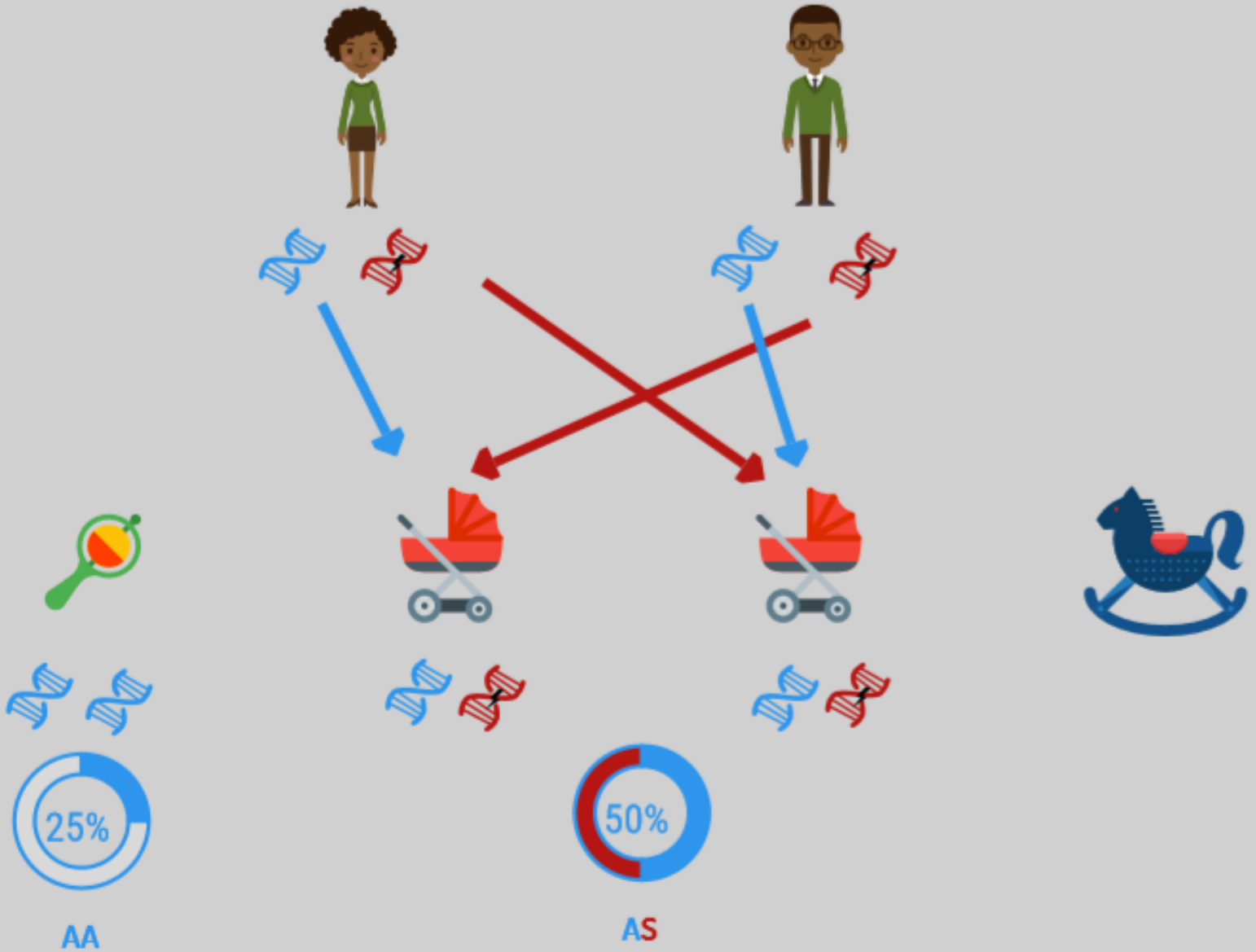

Genetics of Sickle Cell

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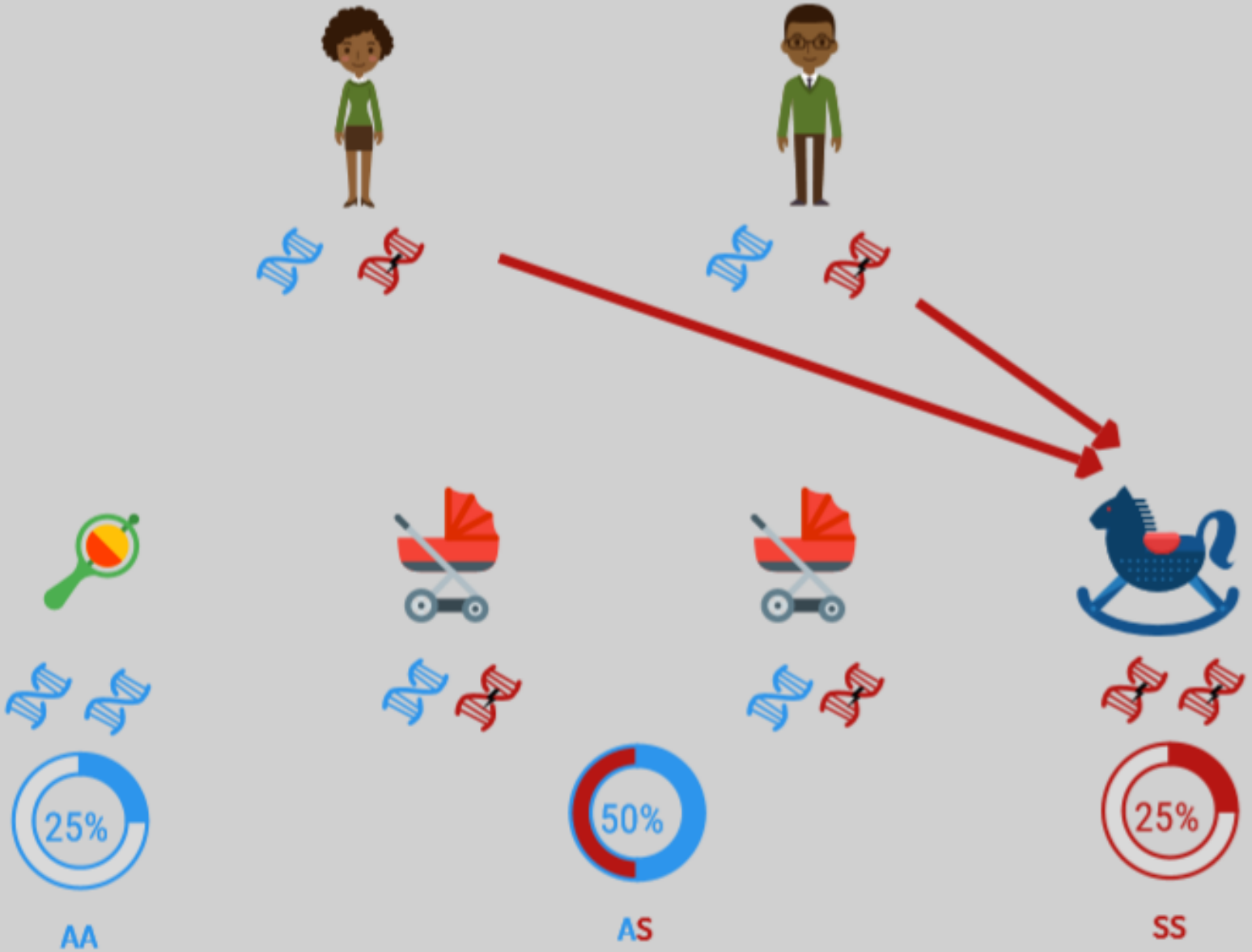

