

Sickle Cell Disease Partnership

GENERAL EDUCATION DECK

Q3 2023



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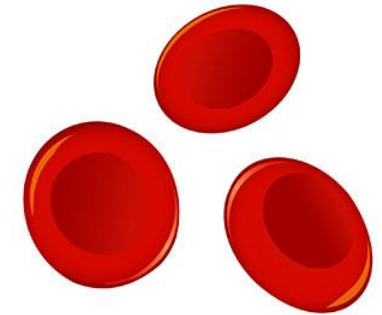
Understanding Sickle Cell Disease



What is sickle cell disease?

Sickle cell disease (SCD) is a group of inherited red blood cell disorders.

- **Healthy cells.** Red blood cells contain hemoglobin, a protein that carries oxygen. Healthy red blood cells are round, and they move through small blood vessels to carry oxygen to all parts of the body.
- **SCD cells.** In someone who has SCD, the hemoglobin is abnormal, which causes the red blood cells to become hard and sticky and look like a C-shaped farm tool called a “sickle.”
- **Problems with SCD cells.** The sickle cells die early, which causes a constant shortage of red blood cells. Also, when they travel through small blood vessels, they get stuck and clog the blood flow. This can cause pain and other serious complications (health problems) such as infection, acute chest syndrome and stroke.



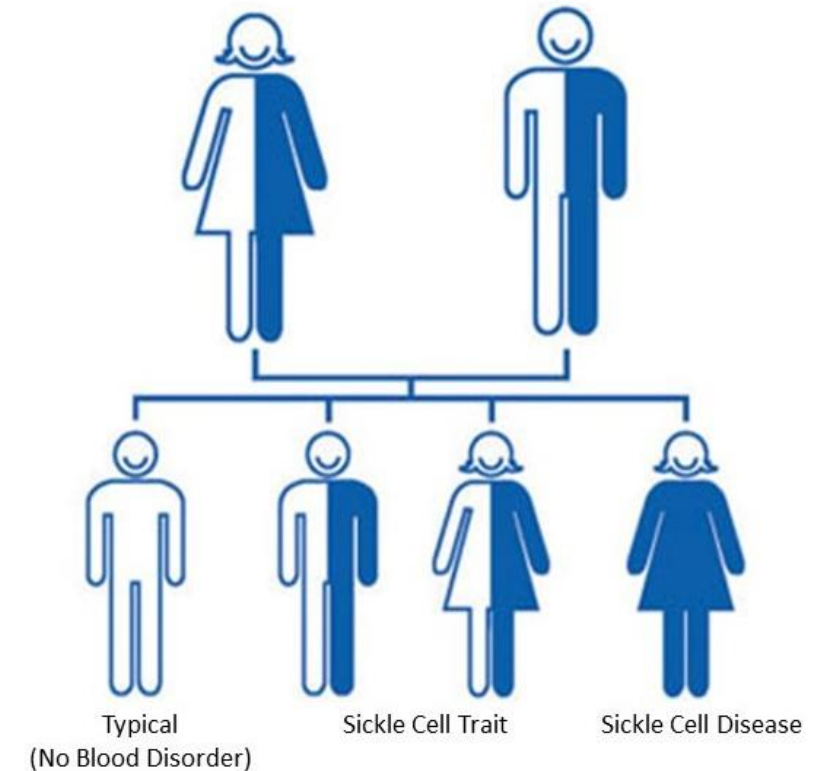
Normal
Red Blood Cell



Sickled
Red Blood Cell

What is the difference between SCD and sickle cell trait?

- Having sickle cell trait (SCT) is different from having SCD.
- When someone has SCD, they have inherited one sickle cell gene and one normal gene.
- People with SCT have both normal red blood cells and some sickle-shaped red blood cells.
- Most people with SCT do not have any symptoms of sickle cell disease.
- As carriers of the sickle cell gene, parents have a 50% chance of passing the gene on to their children. That means people with sickle cell trait can be at risk of having a child with SCT or SCD.



What are the symptoms and complications of SCD? (1 of 4)

Individuals with SCD can experience a myriad of symptoms and complications, ranging from mild to severe/debilitating. Some of the common symptoms and complications are listed below (and slides 5-7).

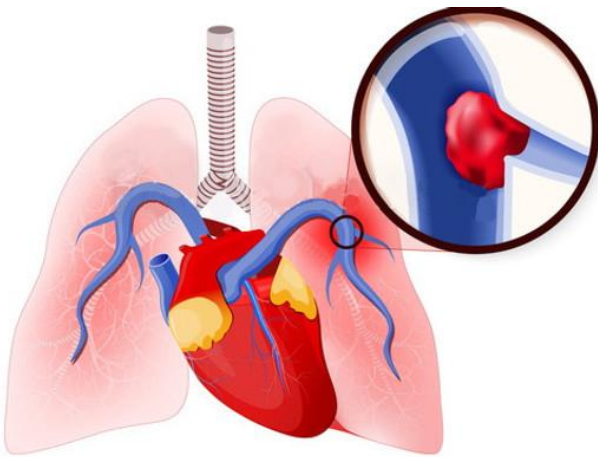
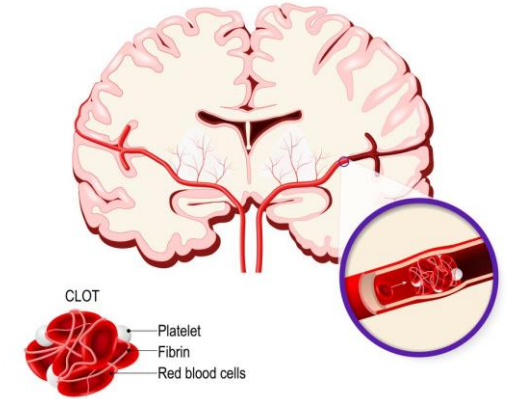
- **Vaso-Occlusive Crisis.** This is the obstruction of blood flow, and is the most common presentation of SCD. Patients complain of severe debilitating pain in any part of the body but typically in the long bones, back, pelvis, chest and the abdomen. Symptoms may start as early as six months of age with pain and swelling in both hands and feet.
- **Acute Chest Syndrome (ACS).** The most common symptoms in patients with ACS are fever, cough, chest pain. Lung exam may show reduced air entry, rales, and sometimes wheeze. ACS can progress rapidly to an abnormally low concentration of oxygen in the blood and respiratory failure if not treated promptly.
- **Infections.** Patients with SCD are especially at risk for infections.



What are the symptoms and complications of SCD? (2 of 4)

- **Pulmonary Hypertension.** This condition occurs when pressure in the blood vessels leading from the heart to the lungs is too high and has an incidence of 6% to 10% and a mortality of 2% to 5%.
- **Cerebrovascular Accidents/Stroke.** CVA can occur in children as young as two years of age, with 11% of patients with SCD having a stroke by 20 years of age. However, silent cerebral infarcts (SCI) are more common than overt strokes, with 34% of patients with SCD having evidence of SCI by age 14 years.

STROKE



- **Pulmonary Embolism (PE).** A PE occurs when a blood clot gets stuck in an artery in the lung, blocking blood flow to part of the lung. There is a 50-fold to 100-fold increase in annual incidence in inpatients with SCD compared to those without SCD.
- **Renal (Kidney) Complications.** Renal complications are extremely common in SCD, with 30% of adults developing chronic renal failure.

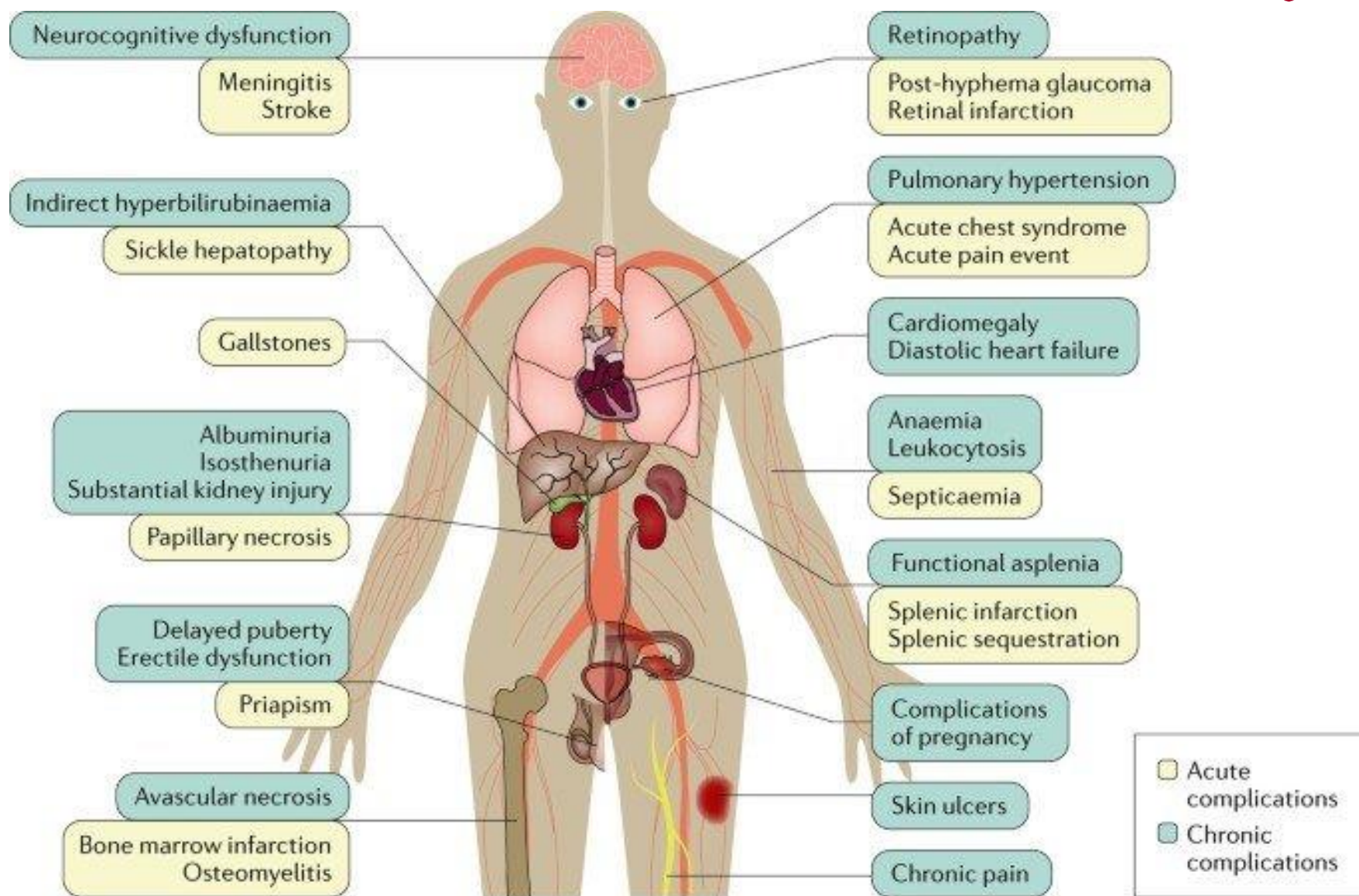
Source: <https://www.ncbi.nlm.nih.gov/books/NBK482384/> ; <https://sicklecellanemianews.com/news/therapy-with-tpa-found-safe-in-scd-sickle-cell-disease-patients-who-had-stroke/> ; <https://www.heartplace.com/what-we-treat-pulmonary-embolism>

