

# Plain English Summary: Exploring the evidence about screening for urea cycle disorders in newborns

## What is the problem?

The UK National Screening Committee (UK NSC) wants to know if screening all newborn babies for Urea Cycle Disorders (UCDs) would help babies and their families.

UCDs are rare inherited conditions, affecting about 1 in every 52,000 babies. UCDs affect how well the body can dispose of the waste nitrogen that is a normal by-product of digesting protein. This happens because 1 of the important enzymes needed for this waste disposal is missing or does not work well. Harmful levels of ammonia can build up in the body. Within days of birth, babies can show symptoms like being sick, not wanting to eat, and feeling very tired. If UCDs are not treated, symptoms can rapidly worsen and lead to serious problems like brain swelling, coma, or even death. How quickly symptoms appear, and how severe they are, depends on which enzyme is affected and how much of it is missing.

Treatments can involve medications, special diets, or filtering the blood. During a serious episode (called a crisis), it is important to lower ammonia levels in the blood very quickly. Sometimes, a liver transplant is needed to help the body manage ammonia better. Although a transplant will not fix brain damage that has already happened, it can prevent future problems and reduce the need for ongoing treatment.

The need for long-term care reflects the severity of the condition. Some people only need to be careful when sick or having surgery. Others need to stay on a low-protein diet and take medicine for life. Some with development disabilities may require additional support.

## Why might screening not be a good idea?

All screening has the potential to cause harm as well as benefit. It can identify things that would never have caused problems, leading to unnecessary worry and treatment. Screening can sometimes raise false alarms when a test result suggests something is wrong but further tests show there's no issue, which can be stressful. Some real cases can also be missed, which can give false reassurance and delay diagnosis and treatment. Before starting or changing any screening programme, we need to understand if it works better than not screening, or better than the current approach.

## What did we do?

Before the UK NSC can make a recommendation, it needs to look at whether there is evidence to support screening. A first step is to check if there is enough reliable evidence to support exploring the topic in more depth.

We looked at 3 questions:

1. Do other countries have recommendations in place about screening for UCDs?
2. How many studies and what type of studies have looked at how well current tests work – how good are they at detecting UCDs in newborns and not wrongly identifying babies who do not have UCDs?
3. How many studies and what type of studies have looked at whether screening and subsequent intervention leads to better health outcomes overall?

## What did we find?

We found very little evidence for each of the 3 questions. For question 1, we found only 2 reports that made recommendations about screening for UCDs. For question 2, we found six studies with some information about how well current tests work. But all 6 studies had some problems in how they were conducted. This means these studies can't reliably tell us how good the tests are at detecting UCDs in newborns. For question 3, we found 7 studies that tried to compare outcomes for treating children with or without symptoms. All these studies were very small and included very few children with UCDs. The evidence is not clear if treating children who have no symptoms but were diagnosed through screening leads to better outcomes for them. Their outcomes were compared to children who were treated after their symptoms started.

## Should UK NSC commission further work on this topic?

Currently, there is not enough evidence to recommend looking at this topic in more depth.