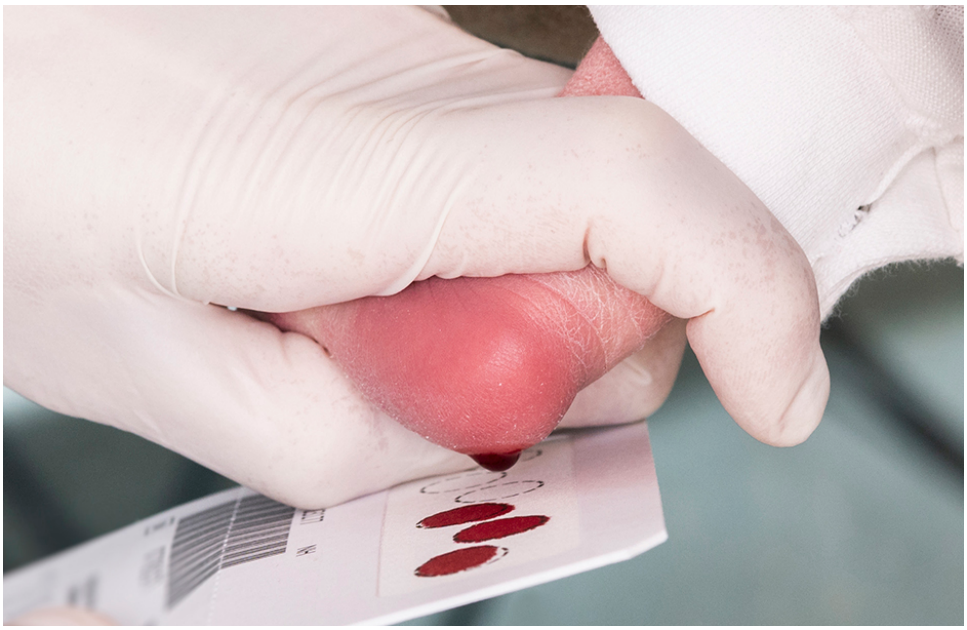
THE NEWBORN BLOOD SPOT SCREENING IN THE NETHERLANDS

MONITOR 2023



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-CvB. 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 2021, 2022 and 2023

	2021	2022	2023
Number of screened children (eligible)	179,095 (180,606)	167,331 (169,196)	164,005 (165,996)
Participation rate	99.2%	98.9%	98.8%
Number referred (incl. OCTN2) (%)	522 (0,29%)	482 (0,29%)	504 (0,31%)
Number with target disease (excl. OCTN2)	206	233	225
Number with still unknown diagnosis	10	1	9
Detection rate per 1000	1.150	1.392	1.372
Positive predictive value (PPV, all target diseases combined)	42%	50%	48%[1]
Sensitivity	99%	99%[2]	99%[2]
Specificity	99.839%	99.861%	99.849%
1st heel prick taken within 168 hours	98.3%	98.3%	98.6%
1st heel prick in recommended period (72-96 hours after birth)	39%	39%	40%
1st heel prick taken 72-120 hours after birth	70%	71%	72%
Repeated 1st heel prick (by condition; %)	0.10 - 0.35 % HbP 0.47%	0.07 - 0.33 % HbP 0.47%	0.09 – 0.22% HbP 0.42%
Timely diagnosis CAH, CH, MD, HbP, CF, SCID, SMA (since 2022)	73, 80, 88, 82, 72, 90%	83, 81, 72, 77, 84, 86, 100%	94, 90, 86, 79, 89, 92, 100%
Costs per child screened	€ 133	€ 146	€ 165
Objection to use of residual blood for scientific research	7.9%	8.9%	11.2%

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

[1] In 2023, target values for the positive predictive value are met for most diseases, but not for CF (63%; target > 65%), HbH (27%; target >50%), SCID (7%; target >10%), and the metabolic diseases CPT1, GALT, VLCAD and MMA (respectively 10%, 17%, 8%, and 6%; target >30%), although there is no clarity for MMA due to the lack of a definition for the target disease.