What are the symptoms and complications of SCD? (3 of 4)

- **Eye Complications.** Proliferative retinopathy is the most common ophthalmologic complication of SCD. This occurs when there is new vessel formation (i.e., neovascularization) on the inner surface of the retina or vitreous, which subsequently can threaten vision by causing retinal detachment or hemorrhage
- **Cholelithiasis.** (gallstones; hardened deposits of digestive fluid that can form in the gallbladder) and biliary sludge develop because of chronic destruction of red blood cells and increased bilirubin turnover.
- **Osteonecrosis.** The death of bone cells due to decreased blood flow can occur because of SCD. The femoral and humeral heads are common sites of osteonecrosis, which occurs because of increased pressure from increased erythrocyte marrow or vascular occlusion.
- **Aplastic Crisis.** A temporary shutdown of red cell production can occur. This self-limited infection typically lasts 7 to 10 days and can be life-threatening.



What are the symptoms and complications of SCD? (4 of 4)



Source: <https://sickle-cell.com/complications>

How prevalent is SCD? (1 of 2)



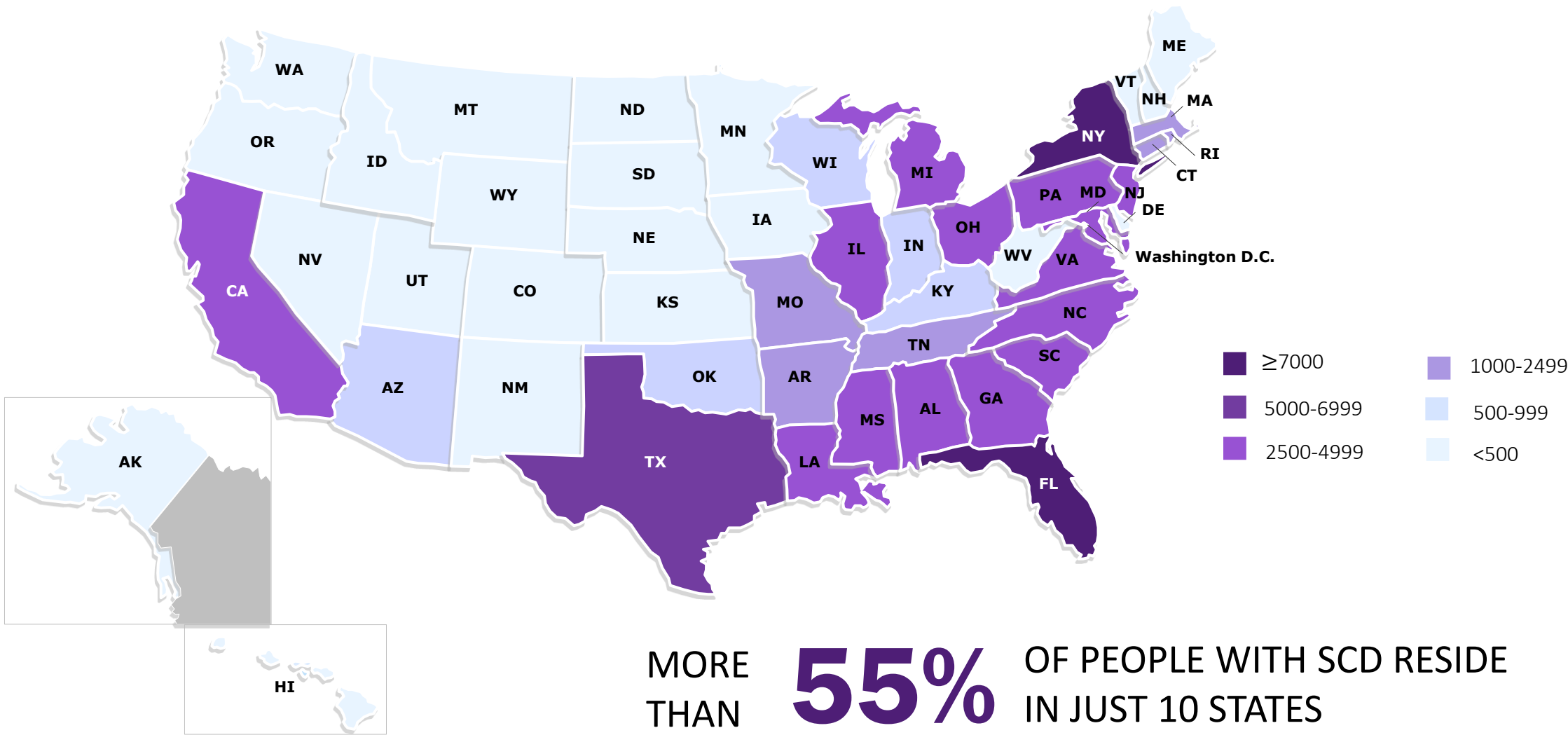
1 out of 365

SCD occurs in about one out of every 365 births of African-American babies.

- Roughly 1 in 100,000 Americans have SCD.
- SCD occurs among about 1 out of every 16,300 Hispanic-American births.
- About 1 in 13 Black or African-American babies is born with sickle cell trait (SCT).

Sources: <https://www.cdc.gov/ncbddd/sicklecell/data.html>; <https://investors.vrtx.com/static-files/7d17ce98-f9e8-45ee-aeb1-1cea0e2a9fef>

How prevalent is SCD? (2 of 2)



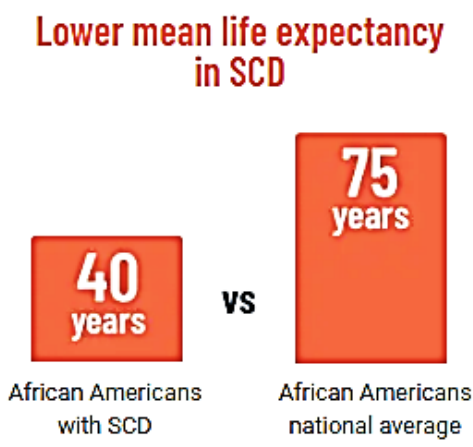
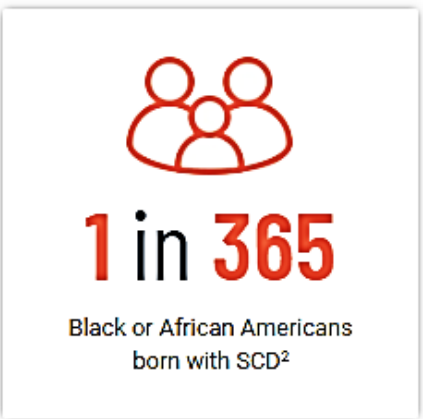
MORE THAN **55%** OF PEOPLE WITH SCD RESIDE IN JUST 10 STATES

Sources: <https://pubmed.ncbi.nlm.nih.gov/20331952/>

How prevalent is SCD compared to other diseases?

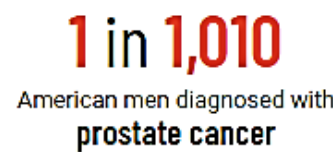
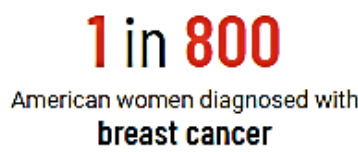
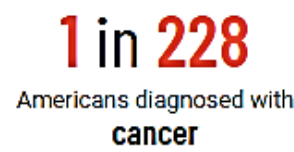