Genetics of Sickle Cell

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My partner has sickle cell trait. Is it possible for us to have a baby with sickle cell disease?

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Testing for sickle cell disease

Newborn Screen

Pros: early detection, most beta traits and disease states detected

Cons: misses beta thal traits

Hemoglobin Profile

Pros: most hemoglobin traits and disease states detected

Cons: should be run >6 months of age; inaccurate after transfusion

Genetic Testing

Pros: able to give exact variant for complex cases

Cons: expensive, results take weeks-months

Sickle Dex

Pros: I'm not sure

Cons: does not differentiate between S trait and disease, only detects S

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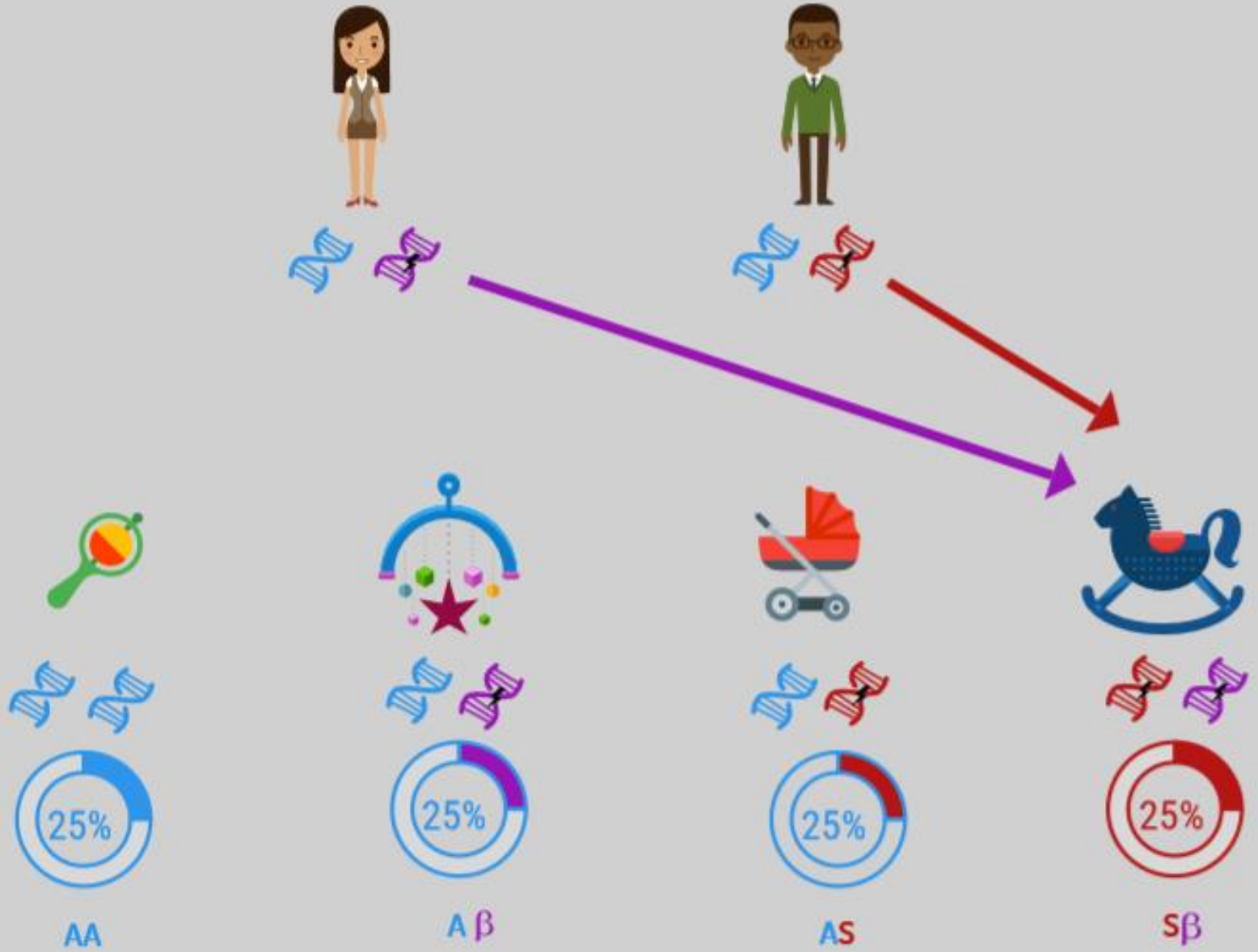

