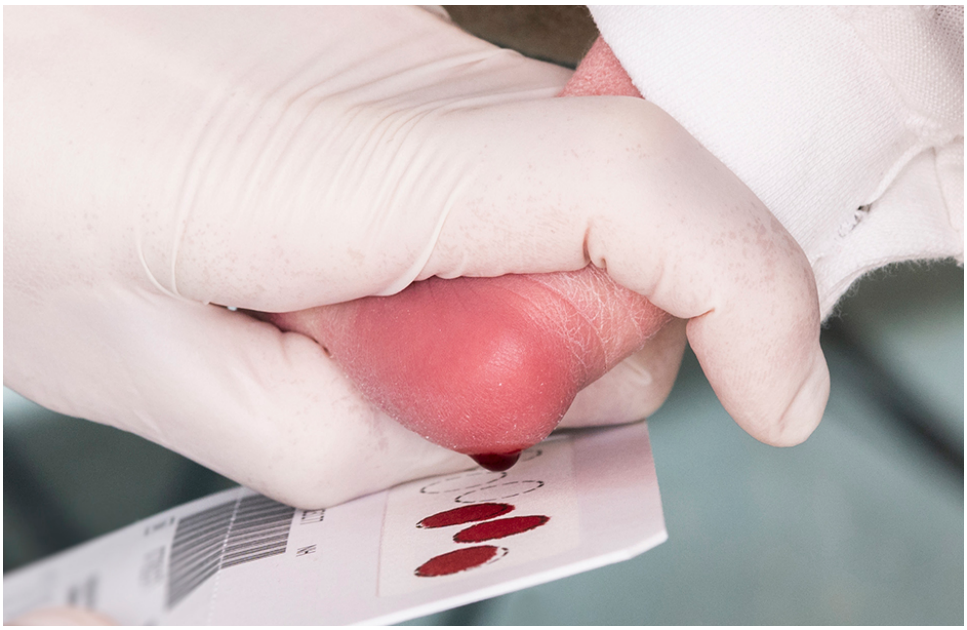
# THE NEWBORN BLOOD SPOT SCREENING IN THE NETHERLANDS

## MONITOR 2024



TNO innovation for life

The aim of the Newborn Blood Spot screening programme (NBS) is the early detection of a number of serious, rare, congenital conditions in newborns. The **target disease** is the variant of the disorder we want to detect with neonatal screening. The screening is designed to preferably detect all children with the target disease and no or as few as possible children with another variant (secondary finding). If these target diseases are detected early, irreversible health damage can be prevented or limited through timely treatment with, for example, medication or diet.

The national monitor with main results of the NBS is carried out annually by TNO at request of the RIVM-Centre for Management of Prevention Programmes and Crisis Management (RPO). The monitor enables insight into the functioning of all aspects of the NBS as well as insight into a possible need for extra measures to allow for an improvement in functioning of the screening programme. A separate monitor is made about the NBS in the Caribbean Netherlands (in Dutch).

# SUMMARY

Table 1
Results of the most important indicators for children born in 2022, 2023 and 2024

| | 2022 | 2023 | 2024 |
|---|---|---|---|
| **Number of screened children (eligible)** | 167,331 (169,196) | 164,005 (165,996) | 165,522 (167,675) |
| **Participation rate** | 98.9% | 98.8% | 98.7% |
| **Number referred (incl. OCTN2) (%)** | 482 (0.29%) | 504 (0.31%) | 517 (0.31%) |
| **Number with target disease (excl. OCTN2)** | 233 | 225 | 222 |
| **Number with still unknown diagnosis** | 1 | 9 | 1 |
| **Detection rate per 1000** | 1.392 | 1.372 | 1.341 |
| **Positive predictive value (PPV, all target diseases combined)** | 50% | 48% | 44%[1] |
| **Sensitivity** | 99% | 99% | 98%[2] |
| **Specificity** | 99.861% | 99.849% | 99.831% |
| **1st heel prick taken within 168 hours** | 98.3% | 98.6% | 98.5% |
| **1st heel prick in recommended period (72-96 hours after birth)** | 39% | 40% | 40% |
| **1st heel prick taken 72-120 hours after birth** | 71% | 72% | 71% |
| **Repeated 1st heel prick (by condition; %)** | 0.07 - 0.33%<br>HbP 0.47% | 0.09 – 0.22%<br>HbP 0.42% | 0.11 - 0.25%<br>HbP 0.42% |
| **Timely diagnosis CAH, CH, MD, HbP, CF, SCID, SMA** | 83, 81, 72, 77, 84, 86, 100% | 94, 90, 86, 79, 89, 92, 100% | 82, 86, 86, 97, 82, 84, 100% |
| **Costs per child screened** | € 146 | € 165 | € 182 |
| **Objection to use of residual blood for scientific research** | 8.9% | 11.2% | 12.2% |

Green: target value met; red: target value not met

[1] In 2024, target values for the positive predictive value are met for most diseases, but not for CF (64%; target > 65%) and the metabolic diseases CPT1, GALT, GA-1, IVA, MMA, TYR-1 and VLCAD (respectively 0%, 13%, 0%, 13%, 4%, 13% and 10%; target >30%), although there is no clarity for MMA due to the lack of a definition for the target disease.