[2] Three children born in 2023 were reported as false-negative (1 for CH, 2 for CF). The target value of 100% for sensitivity of CH and CF was thus not achieved. Furthermore, four children from an earlier birth year were reported as false-negative: 1 child with CH (born in 2021), 2 children with CF (born in 2016 and 2022) and 1 child with homocystinuria (HCU, metabolic disease that is no longer part of the screening, born in 2009).

RECOMMENDATIONS

Existing recommendations that are still valid:

- Intensify actions to improve **timeliness of the first heel prick**. More attention is needed for the optimal period for the 1st heel prick. Furthermore, it is desirable to encourage faster birth registration.
- Screeners check with parents who **refuse** blot spot screening whether they make their choice based on the right information.
- Continued attention to **timely diagnostics, timely and clear registration** of diagnostic data, and continued attention for **false-negative results and missed patients**. Improvement is visible in timeliness and registration. The number of missed patients is very low, but it remains important to investigate the cause and discuss whether this can be prevented.
- **For the metabolic disease MMA, more clarity on the target disease is needed** so that the PPV for MMA can be assessed. In the last 5 years alone, there were more than 100 referrals for MMA, of which, depending on the final definition, potentially >80% may not have a target disease.

New recommendations:

- For the metabolic disease **CPT1**, the last 2 years have seen a relatively high number of false-positive referrals in children screened at an older age. We recommend assessing in the short term whether current screening for CPT1 meets expectations, paying particular attention to the effect of age at screening.
- In children with **SMA** with 2 or 3 SMN2 copies, speeding up blot spot collection, screening and referral may yield health benefits. It is therefore desirable that the number of SMN2 copies can already be determined with the first screening test, so that treatment can be initiated earlier. Furthermore, as long as this is not yet possible, consideration should be given to speeding up all referrals for SMA.

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). Notifications of the Dutch Paediatric Surveillance System (NSCK) have been used to detect possible missed cases until 1st of January 2020. From 1 January 2020, paediatricians report missed patients to RIVM (see 'draaiboek hielprikscreening' (in Dutch)– Kinderarts) because the NSCK has been discontinued. This monitor concerns **children who were born in 2023** (Praeventis reference data: 7-3-2024, NEORAH: 14-5-2024 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) *(**new**, since October 1st, 2023)*
  - Biotinidase deficiency (BIO)
  - Carnitine palmitoyltransferase deficiency type 1 (CPT1)
  - Galactokinase deficiency (GALK)
  - Galactosemia (GALT, formerly called GAL)
  - 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 (MCADD)
  - 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 C0 level for OCTN2 is determined in every child, because a possible deficiency makes the acylcarnitine profile unreliable. This may cause children with the metabolic disorders MCADD, VLCAD, TFP/LCHAD, IVA, GA-1 and 3-MHM to be missed. 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 2023 165,996 children were eligible to participate in the NBS. This is more than 3,000 fewer children than in 2022. A heel prick was performed on 164,005 children. This means that the participation rate in 2023 is 98.8%, which is lower than the signal value of 99.0% (as in 2022). There has been a downward trend since 2020 (Figure 1).

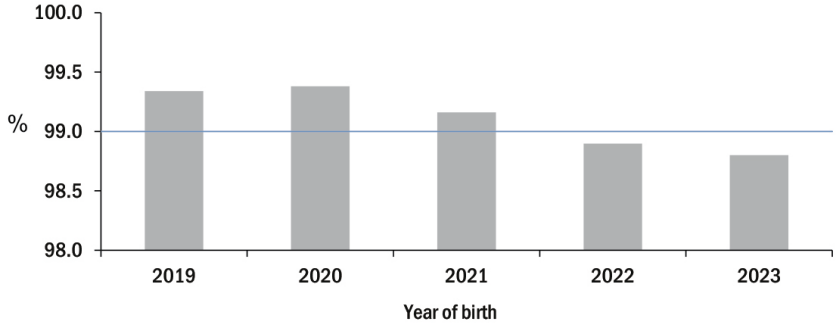


Figure 1
Participation rate of the neonatal screening programme by year of birth (2019-2023); to support readability the y-axis starts at 98%; the blue line indicates the target value.