Genetics of Sickle Cell

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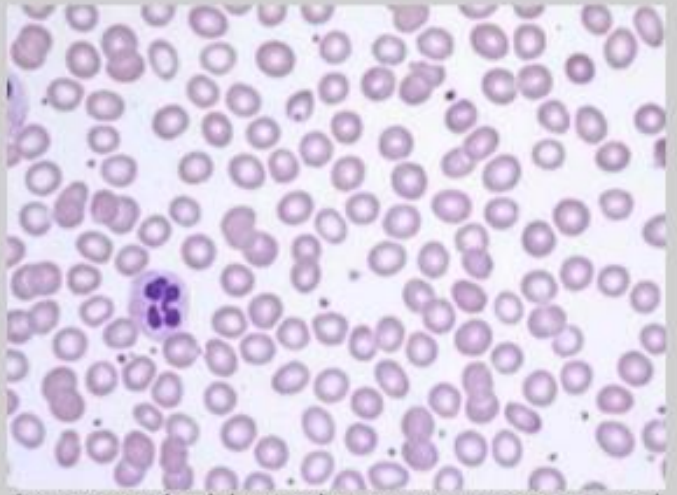
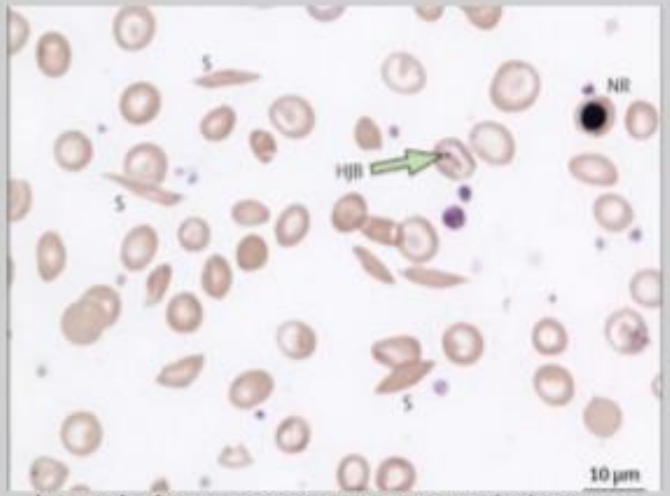
Peripheral Blood Smears



http://imagebank.hematology.org/image/3666/normal-peripheral-blood-smear--1?type=upload

Normal



http://dx.doi.org/10.1016/S0140-6736(10)61029-X

Hemoglobin SS

Source: Lichtman MA, Shafer MS, Felgar RE, Wang N: Lichtman's Atlas of Hematology: http://www.accessmedicine.com

Hemoglobin SC

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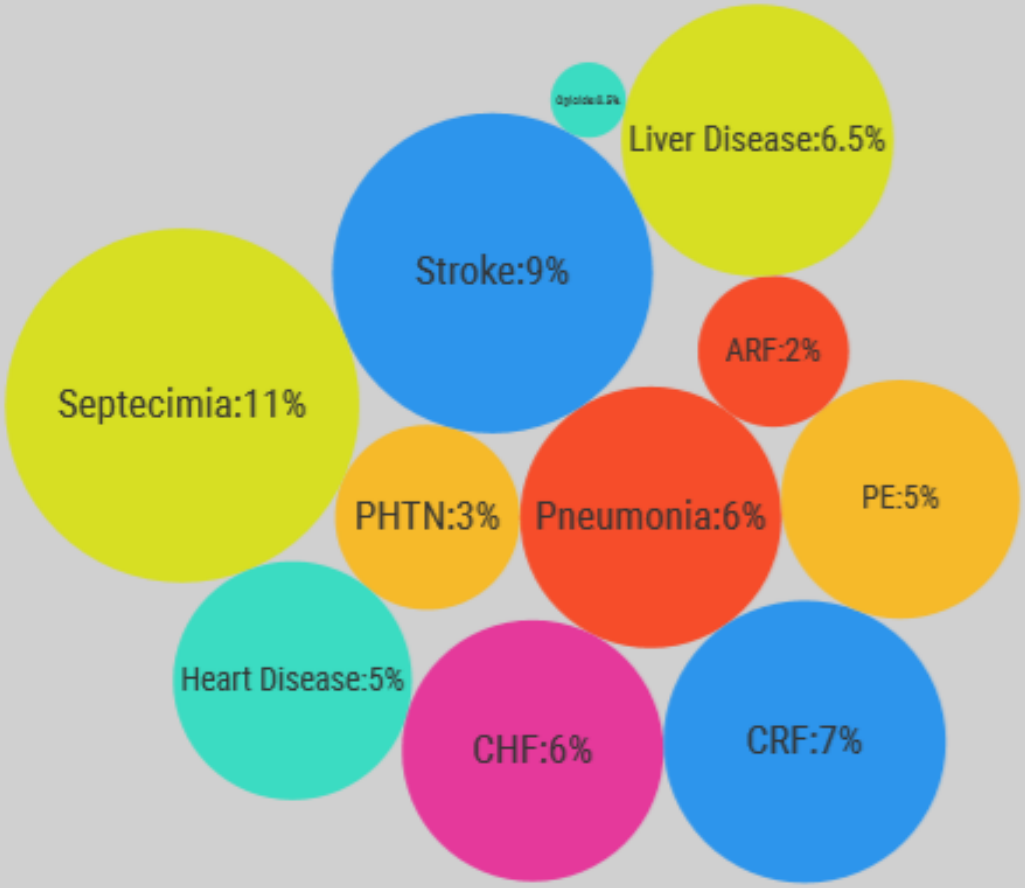
Morbidities in Adulthood