[2] Four children born in 2024 were reported as false negative (all for CF). The target value of 100% for sensitivity of CF was thus not achieved. Furthermore, three children from an earlier birth year were reported as false negative: 1 child with CF (born in 2019), and 2 children with LCHAD (born in 2015 and 2017).

# RECOMMENDATIONS

- Intensify actions to improve **timeliness of the first heel prick.** More attention is needed for the optimal period for the 1st heel prick: this is 72 to 96 hours after birth. It is also desirable to encourage faster birth registration and to speed up the subsequent assignment of blood collection to the screeners. Adding the time of birth to the birth data can help to timely plan heel prick sampling.
- Screeners engage in conversation with parents who **refuse** heel prick screening, and try to ascertain whether the parents have the correct information about the screening. For this, a guideline for screeners would be helpful.
- Continued attention to **timely diagnosis.** Still too many children are older than desirable when they first see the paediatrician.
- Continued focus on **false-negative results** and **missed patients.** Although the number is very low, it remains important to investigate the cause and discuss whether this can be prevented.
- In the case of the metabolic disease **MMA, more clarity is needed regarding the definition of the target disease**, in order to make it possible to assess the PPV for MMA. Over the past five years, there have been 123 referrals for MMA, of which, depending on the final definition, ptentially more than 90% may not have the target disease. **Registration in Neorah** can be improved to clarify which children with a false-positive referral have another treatable condition and therefore still benefit from the referral.
- In the case of the metabolic disease **CPT1,** the number of false-positive referrals has been relatively high for already three years among children who are screened at an older age. The heel prick test is not distinctive enough to detect CPT1 in older children. It is urgent to carry out the evaluation recommended last year as soon as possible and to **implement a change in the test or cut-off values to prevent false-positive referrals for CPT1 in older children.**
- In children with **SMA, accelerating blood collection, screening and referral** can lead to health gains. Some of the children detected with SMA are so severely affected at birth that treatment is not medically viable. These children will pass away. To speed up the process, it can be investigated whether it is possible to adjust the order of analysis in heel prick cards with insufficient blood, giving priority to test for SMA over conditions where timeliness is less important.

### DATA SOURCES

The screening data in this monitor originate from the Praeventis registration system of the RIVM. Diagnostic data originate from the NEORAH registration system of the RIVM (www.neorah.nl). The NEORAH data related to metabolic diseases have been retrieved from the Dutch Diagnosis Registration Metabolic Diseases (www.ddrmd.nl). Paediatricians report missed patients to RIVM (see 'draaiboek hielprikscreening' (in Dutch)– Kinderarts). This monitor concerns children who were born in 2024 (Praeventis reference date: 6-3-2025, NEORAH: 22-4-2025 or later).

## READING GUIDE

This monitor differentiates between the first heel prick, a repeat first heel prick, a second heel prick and a repeat second heel prick:

- First heel prick: the first heel prick that has been carried out;
- Repeat first heel prick: the newborn blood spot collection that is repeated because insufficient blood has been collected during the first heel prick in order to carry out the required laboratory analyses ('insufficient filling') or because the material is unreliable (contamination), or because the first heel prick was taken too early (within 48 hours after birth), or because a child received a blood transfusion within 24 hours before the heel prick was carried out. If a blood transfusion with erythrocytes has been carried out, the heel prick needs to be repeated after 91 days to test for haemoglobinopathies (HbP);
- Second heel prick: carried out if the first heel prick gives an inconclusive laboratory result;
- Repeat second heel prick: redoing the 2nd heel prick for reasons mentioned in the repeated 1st heel prick.

In this monitor the colours green and red indicate whether the results meet the prior indicated signal- or target values.

- The values which fall within the indicated limits are indicated in green.
- Values outside the formulated limits are indicated in red. If possible, actions can be taken to improve the results or to get the results to fall within the limits of the target value.
- Signal- or target values for trends do not exist. Trends which require vigilance, are indicated in orange. Stable trends are indicated in green.

## WHICH CONDITIONS ARE INCLUDED IN THE SCREENING?[1]

- **Congenital adrenal hyperplasia (CAH)**
- **Cystic fibrosis (CF)**
- **Congenital hypothyroidism (CH)**
- **Severe combined immunodeficiency (SCID)** *(since January 1st, 2021)*
- **Spinal muscular atrophy (SMA)** *(since June 1st, 2022)*
- **Hemoglobinopathies (HbP)**
  - Sickle cell disease (SCD)
  - HbH-disease (HbH), a form of alpha-thalassemia
  - Beta-thalassemia major (bTM)
- **Metabolic diseases (MD):**
  - 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)[2]
  - Adrenoleukodystrophy (ALD) *(since October 1st, 2023)*
  - Biotinidase deficiency (BIO)
  - Carnitine palmitoyltransferase deficiency type 1 (CPT1)
  - Galactokinase deficiency (GALK) *(since October 1st, 2020)*
  - Galactosemia (GALT)
  - Glutaric acidemia type I (GA-I)
  - HMG-CoA lyase deficiency (HMG)[2]
  - Isovaleric aciduria (IVA)
  - Maple syrup urine disease (MSUD)
  - Medium-chain acylCoA dehydrogenase deficiency (MCAD)
  - Methylmalonic acidemia (MMA)
  - Mucopolysaccharidose type 1 (MPS I) *(since March 1st, 2021)*
  - Multiple CoA carboxylase deficiency (MCD)[2]
  - Phenylketonuria (PKU)
  - Propionic Acidemia (PA)
  - Trifunctional Protein deficiency/ Long-chain hydroxyacyl-CoA dehydrogenase deficiency (TFP/LCHAD)
  - Tyrosinemia type I (TYR-I)
  - Very-long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