Figure 2 shows that parents more often object to participate than in previous years (0.94% in 2023, versus 0.82% in 2022, 0.61% in 2021 and 0.42% in 2020). 'Tested elsewhere', such as a heel prick abroad, is in 2023 (0.20%) similar to 2020-2022 (respectively 0.18%, 0.19% and 0.20%), and smaller than in 2019 (0.23%). The reasons 'left' (e.g. left the country, or child untraceable) and 'unknown' are rare (respectively 0.04% and 0.02% in 2023).

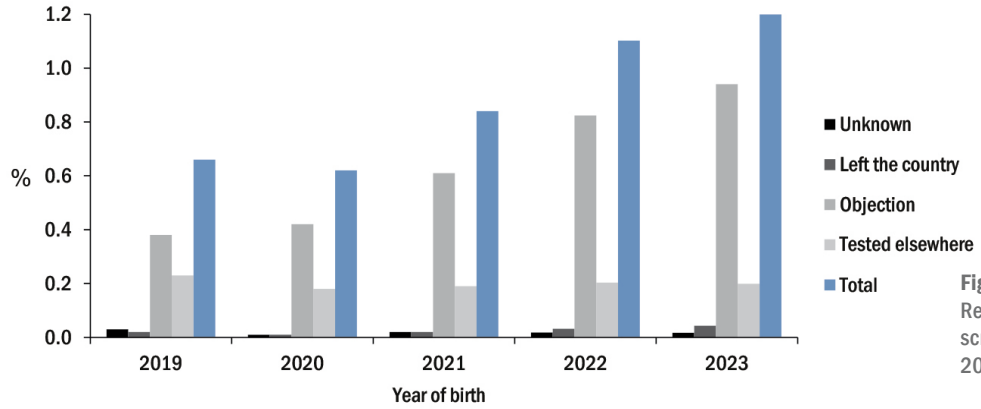


Figure 2
Reasons for non-participation in the neonatal screening programme by year of birth (2019-2023)

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 2023 the percentage of first heel pricks carried out within 168 hours after birth is 98.6% (excluding children born abroad). This is a bit higher than in previous years (98.3% - 98.5% in 2019-2022, 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 78% of the heel pricks is combined with the hearing screening, with the latter to be performed from 96 hours after birth. In 71.7% of children, the heel prick was performed 72-120 hours after birth (target value since 2022: ≥ 80%).

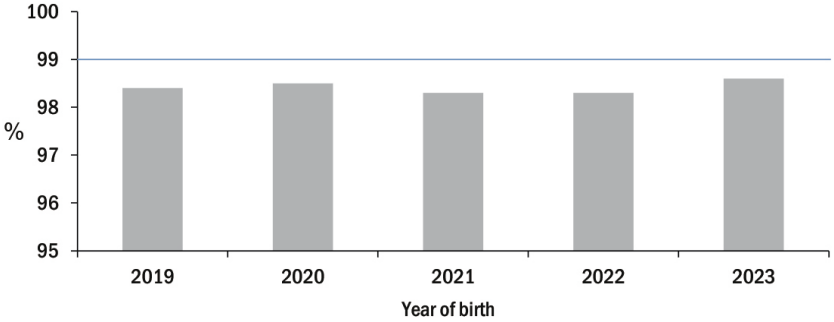


Figure 3
Timeliness of the blood spot collection by year of birth (2019-2023). Children born outside the Netherlands are excluded. To support readability the y-axis starts at 95%. The blue line indicates the target value.

REPEAT FIRST HEEL PRICK

In 2023, 678 children received one or two repeated 1st heel pricks (0.41% of 164,005 participants; 1x in 661, 2x in 17). In 26 of them, the reason was premature 1st collection (not counted in Table 2).

In contrast to 2021 and 2022, the target values (which were tightened in 2021: ≤0.50% for HbP and ≤0.30% for the other conditions) were met for all conditions. From 2019 to 2020, there was a decreasing trend in the percentage of repeat 1st heel pricks in all conditions, and in 2021 and 2022 an increase was actually visible (table 2). In 2023, an improvement is visible: the percentage is decreased or stable in many conditions.

