Newborn Screening for Spinal Muscular Atrophy

A Summary of the Evidence and Advisory Committee Decision

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EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding spinal muscular atrophy (SMA) to the Recommended Uniform Screening Panel (RUSP) in 2018.

About the disorder

SMA is a rare genetic disorder. Studies of patients with symptoms suggest that about 1 out of every 11,000 people has SMA. People with SMA have a change in the *SMN1* gene that prevents it from making enough of the protein that nerve cells need to survive. Some people make enough of this protein with a related gene called *SMN2*. There are different types of SMA. Most children have SMA Type 1, which causes weakness and, without treatment, can worsen quickly and lead to death.

Treatment for SMA

There is no cure for SMA yet, but early diagnosis allows early monitoring and treatment. Nusinersen is a recently approved medicine that can stop SMA problems from getting worse. When used early in the disease process, it can sometimes prevent damage to nerve cells. Other treatments can also help with certain symptoms, at least for a while. The timing and type of treatment for SMA depends on the disease type.

Detecting SMA in newborns

Newborn screening for SMA can be included with routine newborn screening for other disorders during the first few days of life. Newborn screening for SMA looks for problems with the *SMN1* gene. This process uses the same dried blood spots already collected for screening of other disorders. Newborns missing key parts of the *SMN1* gene are at high risk for SMA. They need more testing to know whether they have the disorder and to identify the right treatment.

Public health impact

Based on what is known about screening and the risk of being born with SMA, experts think that screening all newborns in the United States for SMA would find about 364 babies with the disorder each year. Each year, screening could prevent about 50 infants from needing a ventilator (breathing machine) and about 30 deaths due to SMA Type 1.

Committee decision

The Committee voted in 2018 to recommend adding SMA to the RUSP. As of 2018, the RUSP recommends that state newborn screening programs include SMA.

ABOUT THIS SUMMARY

What is newborn screening?

Newborn screening is a public health service that can change a baby's life. Newborn screening involves checking all babies to identify those few who look healthy but who are at risk for one of several serious health disorders that benefit from early treatment.

Certain serious illnesses can be present even when a baby looks healthy. If the baby does not receive screening for these illnesses early in life, a diagnosis may be delayed. Treatment started later might not work as well as earlier treatment. Newborn screening programs have saved the lives and improved the health of thousands of babies in the United States (US).

Who decides what screening newborns receive?

In the US, each state decides which disorders to include in its newborn screening program. To help states determine which disorders to include, the US Secretary of Health and Human Services provides a list of disorders recommended for screening. This list is called the Recommended Uniform Screening Panel (RUSP).

Progress in screening and medical treatments can lead to new opportunities for newborn screening. To learn how a disorder is added to the RUSP, see **Box A**.

What will this summary tell me?

In 2017, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for spinal muscular atrophy (SMA). This summary presents key review information that the Committee used to make its decision about whether to recommend adding SMA to the RUSP. It will answer these questions:

- What is SMA?
- How is SMA treated?
- How are newborns screened for SMA?
- Does early diagnosis or treatment help patients with SMA?
- What is the public health impact of newborn SMA screening in the US?
- Did the Committee recommend adding SMA to the RUSP?

Box A: Adding a Disorder to the RUSP

A committee, called the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), makes a recommendation to the US Secretary of Health and Human Services about adding specific disorders to the RUSP. The Committee bases its decision on a review of the disorder, the screen, the treatment, and the ability of newborn screening programs to check for the disorder. To learn more about the ACHDNC, visit this website.

UNDERSTANDING THE DISORDER

What is SMA?

SMA is a rare genetic disorder. People with SMA have a change in a gene called *SMN1*. Normally, this gene makes a protein that allows healthy nerves to control muscles in the body. In people with SMA, part of the *SMN1* gene is missing, and the gene does not make as much of the protein as normal. Some people with SMA can make enough of this protein with a related gene called *SMN2*. However, the *SMN2* gene does not always produce enough of the protein to keep nerve cells healthy. As a result, nerve cells that control muscles may not work correctly, causing serious health problems that, without treatment, can lead to death in the first months or years of life.

