
Newborn Screening for Mucopolysaccharidosis Type II

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 Mucopolysaccharidosis Type II (MPS II) to the Recommended Uniform Screening Panel (RUSP) in 2022.

About the condition

MPS II is a rare genetic condition caused by changes in a single human gene. Studies of patients with symptoms suggest that fewer than 1 out of every 100,000 people in the United States (US) has MPS II. People with MPS II have low activity of the I2S enzyme that helps break down certain waste products in cells. Babies with MPS II look normal. There are 2 main types of MPS II: the severe type and the attenuated type. Both types of MPS II can cause problems with the liver, spleen, heart, airways, lungs, bones, joints, abdomen, head and neck, ears, mouth, nose, skin, throat, brain, movement, and behavior. People with the severe type of MPS II have more brain and behavior problems. Problems from MPS II can cause early death.

Treatment for MPS II

There is no cure for MPS II. Early diagnosis allows early monitoring and treatment. Enzyme replacement therapy (ERT) is the most common treatment for MPS II. People with MPS II who get ERT have treatment for a few hours once a week at a hospital. ERT can slow down the disease process. It may also help people with both types of MPS II live longer.

Detecting MPS II in newborns

Newborn screening for MPS II can be included with routine newborn screening for other conditions in the first few days of life. Newborn screening for MPS II measures I2S enzyme activity. This process uses the same dried blood spots already collected for screening of other conditions. Newborns with low I2S activity are at a higher risk for MPS II. They need more testing to know if they have MPS II and to find the right treatment.

Public health impact

Experts used what is known about screening and the risk of being born with MPS II to assess the public health impact of screening. They think that screening all newborns in the US for MPS II would find about 59 babies with MPS II each year. This is the same as about 1.6 out of every 100,000 children born.

Committee decision

The Committee voted in 2022 to recommend adding MPS II to the RUSP. As of August 2022, the RUSP recommends that state newborn screening programs include MPS II.

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 find those few who look healthy but who are at risk for one of several serious health conditions 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 conditions to include in its newborn screening program. To help states determine which conditions to include, the US Secretary of Health and Human Services provides a list of conditions 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 condition is added to the RUSP, see **Box A**.

What will this summary tell me?

In 2021, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for Mucopolysaccharidosis Type II (MPS II). This summary presents key information that the Committee used to decide whether to recommend adding MPS II to the RUSP. It will answer these questions:

- [What is MPS II?](#)
- [How is MPS II treated?](#)
- [How are newborns screened for MPS II?](#)
- [Does early diagnosis or treatment help patients with MPS II?](#)
- [What is the public health impact of newborn MPS II screening on the US?](#)
- [Did the Committee recommend adding MPS II to the RUSP?](#)

Box A: Adding a Condition 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 conditions to the RUSP. The Committee bases its decision on a review of the condition, the screen, the treatment, and the ability of newborn screening programs to check for the condition. To learn more about the ACHDNC, visit this [website](#).

UNDERSTANDING THE CONDITION

What is MPS II?

MPS II is a rare genetic condition. People with MPS II have changes in a gene called *IDS*. Normally, this gene makes an *IDS* enzyme that breaks down certain waste products in cells. In people with MPS II, the enzyme does not work properly. This lets waste products build up in the body and causes serious health problems. These problems can start during early childhood.

How common is MPS II?

MPS II is a rare condition. Currently, fewer than 1 out of every 100,000 people in the US are diagnosed clinically with MPS II.

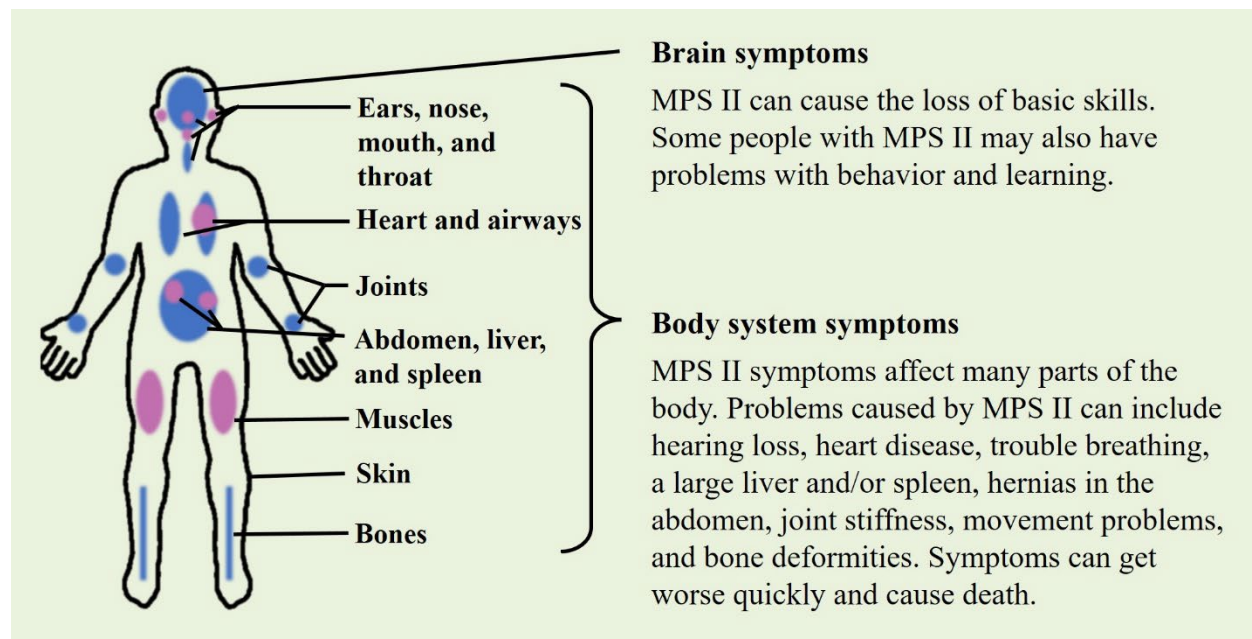
This number is based on people who have symptoms and are diagnosed without newborn screening. Not everyone with MPS II is diagnosed, so the number might be low.