US statistics regarding SCD²⁻⁴



How does this compare to other serious conditions?⁵

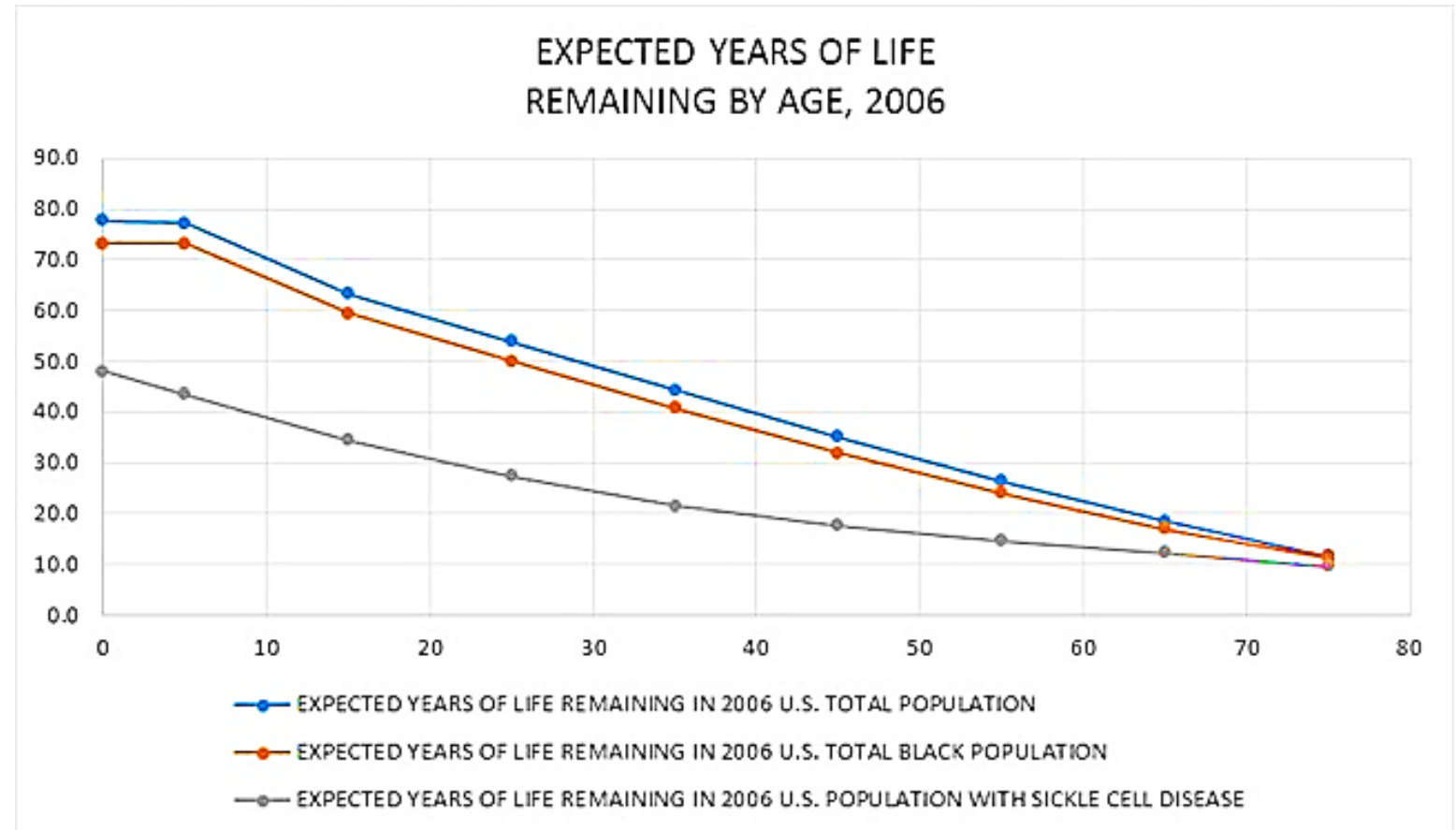
NEWLY DIAGNOSED



Source: <https://www.scdsilentdamage.com/sickle-cell-resources>

What is the life expectancy of people with SCD?

- A 2019 study found that the average lifespan of patients with SCD is roughly **54 years**, which is about 20 years shorter than those without SCD.
- The national median life expectancy for an individual with SCD is roughly 42-47 years.



Sources: <https://www.rarediseaseadvisor.com/hcp-resource/sickle-cell-disease-life-expectancy/#:~:text=Thus%2C%20their%20life%20expectancy%20is,of%20normal%20adults%20without%20SCD.>, <https://www.hematology.org/newsroom/press-releases/2016/rare-patients-with-sickle-cell-disease-live-nearly-twice-as-long-as-average#:~:text=With%20a%20national%20median%20life,%2C%20stroke%2C%20and%20organ%20damage>, <https://www.populationassociation.org/blogs/emily-merchant1/2021/01/31/life-expectancy-sickle-cell>.

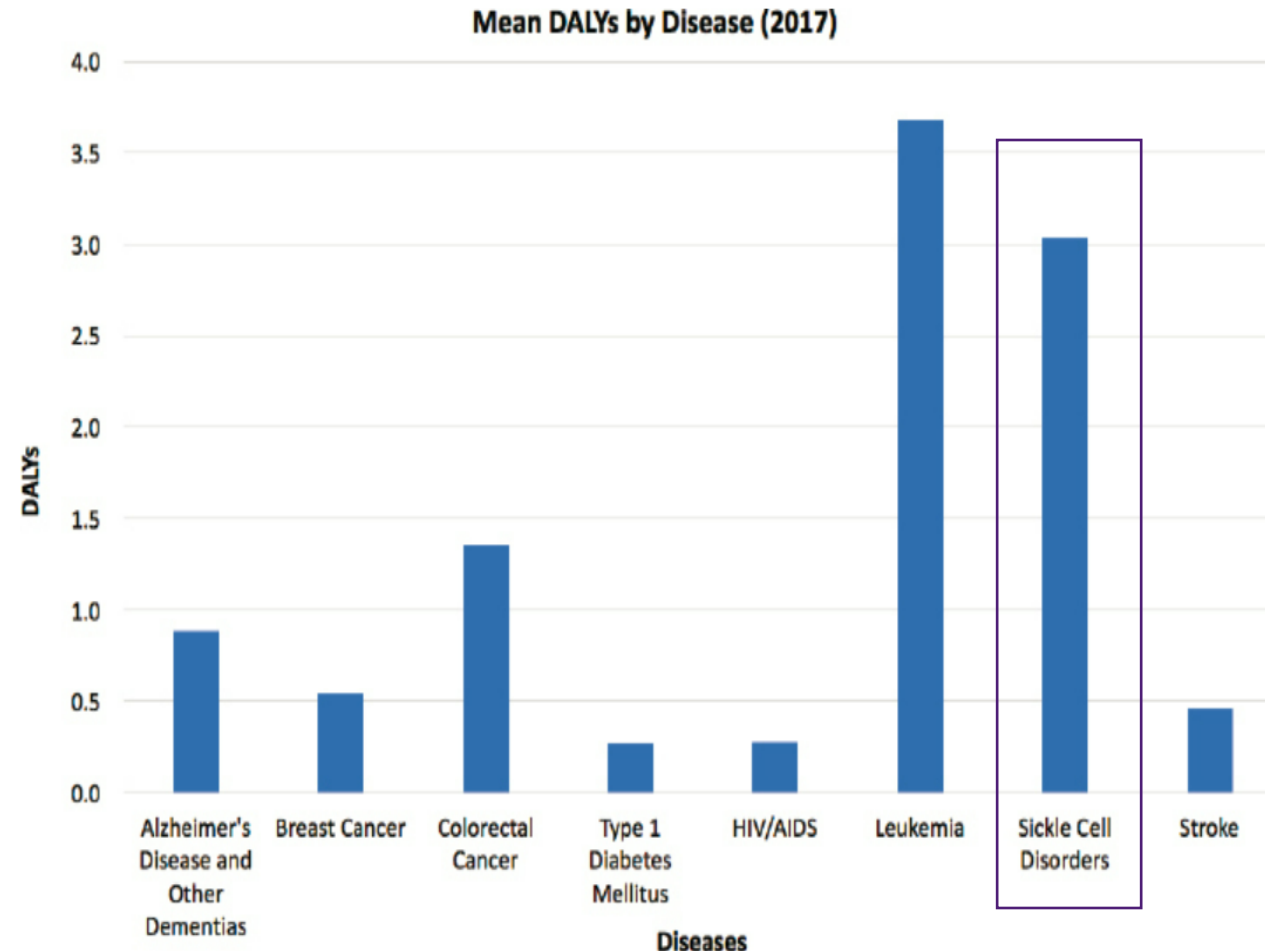
What is the overall disease burden of SCD?

One study in 2017 noted that in the U.S. *each year*, SCD is responsible for:

- **744 deaths**
- **29,284 years of life lost,**
- **3,984 disability-adjusted life-years (DALYs) lost**

When measured by disability-adjusted life-years, the burden of SCD on individual patients exceeds that of numerous other severe illnesses (see graph).

- DALYs measure the potential years of life lost due to premature death and the years of healthy life lost due to disease or disability.
- Another way of thinking of DALYs is as the additional expected years of life and healthy years of life that a patient would have enjoyed if he or she had never been diagnosed with the disease in question.



Source: <https://globalheartjournal.com/articles/abstract/10.1016/j.gheart.2017.11.001/> , <https://www.ncbi.nlm.nih.gov/books/NBK566471/>

What are the estimated average lifetime costs for someone living with SCD?



- A recent, large-scale study published in *Blood Advances* found that nonelderly lifetime burden of total medical costs attributable to SCD was **\$1.7 million**.
- Individuals with SCD incurred **\$44,000** in out-of-pocket costs due to their disease over their nonelderly lifetimes.
- Additionally, these results suggest that the medical costs of treating SCD peak around the age of 13-24 years old and decline with older age.
- **NOTE:** These findings do not encompass the indirect costs one can accumulate when receiving care for SCD (e.g., lost productivity due to being unable to work) and do not include people covered on public insurance plans, like Medicaid.

Sources: <https://www.hematology.org/newsroom/press-releases/2022/the-cost-of-living-with-sickle-cell-disease#:~:text=%E2%80%9COur%20findings%20suggest%20that%20the,of%20Pharmacy%2C%20University%20of%20Washington.>

Access to Care and Treatment



How is Sickle Cell Disease treated?



Current Therapies

Medicine

- Voxelotor to prevent the sickling of red blood cells
- Crizanlizumab-tmca to reduce vaso-occlusive and pain crises
- Hydroxyurea to reduce or prevent multiple complications
- L-glutamine to treat pain
- Penicillin to reduce risk of infection

Transfusion

- There are two kinds of red blood cell transfusions: simple and exchange transfusions.
- Simple transfusions deliver additional healthy red blood cells to an individual's body, while exchange transfusions exchange the individual's sickled blood cells with healthy ones.

Bone Marrow Transplant

- A blood and bone marrow transplant is currently the only cure for SCD, but it is not for everyone.
- Many individuals with SCD do not have a relative who is a close enough genetic match to be a donor.
- Most transplants to treat SCD occur in children.
- Blood and bone marrow transplants are riskier in adults.