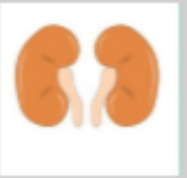
Age 25:
second stroke peak

Acute Chest
Pulmonary Hypertension

Functional
Hyposplenia



Left Ventricle
Dysfunction



Renal Failure
Decreased Epo

Organ Ischemia

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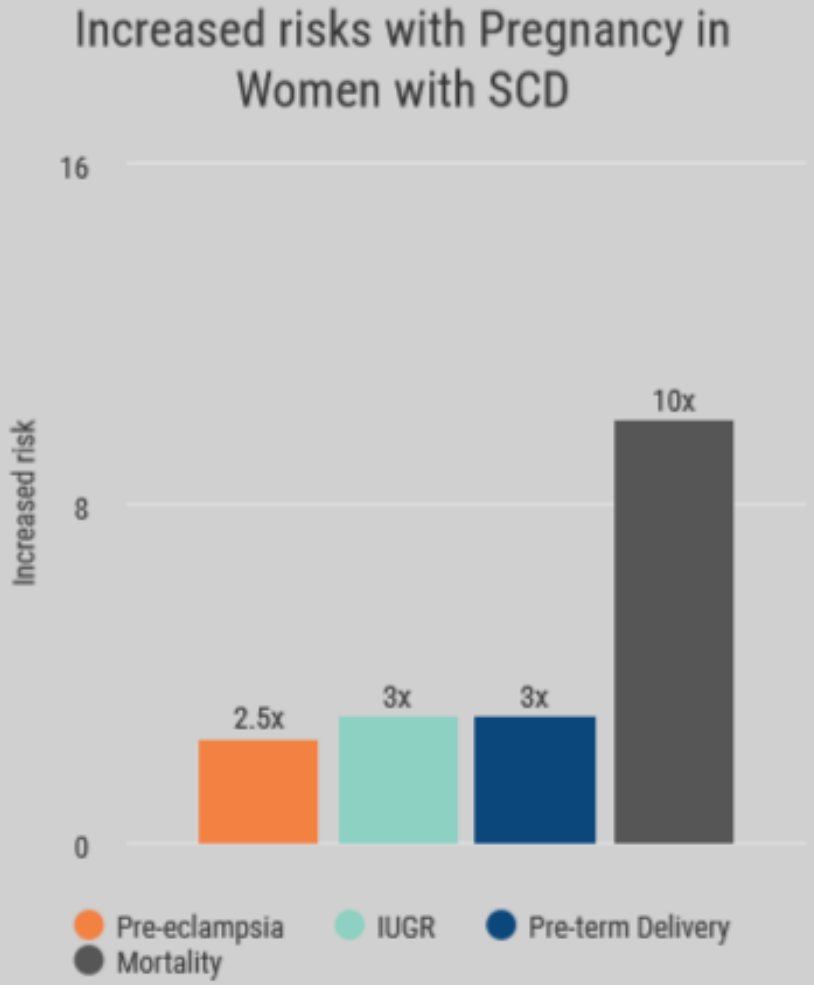
Reproductive Health

1. Limited contraceptive options
2. Safety of medications during pregnancy largely unknown
3. Role of transfusions during pregnancy is unclear



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Oteng-Ntim E. Pregnancy in women with sickle cell disease is associated with risk of maternal and perinatal mortality and severe morbidity. Evid Based Nurs. 2017

Neonates

4x risk of stillbirth

Neonatal alloimmunization due to maternal RBC antibodies

Male Health

Hypogonadism due to testicular infarcts

Erectile dysfunction due to priapism

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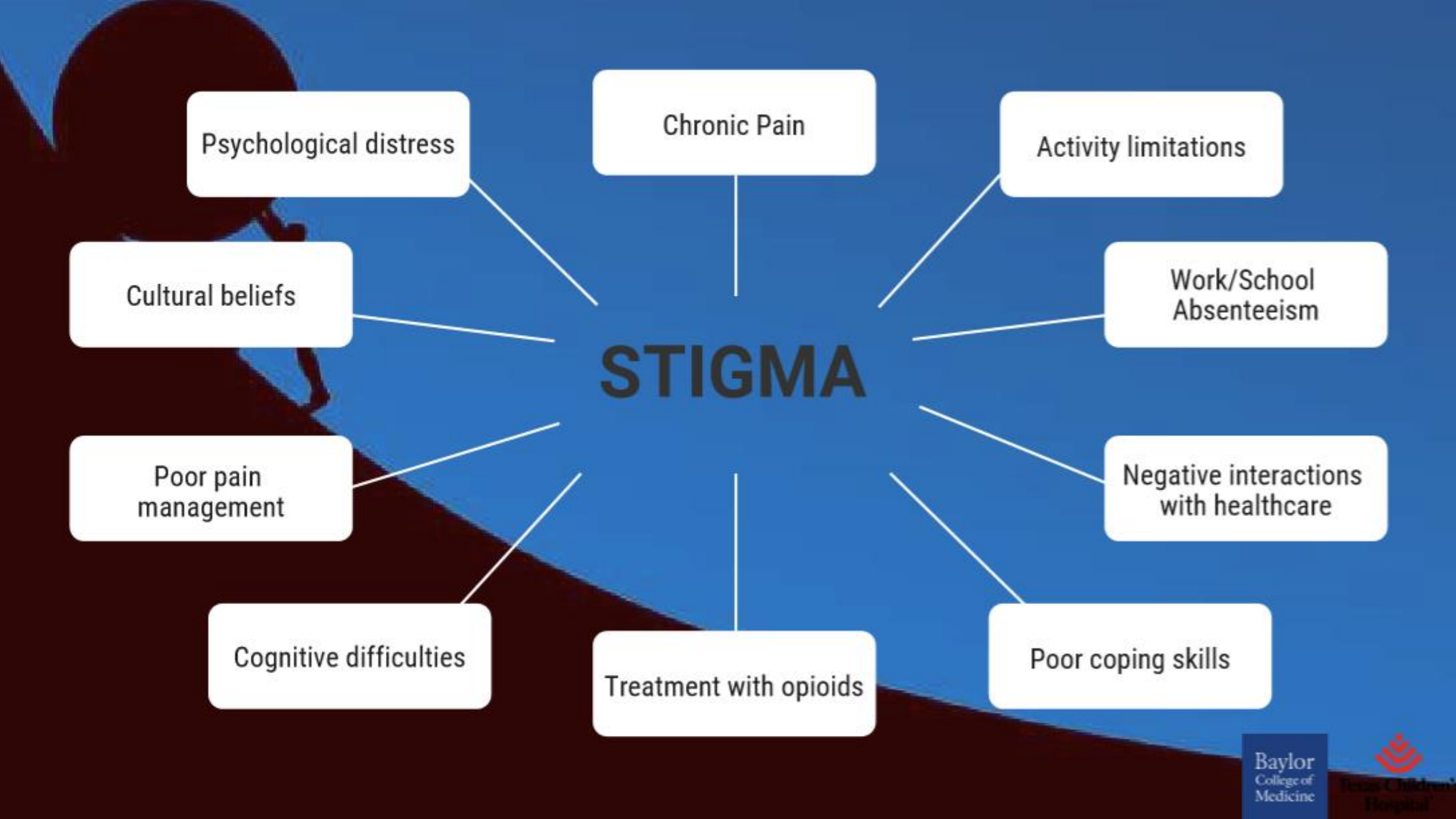
Chronic Pain
Psychological distress
Activity limitations
Cultural beliefs
Work/School Absenteeism
STIGMA
Poor pain management
Negative interactions with healthcare
Cognitive difficulties
Treatment with opioids
Poor coping skills
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How do you know if someone is in pain?