More boys than girls have MPS II.

What kinds of health problems does MPS II cause?

MPS II can hurt many body systems (Figure 1). Babies with MPS II look normal, but their appearance can change over time.

Figure 1: MPS II Symptoms.



Are there different types of MPS II?

Yes. Doctors classify MPS II into 2 main types:

Severe MPS II: This type causes serious brain and behavior problems. People with this type can also have serious health problems in many body systems. Problems from severe MPS II get worse quickly without treatment.

Attenuated MPS II: This type usually causes less serious brain and behavior problems than severe MPS II. Other body systems can have the same problems as in severe MPS II. People with attenuated MPS II can have symptoms that range from mild to severe.

When do MPS II symptoms develop?

The timing and type of problems caused by MPS II vary between people. Table 1 explains when MPS II symptoms may arise.

Table 1: Symptoms and Type.

Age	Symptom	Details
Birth	Signs may not show	MPS II is present at birth. However, babies with MPS II look normal. Parents and doctors cannot tell just by looking if a baby has MPS II.
Childhood	Brain and body symptoms	Symptoms can start early in childhood. Children with MPS II often show symptoms around the age of 1 ½ years. They are often diagnosed by a doctor around age 3. Children with severe MPS II have more brain and behavior problems than children with attenuated MPS II. These problems can get worse quickly.
Adulthood	Worsening brain and body symptoms	People with MPS II have a shortened lifespan. Treatment may help them live longer.

TREATMENT FOR MPS II

How is MPS II treated?

There is no cure for MPS II. Treatment cannot fix problems already caused by MPS II. However, it may slow down the disease process.

Enzyme replacement therapy (ERT)

ERT is the main treatment for MPS II. It is the only treatment for MPS II that is approved by the US Food and Drug Administration (FDA). People who need ERT receive a 3- to 4-hour treatment every week at a hospital.

ERT puts a working I2S enzyme into the blood. This replacement enzyme makes I2S activity levels closer to normal. The most common replacement I2S enzyme cannot get into the brain to help with brain problems. Experts are testing new ways to get working I2S into the brain.

Hematopoietic Stem Cell Transplantation (HSCT)

HSCT is also called a “bone marrow transplant.” HSCT can increase I2S activity by using bone marrow from a donor who does not have MPS II.

People with MPS II who undergo HSCT get new bone marrow that makes blood cells with a working I2S enzyme. People who receive HSCT may or may not need other treatments.

What are the risks of treatment for MPS II?

Some babies have allergic reactions to ERT. Doctors monitor babies closely during treatment. Certain medicines can help with this problem. ERT does not have other major risks.

HSCT is a serious medical procedure. It can increase the risk for serious infections after the procedure and can cause other problems. Risks depend on a few things, like the match between the HSCT (“bone marrow”) donor and the person with MPS II. Because of these risks, HSCT can lead to death. Experts do not normally suggest HSCT as the first treatment for MPS II. Families offered HSCT talk to specialists about whether this treatment is right for their child.

FINDING NEWBORNS WHO HAVE MPS II

How are newborns screened for MPS II?

Newborn screening for MPS II can be included 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 conditions.

To screen for MPS II, laboratories use special equipment to measure I2S enzyme activity in the dried blood spots. Low I2S enzyme activity means a higher risk for MPS II.

When a newborn has low I2S enzyme activity, the baby needs more tests. The newborn screening program works with the baby's doctor when screening results mean that the baby needs other tests or to see a specialist.

How well does screening for MPS II work?

Screening finds babies with low I2S activity. After more testing, some of these babies are diagnosed with MPS II. Others do not have MPS II. Screening cannot diagnose MPS II, but it can find the babies who need more tests or to see a specialist.

What happens if newborn screening indicates a high risk for MPS II?