Future Therapies

Gene Therapy

- Gene therapy involves either restoring a faulty or missing gene or adding a new gene that improves the way the cell works.
- Researchers take blood or bone marrow from a patient and modify their stem cells in a laboratory using genetic therapies.
- Modified stem cells are injected into the blood and begin making healthy red blood cells.
- Only 1/5 individuals in the U.S. with SCD are expected to be eligible for gene therapies.

Source: <https://www.nhlbi.nih.gov/health/sickle-cell-disease/treatment#:~:text=A%20blood%20and%20bone%20marrow,manage%20complications%2C%20including%20chronic%20pain.>

What sources of health coverage do people with SCD have?

- Medicaid has been a key source of insurance coverage for those with SCD.
- CMS 2017 data: 42,000 Medicaid/CHIP beneficiaries with SCD.
- Medicaid covers roughly half the SCD population in the U.S.
- According to older data, Medicaid nationwide covered
 - **66 percent** of SCD hospitalizations in 2004
 - **58 percent** of ED visits for the disease between 1999 and 2007.



Source: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf> ; <https://www.ncbi.nlm.nih.gov/pubmed/20331955>.

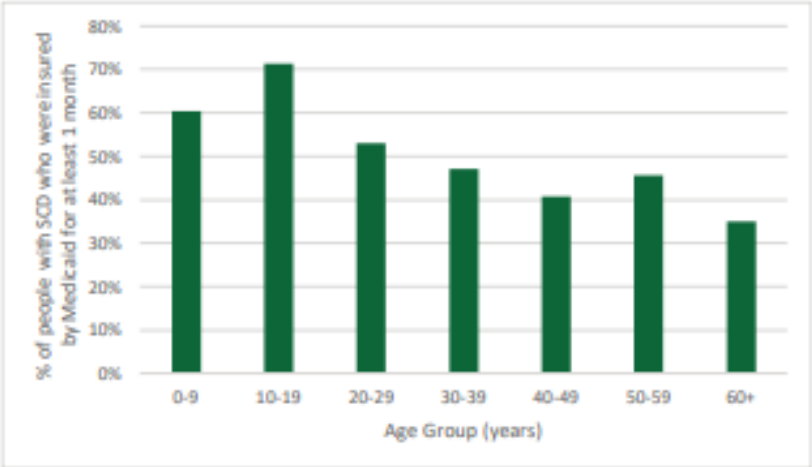
Georgia Medicaid - Individuals with SCD (2014-2016)



GEORGIA
9,382
people with SCD

56%

were insured by Medicaid for at least 1 month



40%

had at least one gap (a period of time when they were not insured by Medicaid) in their coverage

Average length of each gap in coverage:



Source: <https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc.html>.

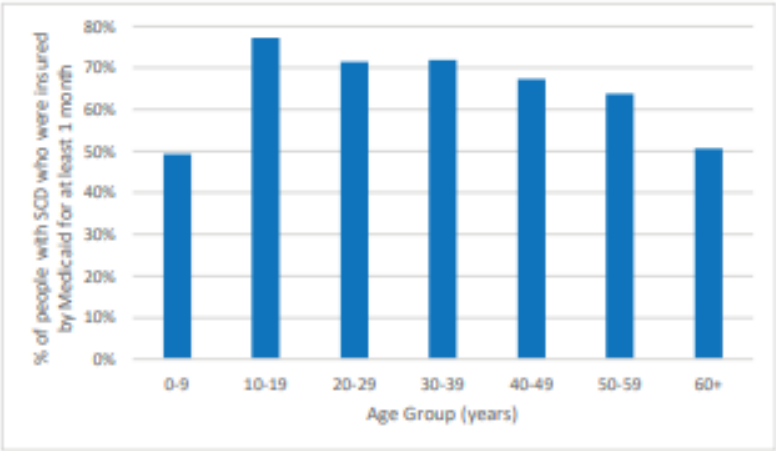
California Medicaid Coverage Patterns for Individuals with SCD (2014-2016)



CALIFORNIA
5,124
people with SCD



66%
were insured by Medicaid for at least 1 month



31%
had at least one gap (a period of time when they were not insured by Medicaid) in their coverage

Average length of each gap in coverage:



Source: <https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc.html>.

What is known about access to care for children with SCD?

CDC data suggests about less than half of children with sickle cell anemia (SCA) – the most severe form of SCD – receive the recommended care for the disease.

- Transcranial Doppler Ultrasound (TCD) screenings are used to identify children who are at risk for stroke.
 - **Fewer than half of children** aged 2–9 years (47%) and 10–16 years (38%) received a TCD screening in 2019.
- Hydroxyurea is a recommended treatment for people with SCD ages 9 months and older, as it is the only effective drug proven to reduce the frequency of painful episodes.
 - However, according to 2019 CDC data, **less than half** of children ages 2-9 **(38%)** and **slightly over half** of children 10–16 years **(53%)** used hydroxyurea.

2 in 5

Only 2 in 5 children 2–9 years used recommended medication that can prevent sickle cell anemia complications in 2019.

50%

Fewer than half of children 2–16 years received the recommended screening for stroke in 2019.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (1 of 7)



KEY FACTS*



41,995

Medicaid and CHIP
beneficiaries
with SCD

74 per 100,000

National prevalence of SCD in the
Medicaid and CHIP population
per 100,000 beneficiaries

43%

Medicaid and CHIP
beneficiaries with SCD
who were over age 20

30%

Beneficiaries with SCD ages
21 to 64 who were dually eligible
for Medicare and Medicaid¹

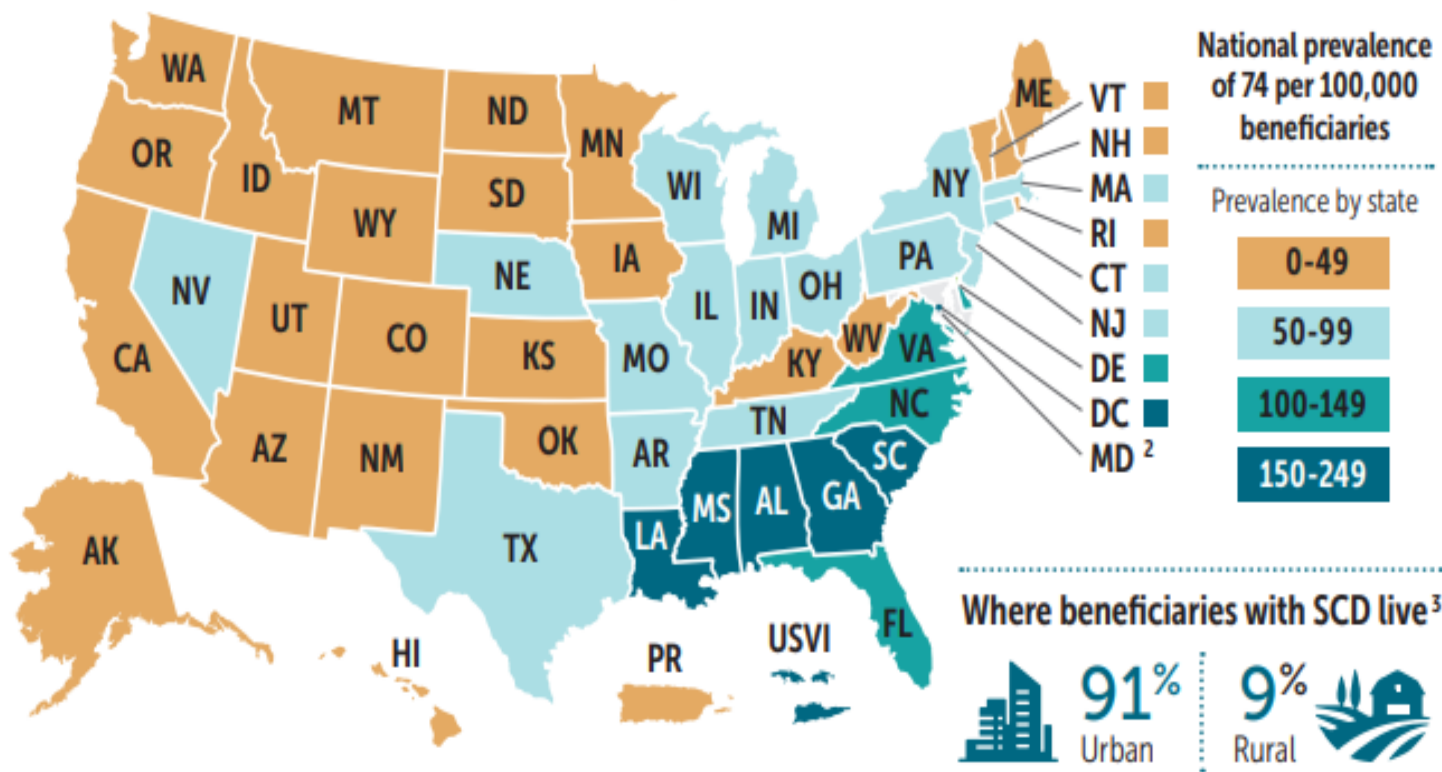
Sources: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf>.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (2 of 7)

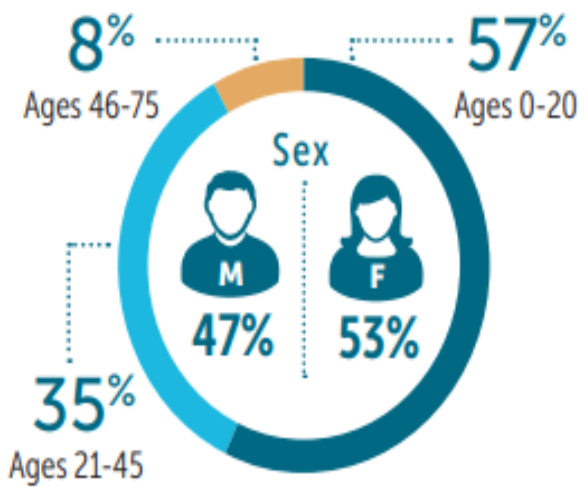


CHARACTERISTICS OF BENEFICIARIES WITH SCD

Geographic Variation in the Number of Medicaid and CHIP Beneficiaries with SCD Per 100,000 Beneficiaries in 2017