More information about these conditions can be found on the RIVM website:
https://www.pns.nl/hielprik

[1] OCTN2 deficiency and SCD carrier status are not part of the screening program; they are secondary findings. The results will be reported back to parents. The SCD carrier status will be reported back only if there is no objection from parents.
[2] These three conditions are reported combined under one name, 3-MHM, since they have the same screening marker.

## PARTICIPATION

In 2024 167,675 children were eligible to participate in the NBS. This is almost 1,700 more children than in 2023. A heel prick was performed on 165,522 children. This means that the participation rate in 2024 is 98.7%, which is lower than the signal value of 99.0% (as in 2022 and 2023). There has been a downward trend since 2020 (Figure 1).

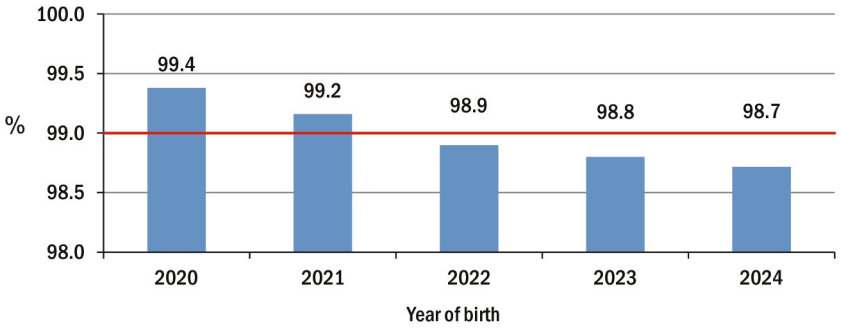



**Figure 1**
Participation rate of the neonatal screening programme by year of birth (2020-2024); to support readability the y-axis starts at 98%; the red line indicates the target value.

Figure 2 shows that parents more often object to participate than in previous years (red bars). The number of children 'Tested elsewhere', such as a heel prick abroad, is in 2024 similar to previous years (0.19% in 2024). The reasons 'left/untraceable' (e.g. left the country, or child untraceable), 'unknown' and 'too old' are rare (respectively 0.05%, 0.02% and 0.03% in 2024).

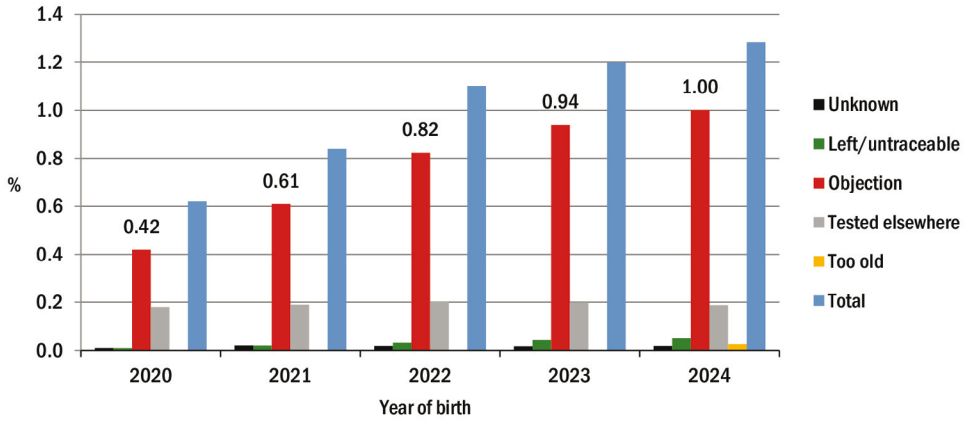



**Figure 2**
Reasons for non-participation in the neonatal screening programme by year of birth (2020-2024)

## TIMELINESS OF BLOOD COLLECTION

The heel prick should be carried out between 72 and 168 hours after birth, but ideally as soon as possible after 72 hours (or after 96 hours in the case of simultaneous neonatal hearing screening). In 2024 the percentage of first heel pricks carried out within 168 hours after birth is 98.5% (excluding children born abroad). This is a similar to previous years (figure 3). The target value of at least 99.0% still has not been achieved. Late birth registration and weekend days complicate timely screening.

In 39.5% of children, newborn blood spots were collected in the recommended period between 72 and 96 hours after birth (table 1). This seems to be a good outcome in the current situation, as we know from the hearing screening monitors that circa 79% of the heel pricks is combined with the hearing screening, with the latter to be performed from 96 hours after birth. In 71.1% of children, the heel prick was performed 72-120 hours after birth (target value since 2022: ≥ 80%).