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How do you know if someone is in pain?

Gross visualization

Laboratory or imaging

Verbalization

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What is chronic pain?

"...pain standing in my way of doing something I want to do."

"I would love to be working, driving a car...have what regular folks have...a family, get married."

"A daily thing...it's a constant battle everyday."

"I'm still fighting depression all the time."

"I changed doctors...with the hopes of finding someone who would listen to my symptoms and do more than just throw pain medicine at me.

"Self-management of chronic pain is a priority, a full-time job, a full-time child, a full-time life."

Porter, JS, et al. Pediatric transition to adult care: Perspecitves of young adults with sickle cell disease. Journal of Pediatric Psychology. 2017.

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Managing Chronic Pain

Individual Factors

Knowing personal triggers
Sites of previous pain events

Pharmacotherapy

Opioids may not be part of a chronic pain treatment plan

Psychology

Recognizing and treating underlying depression or anxiety

Utilizing Healthcare

Positive interactions with primary and emergency providers

Lifestyle

Maintaining productive and active lifestyle

Connections

Talking with others who manage their chronic pain

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Addressing the Stigma

1. Healthcare provider perceptions and treatment influence outcomes in SCD

2. Education is the key

   As little as 90 minutes of education for pediatric residents improved empathy for SCD

3. Opioids and addiction

   1998-2013

   Non-SCD: Mortality rates due to opioids increased by 350%

   SCD: No increase in mortality due to opioids

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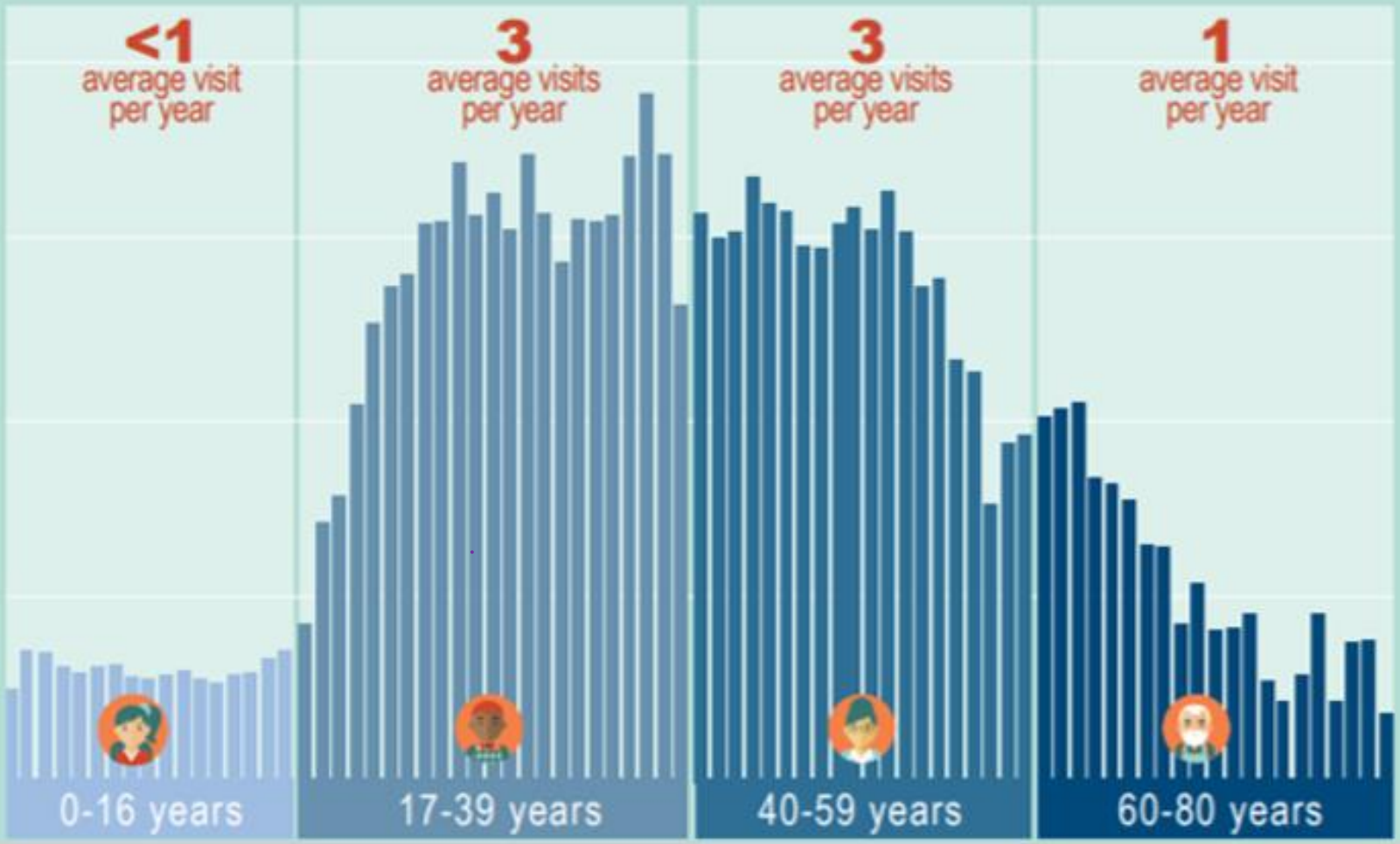
Emergency Department (ED) Visits Among People with Sickle Cell in California, 2005-2014