Beneficiaries by Age and Sex



Distribution of male and female beneficiaries by age

Male		Female
51%	Ages 0-20	49%
42%	Ages 21-45	58%
36%	Ages 46-75	64%

Sources: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf>.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (3 of 7)

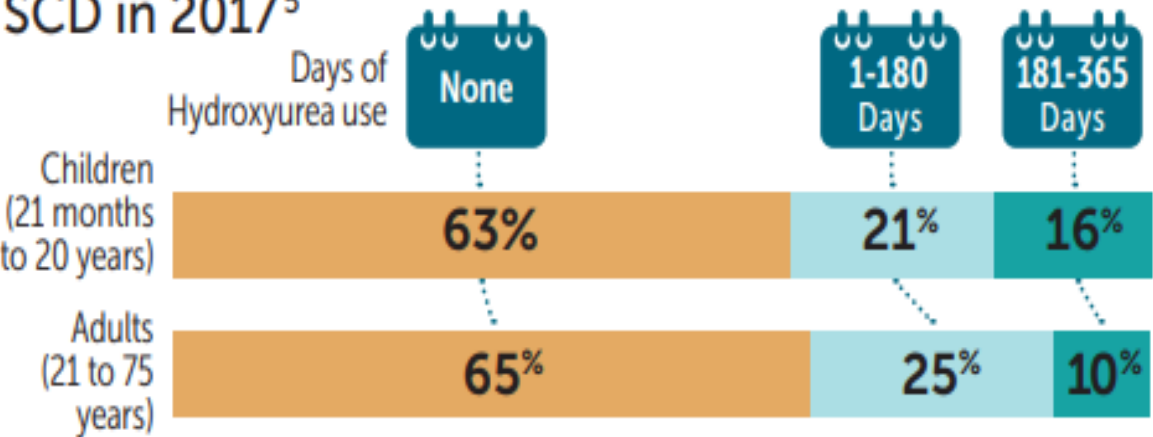
RECOMMENDED CARE FOR SCD

Transcranial Doppler Ultrasound (TCD) Screening⁴

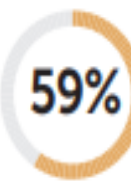


Children ages 2 to 16 with SCD who received a TCD screening in 2017

Hydroxyurea Use among Children and Adults with SCD in 2017⁵



Pneumococcal Vaccination⁶



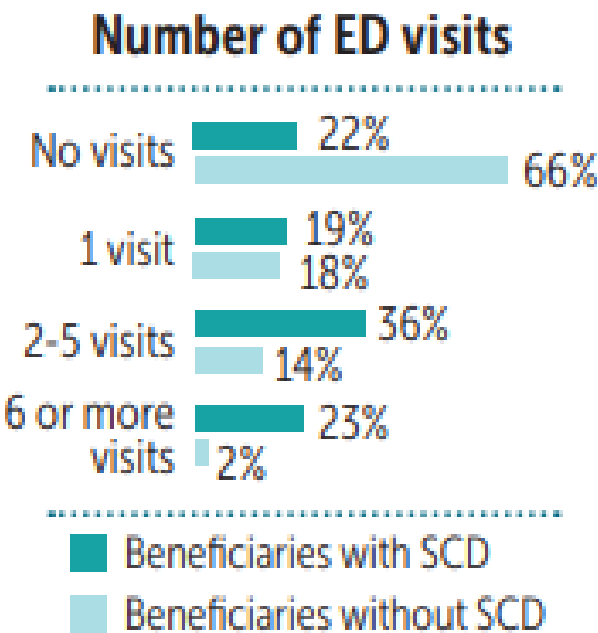
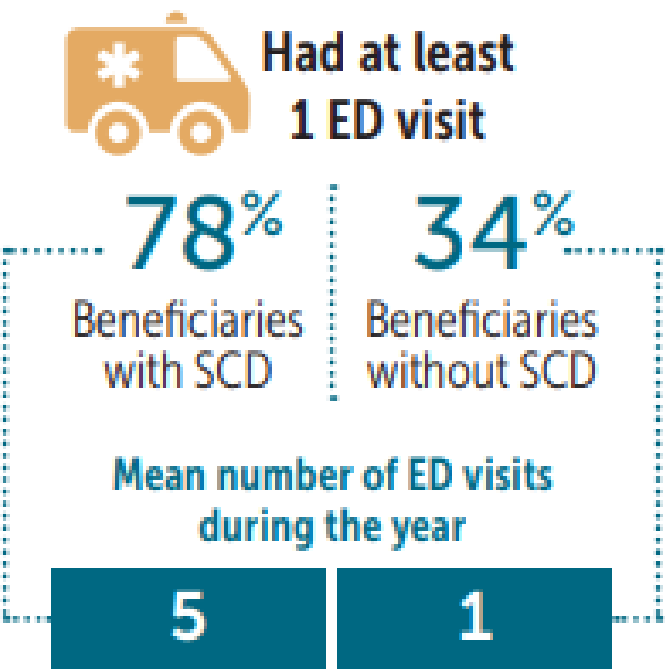
Children under age 2 with SCD who had at least 1 pneumococcal vaccination in 2017

Sources: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf>.

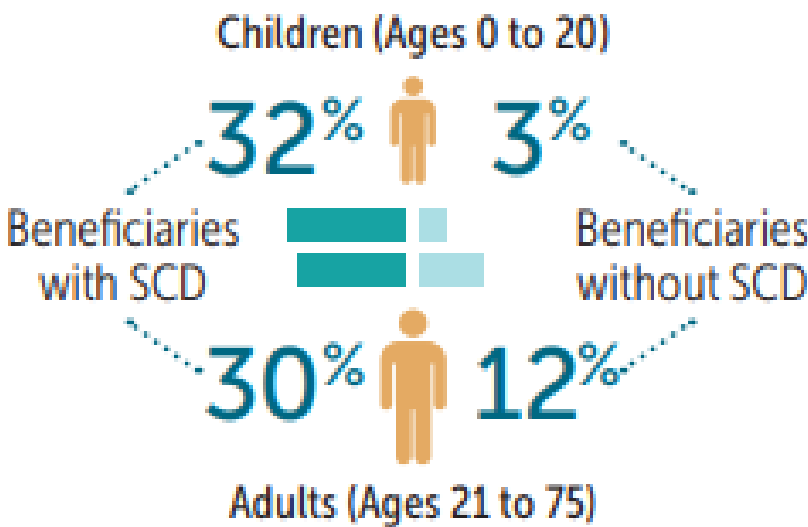
For individuals with SCD enrolled in Medicaid, what is known about their access to care? (4 of 7)

HEALTH CARE UTILIZATION

Emergency Department (ED) Visits in 2017⁷



Percentage of ED visits that led to an inpatient hospital stay



Sources: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf>.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (5 of 7)