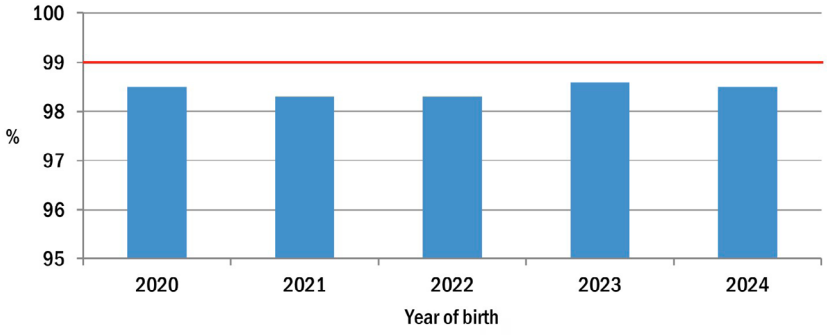



**Figure 3**
Timeliness of the blood spot collection by year of birth (2020-2024). Children born outside the Netherlands are excluded. To support readability the y-axis starts at 95%. The red line indicates the target value.

## REPEAT FIRST HEEL PRICK

In 2024, 733 children received one or two repeated 1st heel pricks (0.44% of participants; 1x in 715, 2x in 18 children). In 26 of them, the reason was premature 1st collection.

As in 2023, the target values were met for all conditions (table 2). Yet, the percentages of repeat first heel pricks increased for all conditions in 2024 compared to 2023, except for HbP and ALD.

**Table 2**
Repeated first heel pricks* according to birth year (2020-2024)

| % of repeated first heel pricks | | 2020 | 2021 | 2022 | 2023 | 2024 | Number in 2024 | Target value |
|---|---|---|---|---|---|---|---|---|
| **CAH** | | 0.04 | 0.06 | 0.07 | 0.09 | 0.11 | 187 | ≤0.30 |
| **CH** | | 0.22 | 0.27 | 0.29 | 0.21 | 0.25 | 420 | ≤0.30 |
| **CF** | | 0.24 | 0.30 | 0.31 | 0.22 | 0.24 | 403 | ≤0.30 |
| **HbP** | | 0.43 | 0.47 | 0.47 | 0.42 | 0.42 | 701 | ≤0.50 |
| **MD** | 3-MHM | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 308 | ≤0.30 |
| | ALD | | | | 0.18 | 0.15 | 246 | ≤0.30 |
| | BIO | 0.26 | 0.35 | 0.32 | 0.21 | 0.24 | 400 | ≤0.30 |
| | CPT1 | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 309 | ≤0.30 |
| | GALK | 0.10 | 0.14 | 0.17 | 0.15 | 0.16 | 263 | ≤0.30 |
| | GALT | 0.11 | 0.13 | 0.16 | 0.14 | 0.16 | 261 | ≤0.30 |
| | GA-1 | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 310 | ≤0.30 |
| | IVA | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 310 | ≤0.30 |
| | MSUD | 0.09 | 0.10 | 0.13 | 0.13 | 0.14 | 238 | ≤0.30 |
| | MCADD | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 310 | ≤0.30 |
| | MMA | 0.12 | 0.14 | 0.16 | 0.18 | 0.19 | 310 | ≤0.30 |
| | MPS I | | 0.33 | 0.33 | 0.22 | 0.25 | 417 | ≤0.30 |
| | PA | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 306 | ≤0.30 |
| | PKU | 0.09 | 0.10 | 0.13 | 0.13 | 0.14 | 238 | ≤0.30 |
| | TFP/LCHAD | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 310 | ≤0.30 |
| | TYR-1 | 0.09 | 0.10 | 0.13 | 0.13 | 0.14 | 238 | ≤0.30 |
| | VLCAD | 0.12 | 0.14 | 0.16 | 0.17 | 0.19 | 310 | ≤0.30 |
| | OCTN2 | 0.10 | 0.10 | 0.13 | 0.13 | 0.14 | 238 | ≤0.30 |
| **SCID** | | | 0.31 | 0.30 | 0.21 | 0.24 | 390 | ≤0.30 |
| **SMA** | | | | 0.32 | 0.22 | 0.25 | 415 | ≤0.30 |

* Based on 'unclassifiable' result for 1st heel prick, i.e. insufficient/unreliable blood or <24 hours after blood transfusion. Heel pricks that were carried out too early (<48 hours after birth, n=26 in 2024) are not included.

## SECOND HEEL PRICK

In 2024 0.32% of the CH results of the first heel prick indicated the need for a second heel prick. For OCTN2, SCID and SMA this was 0.042%, 0.030%, and 0.002% respectively. The target values for this indicator were reached for all target conditions, but not for OCTN2 (table 3).