cdc.gov/ncbddd/sicklecell/documents/Sickle_Cell_Providers.pdf

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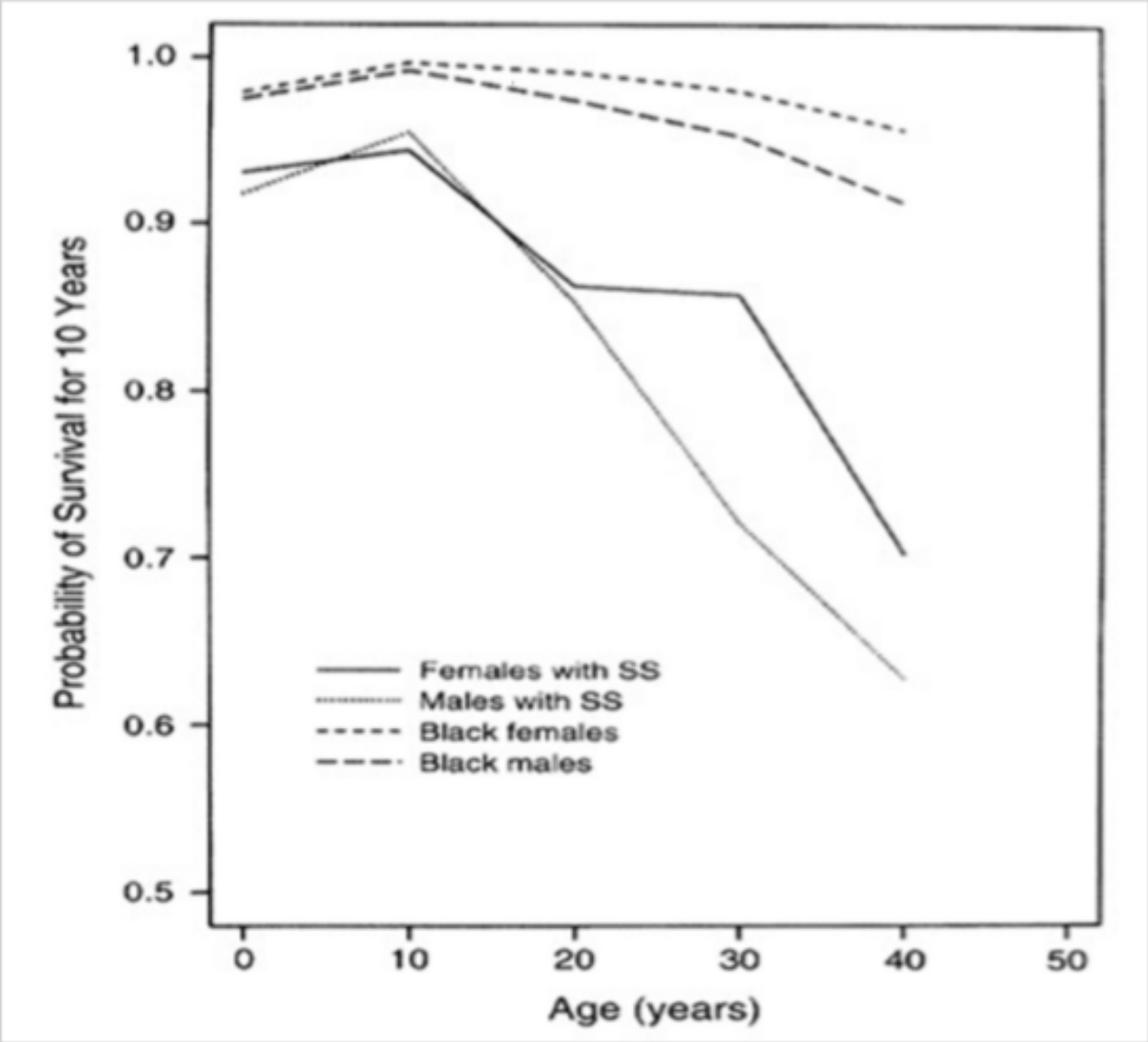
The Adolescent and Young Adult