HEALTH CARE UTILIZATION

Inpatient Hospital Stays in 2017⁸



Had at least 1 inpatient hospital stay

49%

Beneficiaries with SCD

6%

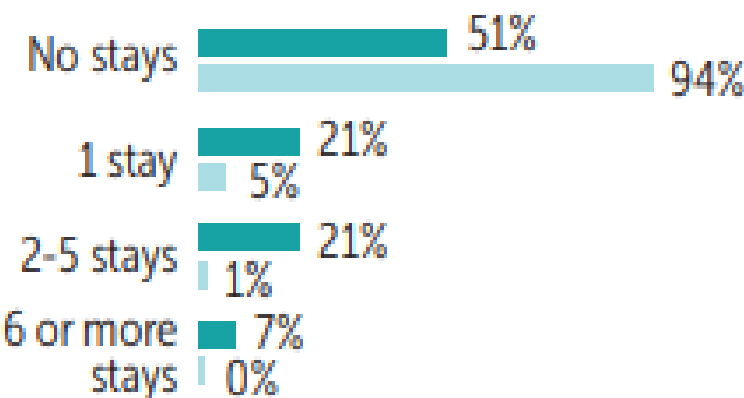
Beneficiaries without SCD

Mean number of hospital days during the year

9

1

Number of inpatient hospital stays



Beneficiaries with SCD
Beneficiaries without SCD

Outpatient Visits in 2017



Had at least 1 outpatient visit with any provider

99.8%

Beneficiaries with SCD

87.1%

Beneficiaries without SCD

Median number of outpatient visits during the year

14

5

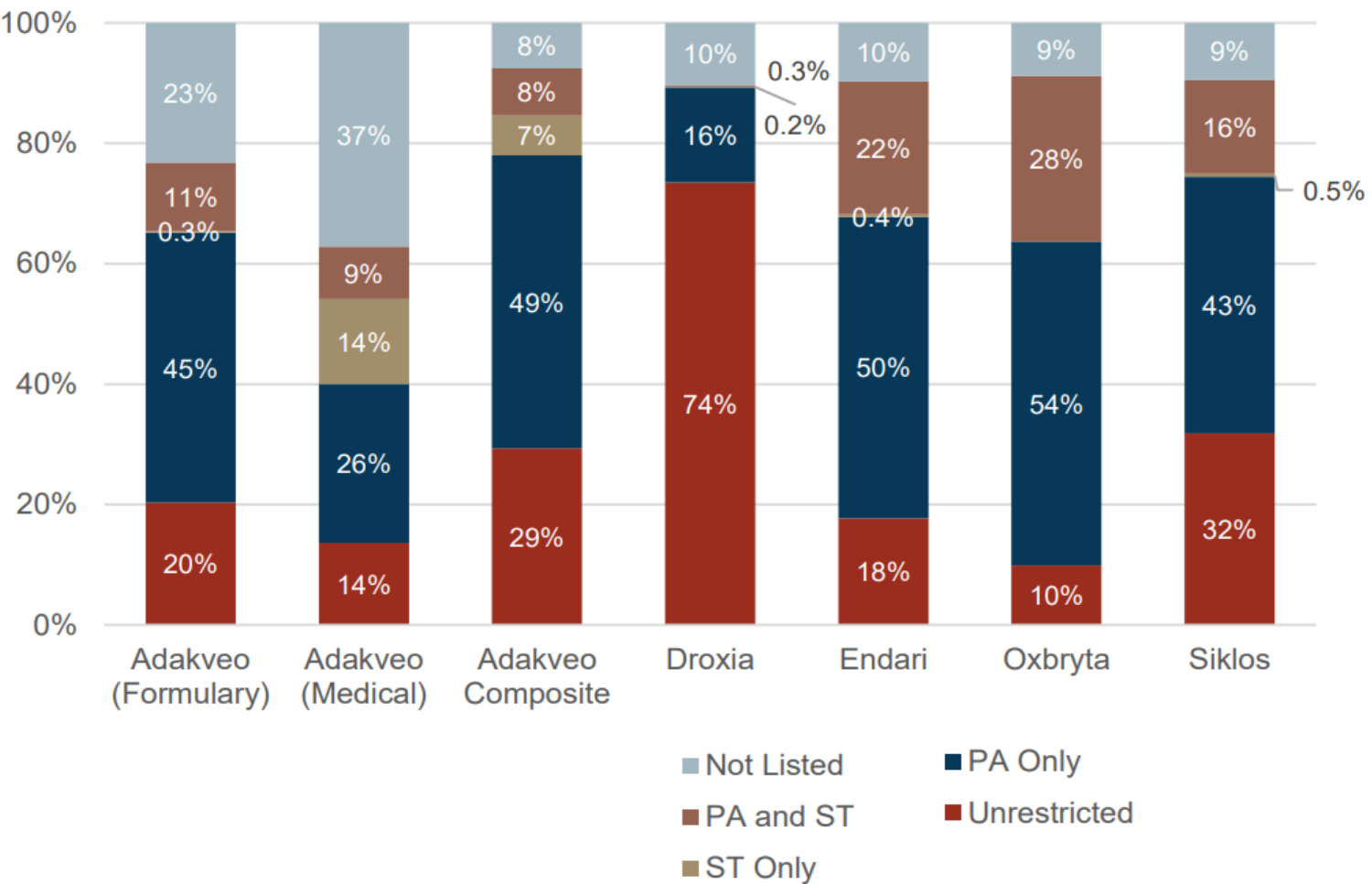
Sources: <https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf>.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (6 of 7)



Figure 3 – Utilization Management Techniques for SCD Therapies, All Medicaid

Looking across all state FFS programs and MCOs, Medicaid payers **require prior authorization and/or step therapy at least 50% of the time** for Adakveo®, Endari, Oxbryta®, and Siklos®



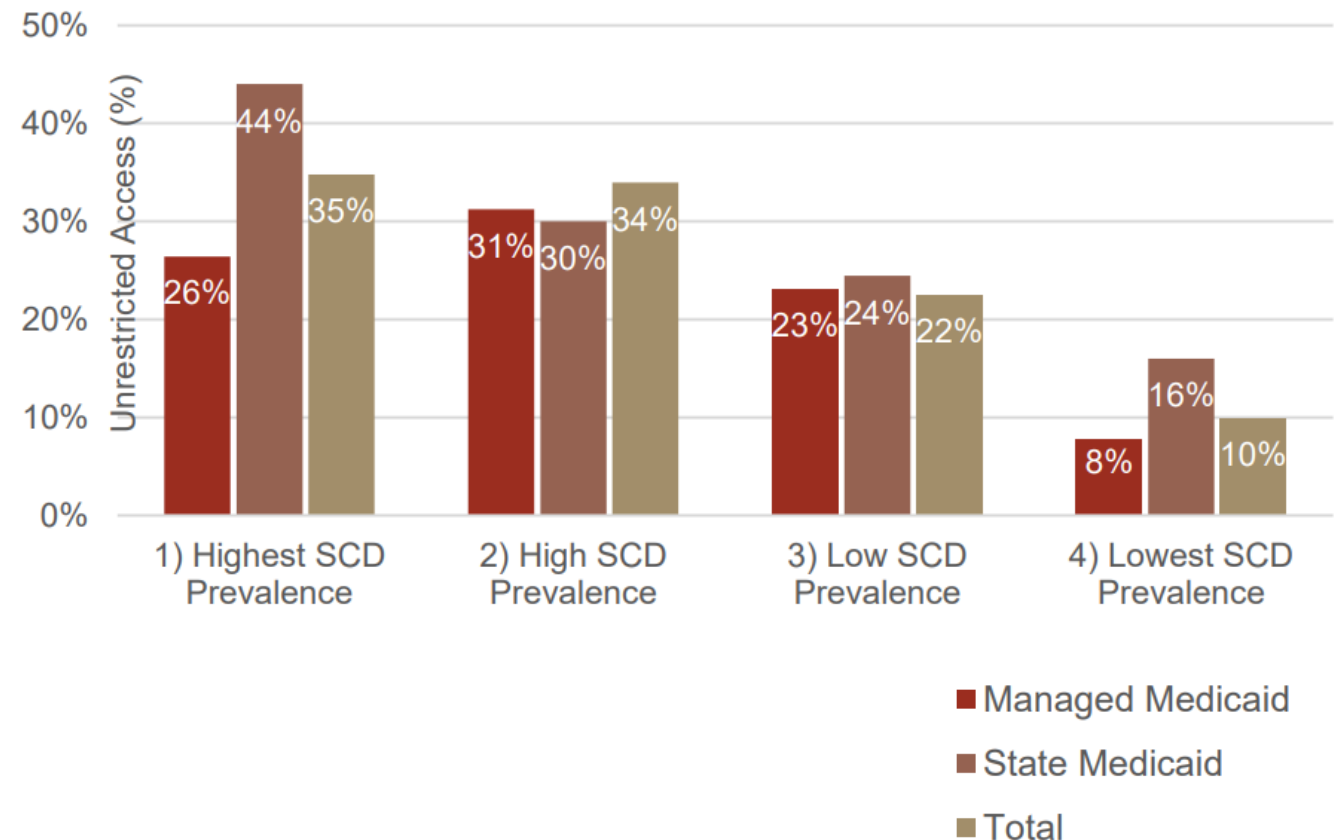
Source: https://sickcells.org/wp-content/uploads/2022/08/Sick-Cells_Medicaid-Access-and-Landscape-Review_Final-Report.pdf.

For individuals with SCD enrolled in Medicaid, what is known about their access to care? (7 of 7)

When states or their MCOs require prior authorization for prescription products that treat SCD, reauthorization is most often required every 6-12 months.

- Shorter reauthorization periods may increase the number of administrative steps that individuals with SCD and their providers must take to obtain therapies.
- Administrative steps for individuals with SCD and their providers associated with prior authorization (and the increased frequency of those requirements) adds to administrative burdens.

Figure 6 – Unrestricted Access by Prevalence Group



What is known about the role that stigma and bias play in access to care for persons with SCD?



- **Discrimination against SCD patients is self-reported as coming from family, friends, peers, co-workers, and community members**, and include examples such as discrediting pain, stigmatizing them as drug seekers, treating patients as though they are weak or lazy, and deeming them incapable, among others.
- **Racism and stigma often leads to inadequate pain management.**
 - A cross-sectional analysis conducted by Haywood et al. found that SCD patients waited **25% longer** than the general population and **50% longer** than those with long bone fractures after considering race and triage priority.
- **Research suggests that stigma has detrimental consequences for individuals with SCD**, including having negative social consequences, impairing healthcare interactions, and hindering physiological and psychosocial wellbeing.

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6186193/> ; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3608692/>

What do experts say about the need to address SCD?

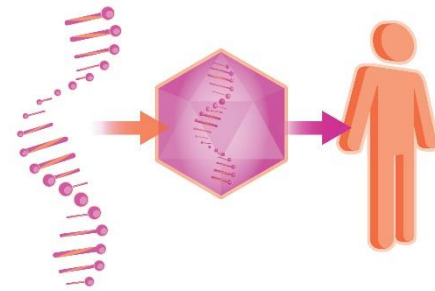
- “Ending sickle cell disease is a matter of racial justice....
- One hundred thousand Americans — the great majority of whom are Black — have sickle cell disease, an excruciatingly painful, terminal disease that on average leads to death before age 50, but for many much younger.
- But my review of Symphony Health Claims Data revealed only 30 percent of these one hundred thousand receive any form of medical treatment despite its widespread availability.
- Can you imagine the outcry if only 30 percent of Americans with cancer received treatment?
- There would be no stronger affirmation of our national commitment to equity and racial justice than to prioritize assistance to those suffering from this disease.”