**Table 3**
Percentage second heel prick according to birth year (2020-2024)

| | 2020 | 2021 | 2022 | 2023 | 2024 | Number in 2024 | Target value |
|---|---|---|---|---|---|---|---|
| **CAH**[1] | 0.049 | 0.044 | | | | | ≤0.09 |
| **CH** | 0.28 | 0.28 | 0.32 | 0.30 | 0.32 | 535 | ≤0.40 |
| **OCTN2**[2] | 0.027 | 0.036 | 0.031 | 0.043 | 0.042 | 70 | ≤0.04 |
| **SCID** | | 0.052 | 0.026 | 0.018 | 0.030 | 49 | ≤0.06 |
| **SMA** | | | 0.001 | 0.001 | 0.002 | 3 | ≤0.02 |

[1] For CAH, second heel pricks has been replaced by an additional analysis on the blood from the first heel prick since October 1, 2021.
[2] OCTN2 is an incidental finding. In the event of an inconclusive result for OCTN2, a second heel prick is performed. If both results are inconclusive, the child will be referred. In that case, other metabolic disorders with a screening based on acylcarnitines are unclassifiable and are further examined in the hospital.

## REFERRALS

In 2024, a total of 517 referrals were made as a result of the heel prick (table 4). This includes 15 referrals for the incidental finding OCTN2. This gives a total referral rate of 0.31% of the number of screened children in 2024. This is equal to 2023 and slightly higher than in the years before.

In 2024, the referral rates for individual conditions are similar to previous years. Only for GA-1 the referral rate in 2024 is higher than in previous years. For CPT1, relatively many children are referred who are already weeks old at blood collection.

**Table 4**
Referrals according to birth year (2020-2024)

| % referrals | | 2020 | 2021 | 2022 | 2023 | 2024 | Number in 2024 | Trend |
|---|---|---|---|---|---|---|---|---|
| **CAH** | | 0.012[1] | 0.012 | 0.004 | 0.010[1] | 0.006 | 11[1] | Low in 2022 |
| **CH** | | 0.135[1] | 0.135[1] | 0.139[1] | 0.129[1] | 0.140[1] | 231[1] | Stable |
| **CF** | | 0.016 | 0.022 | 0.020 | 0.023 | 0.027 | 45 | Stable |
| **HbP** | *subtotal* | *0.022* | *0.025* | *0.029* | *0.029* | *0.022* | *37* | |
| | SCD | 0.014 | 0.017 | 0.019 | 0.019 | 0.016 | 26 | Stable |
| | HbH | 0.004 | 0.005 | 0.003 | 0.007 | 0.003 | 6 | High in 2023 |
| | bTM | 0.004 | 0.003 | 0.008 | 0.004 | 0.003 | 5 | High in 2022 |
| **MD** | *subtotal* | *0.081* | *0.081* | *0.081* | *0.099* | *0.095* | *158* | |
| | 3-MHM | 0.007 | 0.006 | 0.009 | 0.010 | 0.008 | 13 | Stable |
| | ALD | | | | 0.001[2] | 0.001 | 1 | - |
| | BIO | 0.005 | 0.005 | 0.005 | 0.004 | 0.007 | 12 | Stable |
| | CPT1 | 0.001 | 0.002 | 0.002 | 0.006 | 0.006 | 10 | Increase in 2023 |
| | GALK | 0.002[2] | 0.001 | 0.001 | 0 | 0.001 | 2 | Stable |
| | GALT | 0.006 | 0.006 | 0.005 | 0.007 | 0.004 | 8 | Stable |
| | GA-1 | 0.001 | 0.001[1] | 0.001 | 0.002 | 0.005 | 9 | High in 2024 |
| | IVA | 0.004 | 0.003 | 0.003 | 0.003 | 0.004 | 8 | Stable |
| | MSUD | 0.002 | 0.001[1] | 0.001 | 0 | 0.001 | 2 | Stable |
| | MCADD | 0.013[1] | 0.009 | 0.012 | 0.011 | 0.010 | 17 | Stable |
| | MMA | 0.014 | 0.016 | 0.011 | 0.019 | 0.013 | 23 | High in 2023 |
| | MPS I | | 0.003[2] | 0.002 | 0.003 | 0.002 | 3 | Stable |
| | PA | 0.001 | 0.002 | 0.001 | 0.001 | 0.002 | 3 | Stable |
| | PKU | 0.007 | 0.007[1] | 0.011 | 0.009 | 0.008 | 13 | Stable |
| | TFP/LCHAD | 0.001 | 0.001 | 0.001 | 0.002 | 0.001 | 1 | Stable |
| | TYR-1 | 0.005 | 0.004 | 0.001 | 0.001 | 0.004 | 8 | Stable |
| | VLCAD | 0.007 | 0.006 | 0.007 | 0.007 | 0.006 | 10 | Stable |
| | OCTN2 | 0.008 | 0.010 | 0.009 | 0.013 | 0.009 | 15 | Stable |
| **SCID** | | | 0.016 | 0.008[1] | 0.007 | 0.011[1] | 19 | High in 2021 |
| **SMA** | | | | 0.010[2] | 0.010 | 0.010 | 16 | Stable |
| **Total referral rate** | | 0.27 | 0.29 | 0.29 | 0.31 | 0.31 | 517 | Stable |

[1] Excluding children who died before a referral could be made. In 2024, 12 for CH and 2 for SCID.
[2] Number applies to only a part of the year: GALK is added to the screening programme per 1-10-2020, MPS I per 1-3-2021, SMA per 1-6-2022, ALD per 1-10-2023.