Platt OS, et al. Mortality in sickle cell disease. N Engl J Med. 1994

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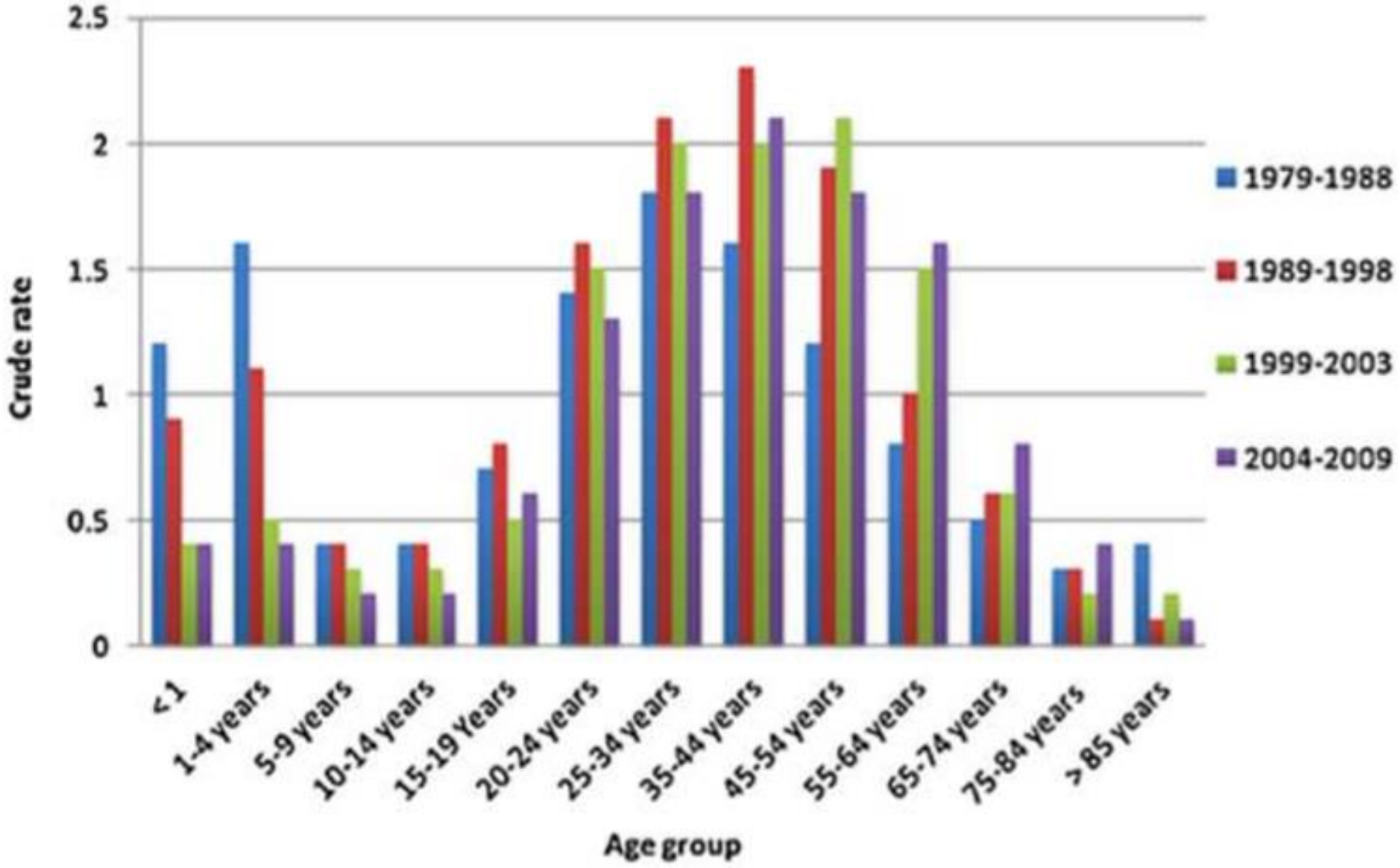
SCD Related Mortality in the US (1999-2009)



Pediatric Blood & Cancer, Volume: 60, Issue: 9, Pages: 1482-1486, First published: 23 April2013, DOI: (10.1002/pbc.24557)

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Comprehensive Care Model

NIH recommends: 1 physician, >1 APP, a health educator, and a medical social worker at a facility with lab/radiology services and a 24-hour blood bank

1. Create an indivualized "Pain Plan" for every patient
2. Increase communication between primary and specialty providers
3. Create multi-disciplinary teams in EDs to treat pain

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A national poll in 2016 found that ____% of primary care providers were comfortable in treating sickle cell disease?

A. 5%
B. 20%
C. 40%
D. 60%
E. 80%

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A national poll in 2016 found that ____% of primary care providers were comfortable in treating sickle cell disease?

A. 5%
B. 20%
C. 40%
D. 60%
E. 80%

20%

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Treatments for SCD

Hydroxyurea (Hydrea®)

Pros:	Cons:
-minimal side effects -once daily oral -preventative -cheap -long-term use studied	-requires lab monitoring -variable response

FDA approved: ≥ 18 years in 1998
≥ 2 years in 2017

Voxelotor (Oxbryta™)

Pros:	Cons:
-once daily oral -no lab monitoring -long-term use being monitored	-expensive -moderate side effects

FDA approved: ≥ 12 years in 2019

Crizanlizumab (Adakveo®)

Pros:	Cons:
-quick infusion -once monthly dosing -well-tolerated -long-term use being monitored	-requires monthly infusion visits -expensive

FDA approved: ≥ 16 years in 2019

Others

L-glutamine (Endari®): FDA approved ≥5 years in 2017
Rivipansel (GMI-1070): failed to meet primary endpoint in Phase 3