Table 2
Repeated first heel pricks* according to birth year (2019-2023)

% of repeated first heel prick		2019	2020	2021	2022	2023	Number in 2023	Target value[1]
CAH		0.06	0.04	0.06	0.07	0.09	143	≤0.30
CH		0.27	0.22	0.27	0.29	0.21	342	≤0.30
CF		0.30	0.24	0.30	0.31	0.22	353	≤0.30
HbP		0.47	0.43	0.47	0.47	0.42	696	≤0.50
MD	3-MHM	0.18	0.12	0.14	0.16	0.17	280	≤0.30
	ALD					0.18	73	
	BIO	0.29	0.26	0.35	0.32	0.21	348	≤0.30
	CPT1	0.15	0.12	0.14	0.16	0.17	281	≤0.30
	GALK		0.10	0.14	0.17	0.15	244	≤0.30
	GALT	0.15	0.11	0.13	0.16	0.14	236	≤0.30
	GA-1	0.18	0.12	0.14	0.16	0.17	281	≤0.30
	IVA	0.18	0.12	0.14	0.16	0.17	281	≤0.30
	MSUD	0.12	0.09	0.10	0.13	0.13	211	≤0.30
	MCADD	0.18	0.12	0.14	0.16	0.17	281	≤0.30
	MMA	0.15	0.12	0.14	0.16	0.18	287	≤0.30
	MPS I			0.33	0.33	0.22	366	≤0.30
	PA	0.15	0.12	0.14	0.16	0.17	286	≤0.30
	PKU	0.12	0.09	0.10	0.13	0.13	210	≤0.30
	TFP/LCHAD	0.18	0.12	0.14	0.16	0.17	281	≤0.30
	TYR-1	0.12	0.09	0.10	0.13	0.13	210	≤0.30
	VLCAD	0.18	0.12	0.14	0.16	0.17	280	≤0.30
	OCTN2	0.12	0.10	0.10	0.13	0.13	209	≤0.30
SCID				0.31	0.30	0.21	346	≤0.30
SMA					0.32	0.22	368	≤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 (n=26 in 2023) are not included.

[1] From 2021, the target values have been tightened, from ≤0.50% for all target diseases except HbP (≤0.80%) to ≤0.30% for all target diseases except HbP (≤0.50%).

SECOND HEEL PRICK

In 2023 0.30% of the CH results of the first heel prick indicated the need for a second heel prick. For OCTN2, SCID and SMA this was 0.043%, 0.018%, and 0.001% respectively. The target values for this indicator were reached for all conditions (table 3), but not for OCTN2.

Table 3
Percentage second heel prick according to birth year (2018-2022)

	2019	2020	2021	2022	2023	Number in 2023	Target value
CAH[1]	0.042	0.049	0.044				≤0.09
CH	0.36	0.28	0.28	0.32	0.30	485	≤0.40
OCTN2[2]	0.054	0.027	0.036	0.031	0.043	71	≤0.04
SCID			0.052	0.026	0.018	29	≤0.06
SMA				0.001	0.001	1	≤0.02

[1] For CAH, 2nd heel pricks were replaced by an additional analysis on the blood from the 1st 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 2023, a total of 504 referrals were made as a result of the heel prick (table 4). This includes 22 referrals for the incidental finding OCTN2. This gives a total referral rate of 0.31% of the number of screened children in 2023. This is slightly higher than in previous years.

The referral rates for individual conditions are similar to previous years. Only for CPT1 and MMA the referral rate in 2023 is higher than in previous years. In CPT1, relatively many children are referred who are already weeks old at blood collection.

Table 4
Referrals according to birth year (2019-2023)