## DIAGNOSTIC RESULTS

In 2024, 502 children (excluding OCTN2) were referred for a target disease of the screening programme. In 222 (44%) cases one of these conditions was confirmed (table 5). This percentage is slightly lower than in 2023 (47%). Children with a referral for OCTN2 deficiency (15 referrals, of which 1 was diagnosed with OCTN2) are not included in these numbers, because this condition is not a target condition of the screening programme, but an incidental finding. For 1 of the 502 referred children, no diagnosis was (yet) known at the time of writing this monitor. Of the children born in 2024, four children were reported with a false-negative result: all for CF.

**Table 5**
Diagnostic results of referred children born in 2024 (excl. OCTN2)

| 2024 | | Referred | Diagnosis confirmed | No target disease | Diagnosis (still) unknown | False negative (test wrongly indicates no need for referral)[1] | Missed/ Other[1] |
|---|---|---|---|---|---|---|---|
| **CAH** | | 11 | 8[2] | 3 | 0 | 0 | 1[3] |
| **CH** | | 231 | 78 | 152 | 1 | 0 | 1[4] |
| **CF** | | 45 | 29[5] | 16 | 0 | 4 | 0 |
| **HbP** | SCD | 26 | 26 | 0 | 0 | 0 | 0 |
| | HbH | 6 | 3 | 3[6] | 0 | 0 | 0 |
| | bTM | 5 | 4 | 1 | 0 | 0 | 0 |
| **MD** | 3-MHM | 13 | 4 | 9 | 0 | 0 | 0 |
| | ALD | 1 | 1 | 0 | 0 | 0 | 0 |
| | BIO | 12 | 6 | 6 | 0 | 0 | 0 |
| | CPT1 | 10 | 0 | 10 | 0 | 0 | 0 |
| | GALK | 2 | 1 | 1 | 0 | 0 | 0 |
| | GALT | 8 | 1 | 7 | 0 | 0 | 0 |
| | GA-1 | 9 | 0 | 9 | 0 | 0 | 0 |
| | IVA | 8 | 1 | 7 | 0 | 0 | 0 |
| | MSUD | 2 | 0 | 2 | 0 | 0 | 0 |
| | MCADD | 17 | 17 | 0 | 0 | 0 | 0 |
| | MMA[7] | 23 | 1[7] | 22[7] | 0 | 0 | 0 |
| | MPS I | 3 | 3 | 0 | 0 | 0 | 0 |
| | PA | 3 | 3 | 0 | 0 | 0 | 0 |
| | PKU | 13 | 13 | 0 | 0 | 0 | 0 |
| | TFP/LCHAD | 1 | 0 | 1 | 0 | 0 | 0 |
| | TYR-1 | 8 | 1 | 7 | 0 | 0 | 0 |
| | VLCAD | 10 | 1 | 9 | 0 | 0 | 0 |
| **SCID** | | 19 | 5 | 14 | 0 | 0 | 0 |
| **SMA** | | 16 | 16 | 0 | 0 | 0 | 0 |
| **Total** | | 502 | 222 | 279 | 1 | 4 | 2 |

[1] 'False negative (test wrongly indicates no need for referral)' refers specifically to children who have not been detected by the screening test. Missed patients for other reasons (e.g. administrative) fall under the indicator 'Missed/other'. 'Other' also includes children with a condition but without an abnormal screening result because they are already receiving treatment.
[2] CAH: 7 of 8 children had classic salt-wasting CAH and 1 child had classic non-salt wasting CAH.
[3] CAH: one child with CAH was detected prenatally. Because treatment had already started before the heel prick was performed, the heel prick test result was negative. This child is therefore not counted as a false negative.
[4] CH: one child with CH was examined in hospital after an inconclusive first heel prick test. As a result, the screening (second heel prick) was not completed.
[5] CF: 4 children with a meconium ileus (MI).
[6] HbH: all 3 children had a mild form of alpha-thalassaemia.
[7] MMA: the definition of target disease is still under review: the diagnostic results may change. Three of the 22 children referred but without MMA had a different condition and 7 had maternal B12 deficiency. As the other causes are not recorded unambiguously in Neorah, this is probably a (substantial) under-estimate of the number explained by vitamin B12 deficiency.

## DETECTION RATES AND VALIDITY

Table 6 shows the detection rates (per 1000 screened children), the positive predictive value (PPV), the sensitivity (Sens) and specificity (Spec) of the programme. An explanation of these indicators can be found elsewhere.

The detection rates of 2024 are comparable to those of previous years for most conditions (stable since 2020).

In 2024, the target values of the PPV (see footnote under table 6) have been reached for CAH, CH, SCD, HbH, bTM, 3-MHM, BIO, MCADD, PKU, SCID and SMA. For CF the target value of >65% was not met. In addition, the signal value of >30% for the other MD with at least 5 referrals was not achieved for CPT1, GALT, GA-1, IVA, MMA, TYR-1 and VLCAD. For CPT1, the test does not appear to work well in children who get the heel prick at an older age. All referrals for these children were false positives. The overall PPV (44%) is similar to the 2020-2024 average.

In 2024, the target values for sensitivity were achieved for all conditions except CF, due to four false-negative results. The target values for specificity were met for all conditions, except MMA.