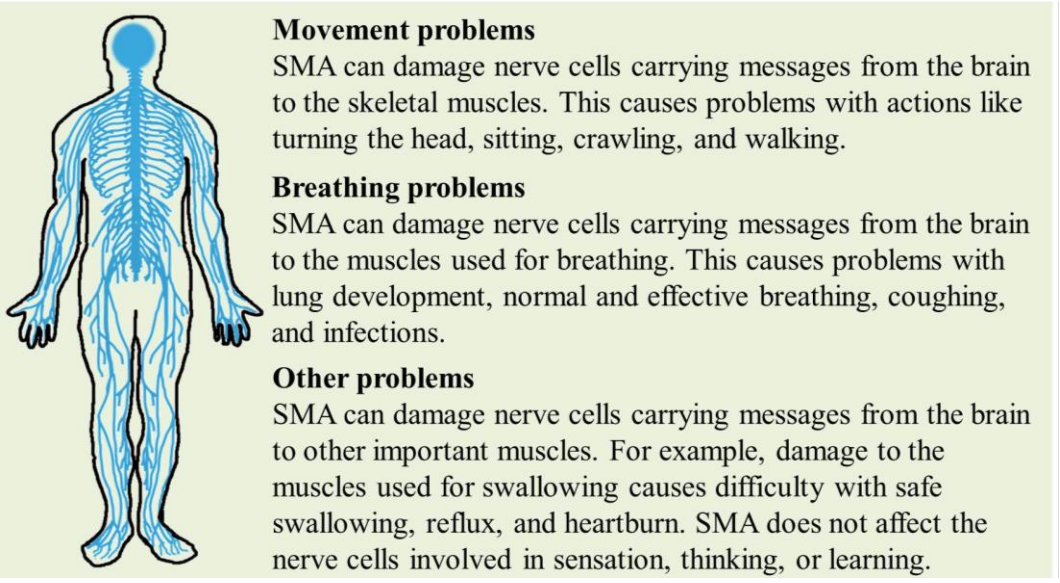
How common is SMA?

- SMA is a rare disorder. About 1 out of every 11,000 people receives a diagnosis of SMA.
- This estimate is based on the number of people who develop symptoms and receive a diagnosis without newborn screening.

What kinds of health problems does SMA cause?

SMA damages the nerve cells that carry messages from the brain to the muscles of the body (Figure 1). This causes muscle weakness and leads to difficulty with many important actions. SMA does not affect nerves involved in sensation, thinking, or learning.

Figure 1: SMA Symptoms.



Are there different types of SMA?

Yes. There are 5 main types of SMA. The types are numbered from 0 to 4 and are based on severity and when symptoms arise. SMA Type 0 can cause miscarriage or death by 6 months of age. SMA Type 1 is the type that most often causes serious symptoms in early childhood. Most babies who have a diagnosis of SMA have Type 1.

When do SMA symptoms develop?

The timing and type of problems caused by SMA vary between the different SMA types. Table 1 explains when and what type of symptoms may arise for each type.

Table 1: Symptom Timing and Type.

SMA Type	Symptom Onset	Symptom Details
0	At birth	● This type can cause miscarriage or death by 6 months of age. ● Breathing problems and weakness are common. ● Babies with this type never learn to roll or sit.
1	<6 months	● Breathing problems and weakness are common. Symptoms get worse over time. ● Babies with this type never learn to sit and may lose the ability to swallow safely. ● Most babies with this type die by 2 years of age.
2	6 to 15 months	● Symptoms include breathing problems and weakness. Symptoms get worse over time. ● Babies with this type learn to sit but not stand. They may lose the ability to sit or swallow safely. ● People with this type usually survive into their 20s.
3	12 months to adolescence	● Symptoms include breathing problems and muscle weakness. Symptoms can worsen over time. ● Babies with this type learn to sit and stand. Children may walk late, have an odd gait, or lose the ability to walk over time. ● People with this type usually have a normal lifespan.
4	Adulthood	● Symptoms include weakness, muscle pain, and muscle loss. Symptoms can worsen over time. ● People with this type usually have a normal lifespan.

TREATMENT FOR SMA

How is SMA treated?

There is no cure for SMA yet. However, a new treatment called nusinersen can stop SMA problems from getting worse.

Nusinersen is a drug that changes the way the body handles the genetic instructions from the *SMN2* gene to help replace the missing protein that the *SMN1* gene normally makes. This helps nerve cells survive. People receiving nusinersen get injections of the drug into the spinal canal every 4 months. This treatment can slow or even prevent SMA symptoms from getting worse. It can improve muscle function and lower the risk of death from SMA.

Other treatments are also being developed for SMA. Gene therapy is one of them. This experimental treatment replaces or corrects the *SMN1* gene. Early results of studies on gene therapy are promising, and experts are working to learn more about how much gene therapy can help people with SMA.

Other treatments for SMA are supportive. They include special nutrition or breathing care. These treatments may prolong life or lengthen the time before a child with SMA needs a ventilator (breathing machine).

What are the risks of treatment for SMA?

Nusinersen is a new treatment for SMA that was approved by the US Food and Drug Administration in December 2016. Nusinersen is a lifelong treatment. Experts are still learning about its risks and benefits.

Risks of nusinersen treatment relate to how it is delivered into the spinal canal. The delivery process can cause side effects, like headache or back pain, in some children. In addition, experts know that other drugs similar to nusinersen can increase the risk of kidney disease. The long-term risks of nusinersen are being studied.

FINDING NEWBORNS WHO HAVE SMA

How are newborns screened for SMA?

Newborn screening for SMA can be included along with other routine newborn screening in the first few days of life. Most newborn screening begins when a doctor or nurse collects a few drops of blood from a baby's heel and dries them onto a special piece of paper. The hospital sends these "dried blood spots" to the state's newborn screening program. The program uses a laboratory to check the dried blood spots for many disorders.