- Dr. Brett Giroir

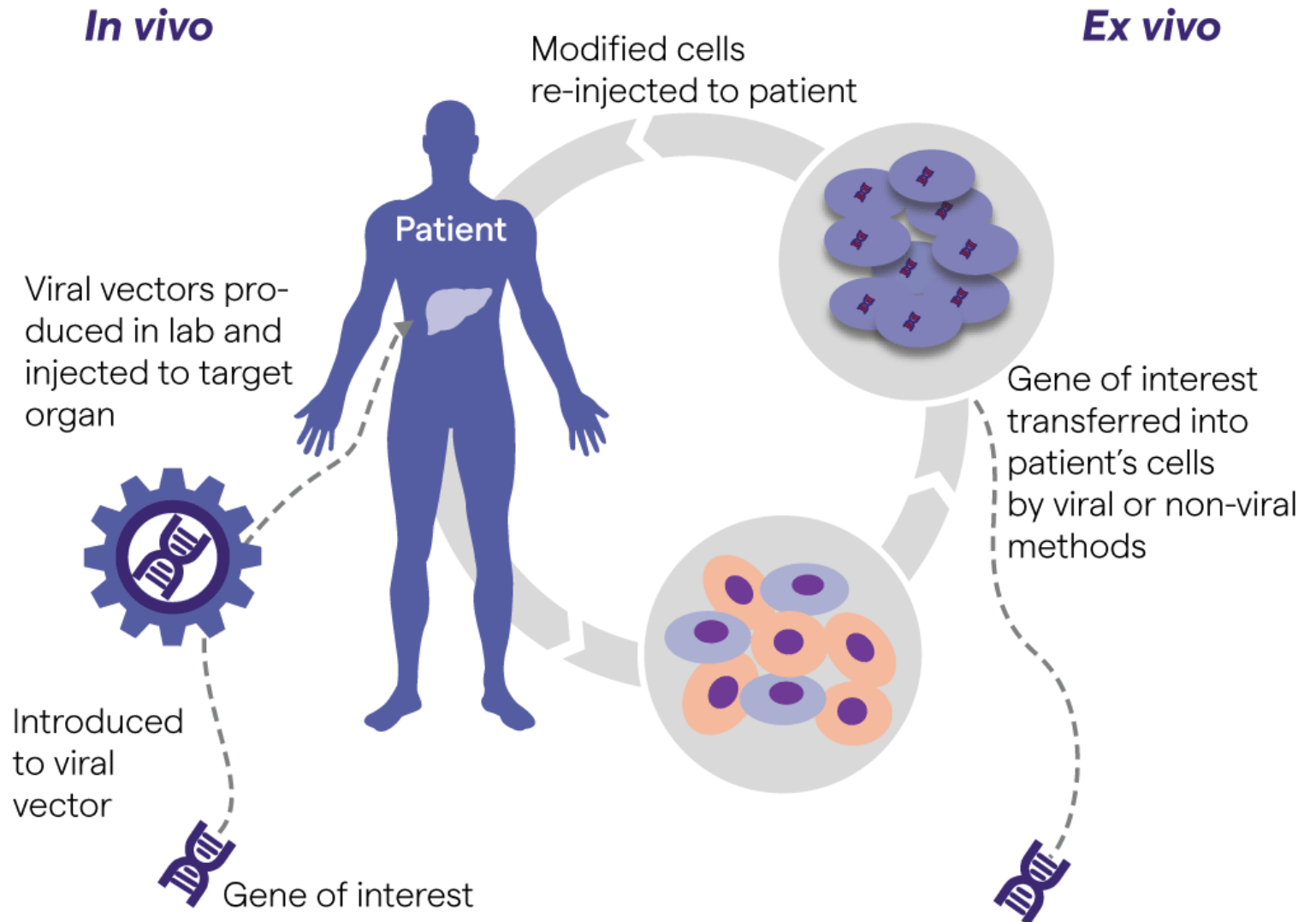
*Former Assistant Secretary of HHS,
Senior Advisor to the SCD Partnership*

New Treatments – Gene Therapies



What is gene therapy?

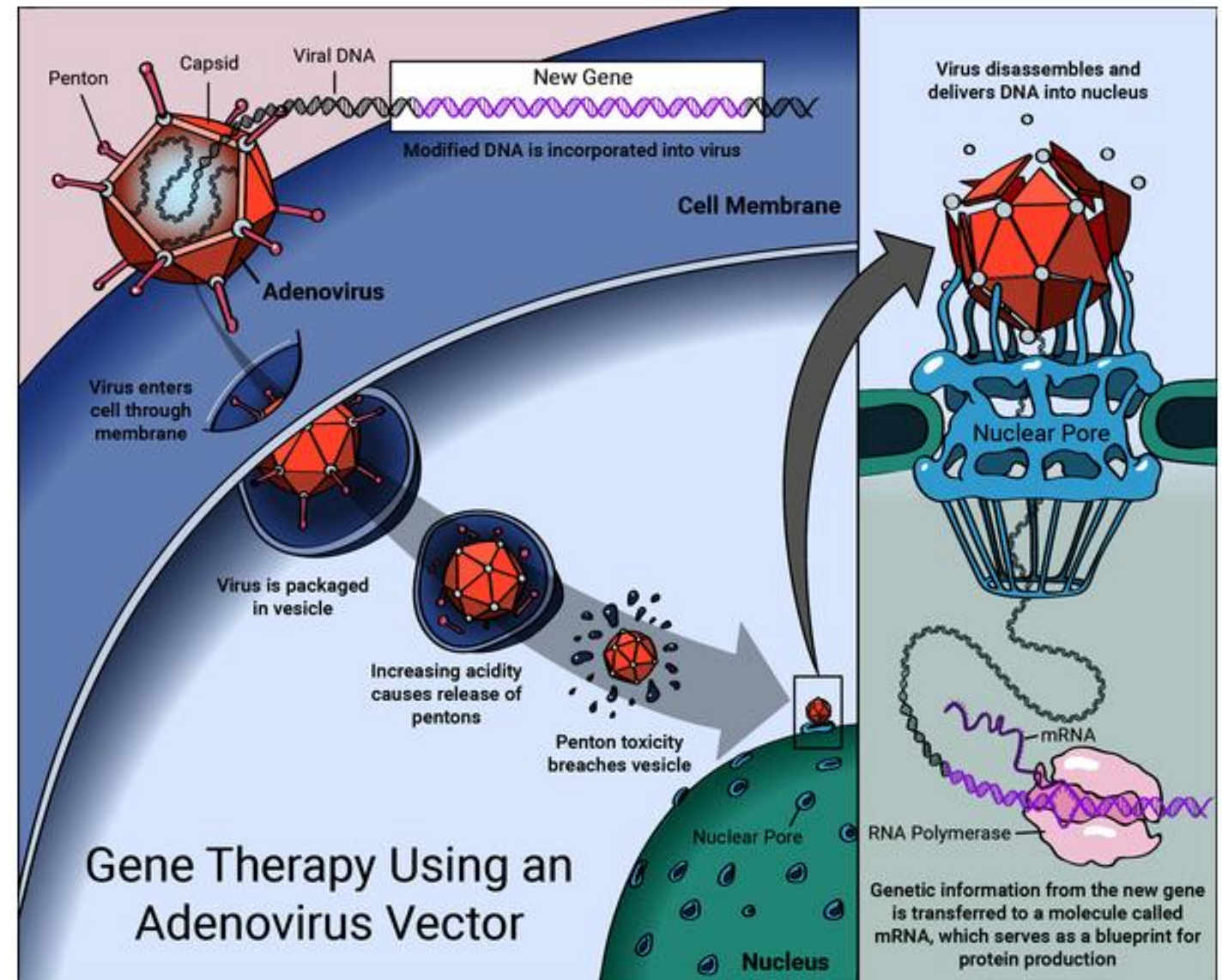
Gene therapy uses DNA or other genetic material to add, correct, or edit genes in order to alter the course of a disease.



Source: <https://www.sparksicklecellchange.com/treatment/sickle-cell-gene> . .

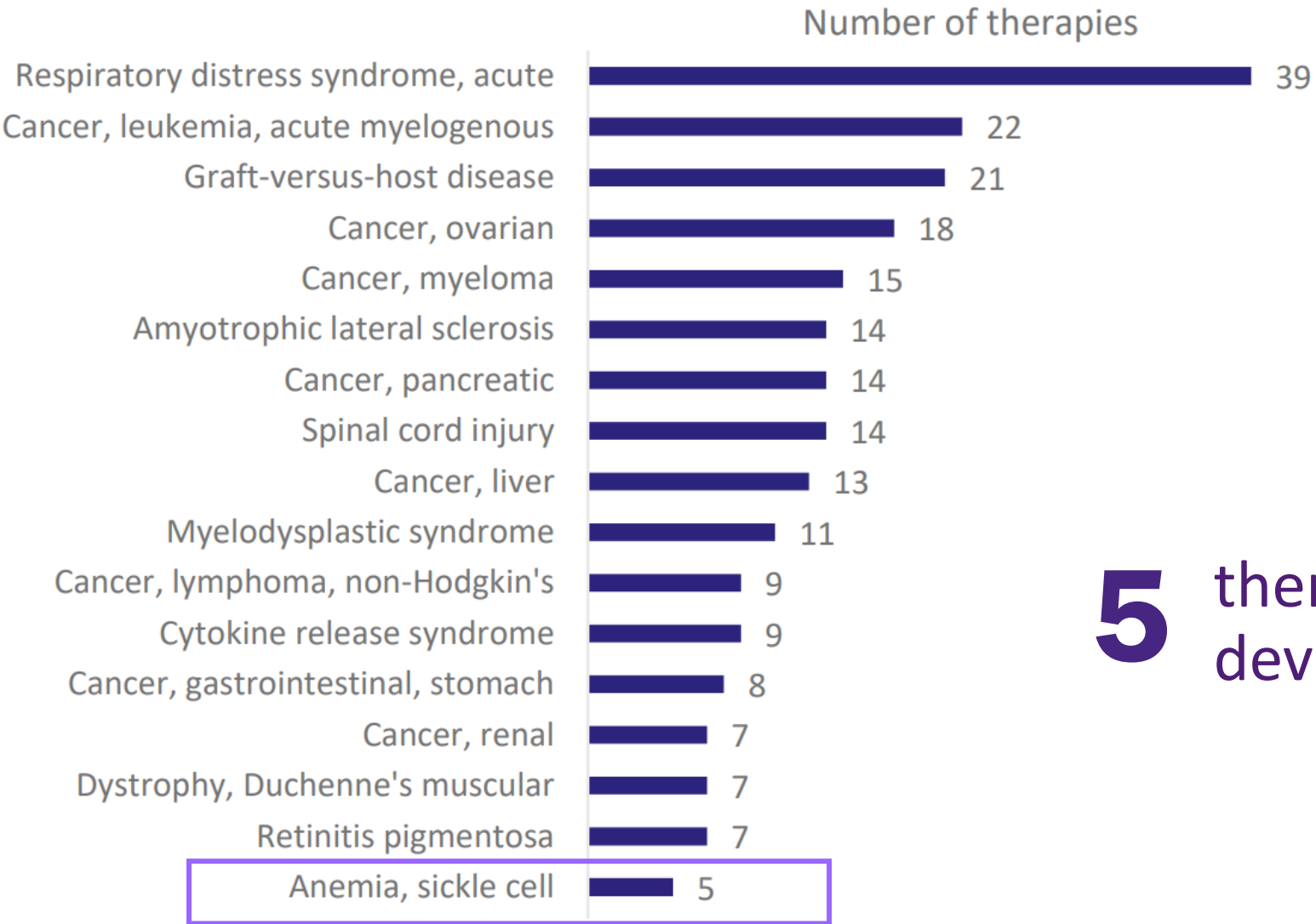
How does a gene therapy work?