**Table 6**
Number referred (N), detection rate, positive predictive value (PPV), sensitivity (Sens) and specificity (Spec) in children born in 2024 and for period 2020-2024 combined (excl. OCTN2)[1]

| | | 2024 | | | | | 2020-2024 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | Detection rate (per 1000) | PPV[3] (%) | Sens (%) | Spec (%) | N | Detection rate (per 1000) | PPV[3] (%) | Sens (%) | Spec (%) |
| **CAH** | | 11 | 0.048 | 73 | 100 | 99.998 | 77 | 0.054 | 61 | 100 | 99.997 |
| **CH** | | 231 | 0.471 | 34 | 100 | 99.908 | 1145 | 0.481 | 36 | 98.8 | 99.915 |
| **CF** incl. MI | | 45 | 0.175 | 64 | 87.9 | 99.990 | 183 | 0.139 | 66 | 91.4 | 99.993 |
| excl. MI | | 41 | 0.151 | 61 | 86.2 | 99.990 | 172 | 0.125 | 63 | 90.6 | 99.993 |
| **HbP** | SCD | 26 | 0.157 | 100 | 100 | 100 | 142 | 0.165 | 99 | 100 | 100 |
| | HbH | 6 | 0.018 | 50 | 100 | 99.998 | 37 | 0.020 | 46 | 100 | 99.998 |
| | bTM | 5 | 0.024 | 80 | 100 | 99.999 | 36 | 0.022 | 53 | 100 | 99.998 |
| **MD** | 3-MHM | 13 | 0.024 | 89 | 100 | 99.995 | 66 | 0.026 | 33 | 100 | 99.995 |
| | ALD[2] | 1 | 0.006 | | 100 | 100 | *2* | *0.025* | *100* | *100* | *100* |
| | BIO | 12 | 0.036 | 50 | 100 | 99.996 | 45 | 0.021 | 40 | 100 | 99.997 |
| | CPT1 | 10 | 0 | 0 | - | 99.994 | 30 | 0.002 | 7 | 100 | 99.997 |
| | GALK[2] | 2 | 0.006 | | 100 | 99.999 | *5* | *0.001* | *20* | *100* | *99.999* |
| | GALT | 8 | 0.006 | 13 | 100 | 99.996 | 49 | 0.014 | 24 | 100 | 99.996 |
| | GA-1 | 9 | 0 | 0 | - | 99.995 | 17 | 0.002 | 12 | 100 | 99.998 |
| | IVA | 8 | 0.006 | 13 | 100 | 99.996 | 30 | 0.011 | 30 | 100 | 99.998 |
| | MSUD | 2 | 0 | | - | 99.999 | 8 | 0.001 | 13 | 100 | 99.999 |
| | MCADD | 17 | 0.103 | 100 | 100 | 100 | 93 | 0.101 | 91 | 100 | 99.999 |
| | MMA | 23 | 0.006 | 4 | 100 | 99.987 | 123 | 0.011 | 7 | 100 | 99.987 |
| | MPS I[2] | 3 | 0.018 | | 100 | 100 | *16* | *0.020* | *81* | *100* | *100* |
| | PA | 3 | 0.018 | | 100 | 100 | 11 | 0.009 | 73 | 100 | 100 |
| | PKU | 13 | 0.079 | 100 | 100 | 100 | 69 | 0.077 | 94 | 100 | 100 |
| | TFP/LCHAD | 1 | 0 | | - | 99.999 | 15 | 0.005 | 27 | 100 | 99.999 |
| | TYR-1 | 8 | 0.006 | 13 | 100 | 99.996 | 26 | 0.004 | 12 | 100 | 99.997 |
| | VLCAD | 10 | 0.006 | 10 | 100 | 99.995 | 57 | 0.018 | 26 | 100 | 99.995 |
| **SCID[2]** | | 19 | 0.030 | 26 | 100 | 99.992 | *74* | *0.010* | *9* | *100* | *99.990* |
| **SMA[2]** | | 16 | 0.097 | 100 | 100 | 100 | *43* | *0.100* | *100* | *100* | *100* |
| **Total[2]** | | 502 | 1.341 | 44 | 98.2 | 99.831 | 2259[2] | 1.183 | 45 | 98.4 | 99.872 |

[1] The PPV, Sens and Spec are also calculated for five years combined because for some conditions only few children are referred per year. For these conditions a calculation over several years gives a more stable outcome.
[2] The total at the bottom of the table excludes conditions added to the heel prick screening less than 5 years ago. The total is thus without GALK (per 1-10-2020), SCID (per 1-1-2021), MPS I (per 1-3-2021), SMA (per 1-6-2022), and ALD (per 1-10-2023). However, the average of these conditions is shown (in italics) over the period from the start of screening until 2024.
[3] The PPV for 2024 is shown for conditions with 5 or more referrals. For the 5-year average, for the MD with 50 or more referrals, PPVs below the signal values are shown on a red background, while the unmet signal values with less than 50 referrals are shown in red numbers.
The target values for the PPV are: CAH >60%, CH >30%, SCD >90%, bTM and HbH >50%, CF >65%, SCID >10%, SMA >95%, and for the metabolic diseases PKU >60%, MCADD >70%, MPS I >50%, ALD >90% and for remaining metabolic diseases >30%.