Doctors refer newborns whose screening results show high MPS II risk for more testing. This testing involves more tests on the dried blood spots, urine tests, and an exam by a special doctor. Tests may also look at the baby's *IDS* gene. Changes in this gene can sometimes explain a baby's low I2S activity level.

Even with screening, sometimes it is still hard to tell if babies have MPS II. MPS II problems may not arise during infancy. Doctors monitor babies at high risk for MPS II when they cannot make a clear diagnosis right away.

What are some of the benefits and risks of newborn MPS II screening?

Table 2 lists the benefits and risks of newborn MPS II screening as of 2022.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
Earlier identification and assessment of babies at high risk for MPS II.	Many babies identified from newborn screening do not have MPS II. All babies with low I2S activity need more testing.
Earlier diagnosis.	The timing and type of problems caused by MPS II are hard to predict.
Earlier treatment, which may slow the disease process.	Earlier exposure to treatment risks.
More time to plan for the future.	More worry about the future.
Health counseling and family planning for family members.	Some people do not want to know genetic risks. Some families do not like sharing health information.
Reassurance for the families of babies with normal I2S activity.	Unnecessary worry for families of babies with low I2S activity who do not have MPS II.

Does early diagnosis or treatment help patients with MPS II?

Early diagnosis allows **early monitoring and treatment**, which can improve outcomes for people with MPS II.

Box B: Where Can I Learn More?

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

- To learn more about MPS II, visit the [National Institutes of Health MPS II](#) website.
- Visit the Committee's website to learn more about:
 - [Nominating conditions to the RUSP.](#)
 - [The full MPS II evidence report.](#)
 - [The ACHDNC recommendation to the Secretary to add MPS II to the RUSP.](#)
 - [The Secretary's letter to accept the ACHDNC's recommendation to add MPS II to the RUSP.](#)

PUBLIC HEALTH IMPACT

How would newborn MPS II screening affect the health of the country?

Experts used what is known about screening and the risk of being born with MPS II to assess the public health impact of screening. They think that screening all newborns in the US for MPS II would find about 59 babies with MPS II each year. This is the same as about 1.6 out of every 100,000 children born.

Without screening, diagnosing MPS II can take time. Most babies with MPS II will not have symptoms right away. Newborn screening for MPS II may allow for diagnosis in the first weeks of life, when treatment could be most effective.

What is the status of newborn MPS II screening in the US?

At the time of the report, 2 states (Illinois and Missouri) screened newborns for MPS II. Two more states (New York and North Carolina) had projects that were assessing how to screen. One state (West Virginia) had a requirement to start screening but had not started as of the report date.

Most screening programs estimated that adding newborn MPS II screening would take 1 to 3 years.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The Committee voted in February 2022 to recommend adding MPS II to the RUSP. The Committee based its decision on the ability of screening to find babies with MPS II and evidence that early treatment was better than later treatment. In August 2022, the US Secretary of Health and Human Services accepted the Committee's recommendation. The RUSP now recommends that state newborn screening programs include MPS II.

Each state will decide whether to screen newborns for MPS II. To screen for any condition, 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 condition and, if so, the best treatment.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	<u>A</u> dvisory <u>C</u> ommittee on <u>H</u> eritable <u>D</u> isorders in <u>N</u> ewborns and <u>C</u> hildren. The committee that oversees the RUSP.
Attenuated MPS II	A type of MPS II that can cause serious brain, behavior, and other body system problems. Symptoms can range from mild to severe.
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 conditions.
ERT	<u>E</u> nzyme <u>r</u> eplacement <u>t</u> herapy. A treatment for MPS II that uses a replacement I2S enzyme to make I2S activity closer to normal.
FDA	<u>F</u> ood and <u>D</u> rug <u>A</u> dministration of the United States.
HSCT	<u>H</u> ematopoietic <u>S</u> tem <u>C</u> ell <u>T</u> ransplantation.
<i>IDS</i> gene	The gene responsible for causing MPS II.
I2S enzyme	An enzyme from the <i>IDS</i> gene that normally breaks down certain waste products in cells.
MPS II	<u>M</u> ucopolysaccharidosis <u>T</u> ype <u>I</u> I. A rare genetic condition that causes serious health problems in many body systems.
RUSP	<u>R</u> ecommended <u>U</u> niform <u>S</u> creening <u>P</u> anel. The list of conditions 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 conditions to the RUSP.
Severe MPS II	A type of MPS II causing serious brain, behavior, and body system problems that get worse quickly.
Specialist	A doctor with expertise in a specific area of medicine.
US	<u>U</u> nited <u>S</u> tates.

Source

The information in this summary comes from the report *Evidence-Based Review of Newborn Screening for Mucopolysaccharidosis Type II: Final Report* (02/20/2022). This report was commissioned by the ACHDNC. It reviewed evidence on MPS II screening and treatments in children through December 31, 2021. The report included both published and unpublished research. To see a copy of this report, visit this [page](#).