- Gene therapy works via alteration of an individual's genetic code in order to restore the lost function of critical proteins.
- This alteration is initiated by a vector, which can be delivered intravenously and directly infects the cell without causing disease in the individual.



Source: <https://medlineplus.gov/genetics/understanding/therapy/procedures/>.

Are there new cell or gene therapies in development to treat SCD?



5 therapies are in development for SCD...

Source: https://asgct.org/global/documents/asgct-citeline-q3-2022-report.aspx?_zs=FbBCc&_zl=T2qI3.

New gene therapies in development to treat SCD?



Yes, there are TWO potential gene therapies on the near-term horizon.



Exa-cel

Q1 2023 projected
completion of US
submission package



Beti-cel, Eli-cel

Q1 2023 projected
submission of biologics
licensing application

Sources: <https://investors.vrtx.com/news-releases/news-release-details/vertex-and-crispr-therapeutics-announce-global-exa-cel>, <https://investor.bluebirdbio.com/news-releases/news-release-details/bluebird-provides-update-fda-review-timelines-betibeglogene>.

What will the process be like for a patient with SCD to receive a gene therapy? (1 of 2)



There are four steps to the SCD gene therapy treatment process:



STEP 1: CONSULTATION

- Patients and their doctor/care team will discuss risks/benefits
- Ensure appropriateness and eligibility (**NOTE:** not many individuals with SCD are eligible for gene therapy)
- Discuss steps to plan for therapy (e.g., health coverage, chemotherapy, side effects)
- The consultation step can take **weeks to months**



STEP 2: PREPARATION

- Will include the stem cell collection needed for manufacturing gene therapy *ex vivo*
- Usually requires a few days for the patient to stay in the hospital for stem cell collection.
- After the collection, it will usually take a **few months** for the lab to modify the stem cells to create the gene therapy

What will the process be like for a patient with SCD to receive a gene therapy? (2 of 2)



There are four steps to the SCD gene therapy treatment process:



STEP 3: TREATMENT

- Conditioning with chemotherapy
- Gene therapy treatment that was prepared is infused back in.
- After treatment, the individual will remain in the hospital for **several weeks**—this time span includes a recovery period and the time needed for the stem cells enter the blood and start making new blood cells



STEP 4: RECOVERY/FOLLOW-UP

- Individual is discharged
- May include several follow-up appointments at a specialized treatment center or home healthcare
- This is a critical step and can last for **several years**. The individual will regularly work with their physicians to monitor the effect of treatment for the long-term.

Source: <https://www.sparksicklecellchange.com/treatment/sickle-cell-gene-therapy>

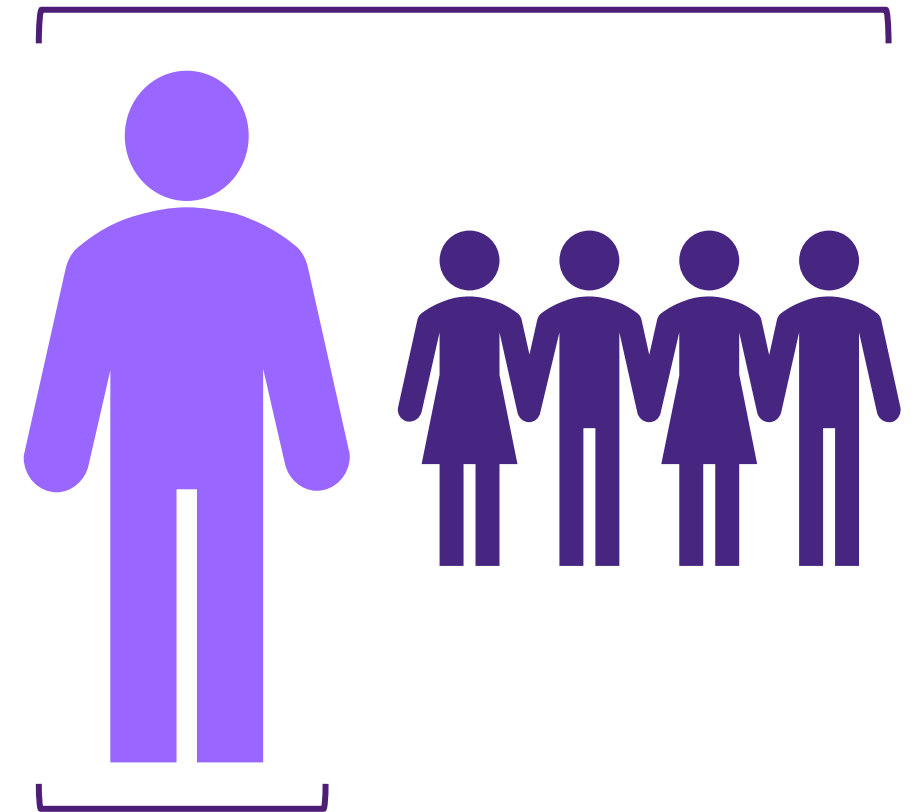
What part of the population with SCD is expected to be eligible for a new gene therapy?

Current publicly available information suggests the most likely candidates for gene therapy are individuals with severe SCD disease.

That means only about 1 in 5 individuals in the U.S. with SCD are likely to be eligible for gene therapy.

Given limited eligibility and even lack of interest among SCD warriors to undergo gene therapy, access to and coverage of existing disease-modifying drugs remains crucial.

All individuals with SCD.



*Expected eligible
for gene therapy.*

How many gene therapies have been approved?

- **There are 11 FDA-approved gene therapies across disease states.**
- The most recent gene therapies to be approved in the U.S.:
 - Zynteglo for beta thalassemia
 - Skysona for cerebral adrenoleukodystrophy
- Oncology and rare diseases remain the top areas of development overall.

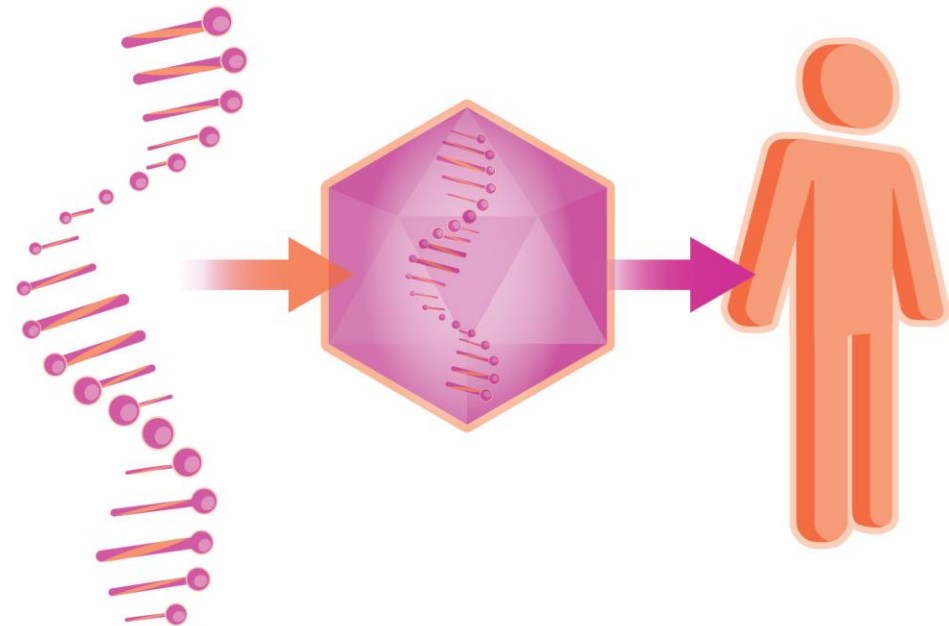


FDA

Source:

Will gene therapies for SCD be safe?

- As with any treatment, there are risks associated with gene therapies and there could be downstream effects.
- Patients need to be informed of these risks, as well as the risks of their underlying condition.
- The FDA's gold standard is safety and effectiveness of any approved therapy or drug.
- Regulators continue to adhere to these statutory standards.



Source:

What could a gene therapy for SCD mean for individuals with this rare blood disease?

- **Life without future treatments?** Gene therapy could enable some individuals with SCD to live without the need for ongoing treatments or the burden of daily disease management.
- **New hope when other treatments fail?** Gene therapy could provide alternative treatment options for individuals with SCD that do not respond to other available therapies.
- **Dramatically improved quality of life?** Gene therapy could dramatically improve an individual's quality of life, allowing them to live pain-free, be active, work, etc.

“People with sickle cell disease live in constant fear of the next pain crisis. This treatment could give people with this disease their life back. We hope [gene therapy] will also be successful in younger patients so they can grow up without experiencing pain crises and live longer.”

- Dr. Markus Mapara, professor of medicine at Columbia University Vagelos College of Physicians and Surgeons

What is it like to be cured from SCD?

Phillip Sanders, a member of the Partnership who was cured of SCD via stem cell transplant, reflects on his experience undergoing his transplant and his future now that he is cured:

- “You could see the bag with the stem cells in it. They put a light on it and you could see them. **You could see your cure and see your life change. It’s in that bag. It’s surreal. That bag was worth more to me than any lottery.**”
- “**My future looks bright, brighter than it ever has been.** I am trying to get my life back to that active life I had. I will. That’s what I want.”



Source: <https://news.uams.edu/2020/06/15/cured-arkansas-man-sickle-cell-disease-eliminated-by-bone-marrow-transplant/>.

What can be done to help Americans with SCD?

- The Sickle Cell Disease Partnership, founded in early 2022, is a multi-sector public policy and advocacy collaboration committed to advancing actionable federal healthcare policies that will improve the lives of patients living with SCD.
- The Partnership's work is grounded in the National Academies of Science, Engineering, and Medicine (NASEM) report, released in 2020: [Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action.](#)
- The Partnership has identified specific recommendations, based on the National Academies' report, that could have significant impact on the lives of those with SCD.
- There is an immense opportunity to advance policies that improve access to care and treatment, strengthen health equity, and improve patient outcomes.



Americans with SCD need Congressional and Administration action.

What can be done to help Americans with SCD?



Learn more about what you can do to help:

www.SickleCellPartnership.org

The time for change is now.

Come and join us.