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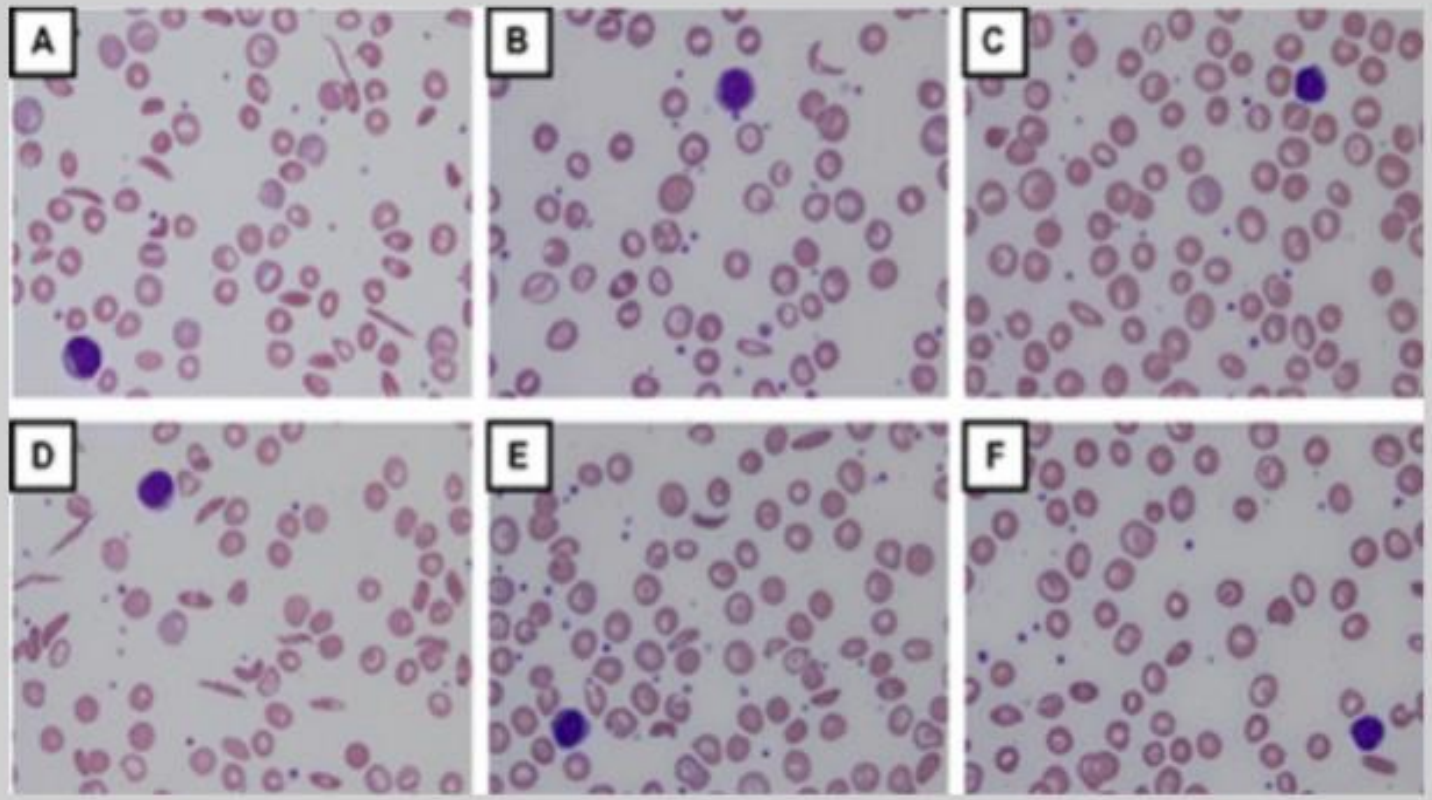
Effects of Hydroxyurea



http://www.bloodjournal.org/content/115/26/5300?sso-checked=true

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Future Directions

1. Improving therapies for prevention and treatment of complications
2. Tackling the global burden of sickle cell
3. Improving outcomes of stem cell transplant
4. Perfecting gene therapy

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Your role in treating sickle cell disease

Educate yourself and others on the impact that appropriate medical management can have on patients' quality of life and health status.

Identify other providers in your community who are interested in sickle cell disease and keep lines of communication open.

Research current and updated options for treatment of sickle cell disease.

Educate your patients on their disease, their pain management strategies, their goals for care

Advocate for the patient with sickle cell disease.

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Resources

American Society of Hematology Guidelines (2019):
https://www.hematology.org/Clinicians/Guidelines-Quality/Guidelines.aspx#scd

National Heart, Lung and Blood Institute Guidelines (2014):
https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/evidence-based-management-sickle-cell-disease-expert-0

Center for Disease Control Fact Sheet for Emergency Room:
https://www.cdc.gov/ncbddd/sicklecell/documents/Sickle_Cell_Providers.pdf

Nursing implications for Sickle Cell Disease:
https://www.cdc.gov/ncbddd/sicklecell/documents/Sickle_Cell_Providers.pdf

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References

Chaturvedi S, DeBaun MR. Evolution of sickle cell disease form a life-threatening disease of children to a chronic disease of adults: The last 40 years. Am J Hematol. 2016;91:5-14.

Davis H, Schoendorf KC, Gergen PJ, Moore RM. National trends in the mortality of children with sickle cell disease, 1968 through 1992. Am J Public Health. 1997;87:1317-1322.

Yanni E, Crosse SD, Yang Q, Olney RS. Trends in pediatric sickle cell disease-related mortality in the United States, 1983-2002. J Ped. 2009;154(4):541-545.

McLaughlin JF, Ballas SK. High mortality among children with sickle cell anemia and overt stroke who discontinue blood transfusion after transition to an adult program. Transfusion. 2016;56:1014-1021.

Serjeant, GR. The natural history of sickle cell disease. Cold Spring Harb Perspect Med. 2013;3:a011783.

Platt OS, Brambilla DJ, et al. Mortality in sickle cell disease. N Engl J Med. 1994;330:1639-44.

Rizk S, Pulte ED, Axelrod D, Ballas SK. Perinatal maternal mortality in sickle cell anemia: two case reports and review of the literature. Hemoglobin. 2017; 41:4-6, 225-229.

Vichinsky E, Hurst D, Earles A, et al. Newborn screening for sickle cell disease: Effect on mortality. Pediatrics. 1988;81:749-755.

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References

Porter JS, Wesley KM, et al. Pediatric to adult care transition: Perspectives of young adults with sickle cell disease. Journal of Pediatric Psychology. 2017;42(9):1016-1027.

Cappelli B, Volt F, et al. Risk factors and outcomes according to age at transplantation with an HLA-identical sibling for sickle cell disease. Haematologica. 2019;e104-xxx.

Calhoun CL, Abel RA, Pham HA, Thompson S, King AA. Implementation of an education intervention to optimize self-management and transition readiness in young adults with sickle cell disease. Pediatr Blood Cancer. 2019;66:e27722.

Lanzkron S, Carroll CP, Haywood C. Mortality rates and age at death from sickle cell disease: U.S., 1979-2005. Public Health Reports. 2013;128:110-116.

Oteng-Ntim E. Pregnancy in women with sickle cell disease is associated with risk of maternal and perinatal mortality and severe morbidity. Evid Based Nurs. 2017;20(2):43.

Liu L, Ozo S, Hogan D, et al. Global, regional and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385:430-439.

Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle cell anaemia: A multicentre, randomized, controlled trial. Lancet. 2011;377:1663-1672.

Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. N Engl J Med. 1998; 339:5-11.

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Thank You

Thank you for your attention and staying until the end.
Please stay safe and healthy.

Please feel free to email me for any questions at sekirk@bcm.edu.

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