## TIMELINESS OF DIAGNOSTICS

The timeliness of diagnostics (based on date of first contact with peadiatrician) is calculated using data from all referred children (see Indicators). After an improvement in timeliness for all conditions in 2023 (compared to 2022), the timeliness has decreased in 2024 for CAH, CH, CF and SCID. For HbP, timeliness has actually improved significantly and is (well) above the target value for the first time. In 2024, the target values are not achieved for CAH, CH, CF, MD and SCID (table 7).

**Table 7**
Timeliness of diagnostics among referred children born in 2020-2024

| Screening | 2020 | 2021 | 2022 | 2023 | 2024 | Target value |
|---|---|---|---|---|---|---|
| **CAH** | 90 | 73 | 83 | 94 | 82 | ≥90% <15 days |
| **CH** | 88 | 80 | 81 | 90 | 86 | ≥90% <15 days |
| **CF** all referrals | 77 | 72 | 72 | 89 | 82 | ≥90% <30 days |
| excl. MI | 74 | 70 | 70 | 89 | 80 | ≥90% <30 days |
| **HbP**[1] | 81 | 82 | 77 | 79 | 97 | ≥90% ≤6.0 weeks |
| **MD** (excl. OCTN2) | 89 | 88 | 84 | 86 | 86 | ≥90% <10 days (most MD), <14 days (PA/MMA) or <30 days (MPS I) |
| **SCID** | | 90 | 86 | 92 | 89 | ≥90% <15 days if TREC ≤2; <30 days if TREC >2–≤10; <15 days from aterme date for preterm children |
| **SMA** | | | 100 | 100 | 100 | ≥90% <15 days |

[1] All children referred for HPLC patterns matching with sickle cell disease, HbH-disease and beta-thalassemia.

## COSTS

In 2024, the costs of the screening programme (excluding diagnostics) were about 30.2 million euro (source: Final bill NBS, RIVM-RPO, excluding the costs for Caribbean Netherlands). Screening costs per child are approximately 182 euro. Compared to last year, there is a cost increase of approximately 10% per child screened (figure 4). This increase is mainly explained by ALD (added per 1 October 2023) being included in the costs for a full year for the first time, and by indexation of the rates for blood collection and laboratory analyses due to high inflation (6-7%). Furthermore, organisational costs have risen due to an increase in the hourly rates of RIVM, higher costs for contracts and management, a quality upgrade to comply with legislation and regulations, and requirements in the field of IT/automation. In 2024, total costs increased more than in previous years (11% relative to 27.1 million in 2023) due to the increase in the number of performed heel pricks in 2024. Over the past 5 years, screening costs have increased by 58%.

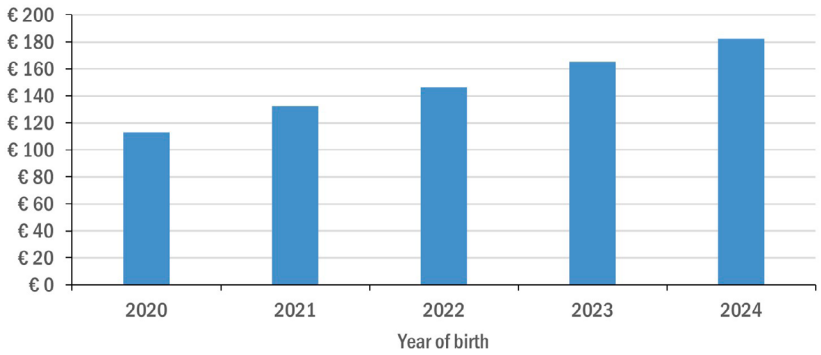



**Figure 4**
Costs of the screening programme per screened child according to year of birth (2020-2024)

## OBJECTIONS AGAINST STORAGE OF NEWBORN BLOOD

In 2023, the way parents can object to the retention of residual blood for (non-identifiable) scientific research has changed. The screener now asks parents whether they give their consent to this. Until 2023, parents could also object but were not actively asked.

In 2024 12.2% of parents objected against the storage of the NBS blood residuals for the purpose of (non-identifiable) scientific research. This percentage already showed an upward trend over time, and has risen further by 2024 (Figure 5).

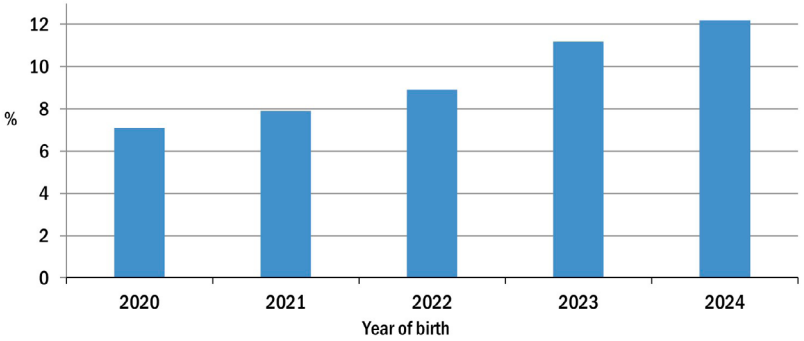



**Figure 5**
Objection of parents against the storage of NBS remnants for non-identifiable scientific research, by year of birth (2020-2024)

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