Laboratories use special tools to look for problems with the *SMN1* gene in the dried blood spots. Screening detects whether key parts of this gene are missing. Babies who are missing key parts of the *SMN1* gene have a high risk for SMA.

How well does screening for SMA work?

Experts know that screening detects most babies with SMA (about 95%). It will not find all babies with SMA. Screening does not identify what type of SMA a baby has or when a baby with SMA will develop symptoms.

What happens if newborn screening indicates a high risk for SMA?

When newborn screening results show that part of the *SMN1* gene is missing, the baby needs more blood tests. The newborn screening program works with the baby's doctor and specialists to see if the baby has SMA and to help predict when symptoms may begin, if the baby does not already have symptoms.

What are some of the benefits and risks of newborn SMA screening?

Table 2 describes the benefits and risks of newborn SMA screening as of 2018.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
• Earlier identification and diagnosis of babies with SMA.	• Screening and follow-up testing require taking blood, which can cause pain. • The timing and type of problems caused by SMA can be hard to predict based on screening and follow-up testing.
• Earlier treatment, which might improve motor function and survival.	• Earlier exposure to the possible risks of treatment. • Some babies with SMA detected through newborn screening may not need treatment right away.
• More time to plan for the future.	• Screening and follow-up testing cannot always predict the type of SMA a newborn has. This might cause more anxiety about the future.
• Health counseling and family planning for family members.	• Sometimes, people do not want to know genetic risks. Some families do not like sharing health information.

Does early diagnosis or treatment help patients with SMA?

Early diagnosis allows **early monitoring and treatment**, which seem to improve outcomes for people with SMA. Some research suggests that early treatment (when treatment begins before symptoms develop) improves motor outcomes and lowers the risk of death or needing a ventilator in people with SMA.

Experts need to learn more before they can say for sure that early treatment helps in SMA.

Box B: Where Can I Learn More?

Follow the links below to learn more about information from this summary.

- To learn more about SMA, visit the National Institutes of Health SMA website.
- Visit the Committee's website to learn more about:
  - Nominating conditions to the RUSP.
  - The full SMA evidence report.
  - The ACHDNC recommendation to the Secretary to add SMA to the RUSP.

PUBLIC HEALTH IMPACT

How would newborn SMA screening affect the health of the country?

Based on what is known about screening and the risk of being born with SMA, experts think that screening all newborns in the US for SMA would do the following:

- Find about 364 babies with SMA each year.
- Prevent between 16 and 100 children with SMA Type 1 from needing a ventilator each year.
- Prevent between 14 and 68 deaths due to SMA Type 1 each year.

Without screening, diagnosing SMA can take time because most babies with SMA will not have symptoms right away. Newborn screening for SMA allows diagnosis in the first weeks of life (even if a baby has no symptoms), when treatment may be most effective.

What is the status of newborn SMA screening in the US?

- At the time of the 2018 evidence review, 2 states (Massachusetts and Utah) screened newborns for SMA. Two more states (Minnesota and Missouri) had mandates to start screening for SMA.
- Most states estimated that implementing newborn SMA screening would take 1 to 3 years.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The Committee voted in 2018 to recommend adding SMA to the RUSP. The Committee based its decision on the ability of screening to find babies with SMA and evidence that early treatment was better than later treatment. In 2018, the US Secretary of Health and Human Services recommended that all newborns receive SMA screening.

To screen for any disorder, states must be prepared. They must have the right equipment and procedures. There must also be specialists who can work with families to determine whether a baby has the disorder and, if so, the best treatment.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	Advisory Committee on Heritable Disorders in Newborns and Children. The committee that oversees the RUSP.
Dried blood spot	A drop of blood that is collected from a baby's heel, dried onto a special piece of paper, and used to screen for many disorders.
Gene therapy	A type of treatment for SMA that replaces or corrects the *SMN1* gene.
Nusinersen	A treatment for SMA that can stop SMA problems from getting worse.
SMA	Spinal muscular atrophy. A rare disorder affecting the nerves that control muscles of the body.
RUSP	Recommended Uniform Screening Panel. The list of disorders recommended for newborn screening.
Secretary of Health and Human Services	The head of the US Department of Health and Human Services. This person decides whether to add disorders to the RUSP.
SMN1	The gene responsible for causing SMA. In people with SMA, part of this gene is missing.
SMN2	A gene similar to *SMN1* that is targeted in SMA treatment.
Specialist	A doctor with expertise in a specific area of medicine.
Ventilator	A machine that helps with breathing.

Source

The information in this summary comes from the report *Evidence-Based Review of Newborn Screening for Spinal Muscular Atrophy (SMA): Final Report (v5.2)* (13 March 2018), commissioned by the ACHDNC. The report reviewed evidence on SMA screening and treatments in children through January 2018. It included both published and unpublished research. To see a copy of the report, visit this page.