% referrals		2019	2020	2021	2022	2023	Number in 2023	Trend
CAH		0.012	0.012[1]	0.012	0.004	0.010[1]	17[1]	2022: low
CH		0.148	0.135[1]	0.135[1]	0.139[1]	0.129[1]	211[1]	stable
CF		0.022	0.016	0.022	0.020	0.023	37	stable
HbP	*subtotal*	*0.032*	*0.022*	*0.025*	*0.029*	*0.029*	*48*	
	SCD	0.024	0.014	0.017	0.019	0.019	31	fluctuates
	HbH	0.006	0.004	0.005	0.003	0.007	11	2023: high
	bTM	0.002	0.004	0.003	0.008	0.004	6	2022: high
MD	*subtotal*	*0.079*	*0.081*	*0.081*	*0.081*	*0.099*	*162*	
	3-MHM	0.006	0.007	0.006	0.009	0.010	16	stable
	ALD					0.001[2]	1	-
	BIO	0.010	0.005[3]	0.005	0.005	0.004	7	stable since 2020
	CPT1	0.002[2]	0.001	0.002	0.002	0.006	10	2023: high
	GALK		0.002[2]	0.001	0.001	0	0	stable
	GALT	0.004[3]	0.006	0.006	0.005	0.007	12	stable
	GA-1	0.002	0.001	0.001[1]	0.001	0.002	3	stable
	IVA	0.002	0.004	0.003	0.003	0.003	5	stable
	MSUD	0.003	0.002	0.001[1]	0.001	0	0	stable
	MCADD	0.013	0.013[1]	0.009	0.012	0.011	18	stable
	MMA	0.013[2]	0.014	0.016	0.011	0.019	31	2023: high
	MPS I			0.003[2]	0.002	0.003	5	stable
	PA	0.007[2]	0.001	0.002	0.001	0.001	1	stable
	PKU	0.008	0.007	0.007[1]	0.011	0.009	14	stable
	TFP/LCHAD	0.002	0.001	0.001	0.001	0.002	3	stable
	TYR-1	0.002[4]	0.005[4]	0.004	0.001	0.001	2	stable
	VLCAD	0.007	0.007	0.006	0.007	0.007	12	stable
	OCTN2	0.014	0.008	0.010	0.009	0.013	22	stable
SCID				0.016	0.008[1]	0.007	12	2021: high
SMA					0.010[2]	0.010	17	-
Total referral		0.29	0.27	0.29	0.29	0.31	504	stable

[1] Excluding children who died before a referral could be made. In 2023, 1 for CAH and 7 for CH.
[2] Figure applies to only a part of the year: PA, MMA and CPT1 added to the screening programme per 1-10-2019, GALK per 1-10-2020, MPS I per 1-3-2021, SMA per 1-6-2022, ALD per 1-10-2023.
[3] BIO: possibly as a result of adapted reference values for BIO per 27-1-2020.
[4] TYR-1: possibly as a result of adapted reference values per 1-4-2019.

DIAGNOSTIC RESULTS

In 2023, 482 children (excluding OCTN2) were referred for a target disease of the screening programme. In 225 (47%) cases one of the conditions was confirmed (table 5). This percentage is slightly lower than in 2022 (50%). Children with a referral for OCTN2 deficiency (22 referrals, of which 3 were 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 9 of the 482 referred children, no diagnosis was yet known at the time of writing this monitor. Of the children born in 2023, three children were reported with a false-negative result: 1 for CH, and 2 for CF.

Table 5
Diagnostic results of referred children born in 2023 (excl. OCTN2)

		Referred	Diagnosis confirmed	No target disease	Diagnosis (still) unknown	False-negative (test wrongly indicates no need for referral)[1]	Missed/ Other[1]
CAH		17	13[2]	4	0	0	0
CH		211	82	123	6	1	0
CF		37	22[3]	13	2	2	0
HbP	SCD	31	30	0	1	0	0
	HbH	11	3	8[4]	0	0	0
	bTM	6	3	3	0	0	0
DZ	3-MHM	16	5	11	0	0	0
	ALD[5]	1	1	0	0	0	0
	BIO	7	3	4	0	0	0
	CPT1	10	1	9	0	0	0
	GALK	0	0	0	0	0	0
	GALT	12	2	10	0	0	0
	GA-1	3	2	1	0	0	0
	IVA	5	2	3	0	0	0
	MSUD	0	0	0	0	0	0
	MCADD	18	16	2	0	0	0
	MMA[6]	31	2[6]	29[6]	0	0	0
	MPS I	5	5	0	0	0	0
	PA	1	1	0	0	0	0
	PKU	14	14	0	0	0	0
	TFP/LCHAD	3	0	3	0	0	0
	TYR-1	2	0	2	0	0	0
	VLCAD	12	1	11	0	0	0
SCID		12	0	12	0	0	0
SMA[6]		17	17	0	0	0	0
Total		482	225	248	9	3	0

[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: all 13 had classic salt-wasting CAH.
[3] CF: in 2023, no children were known to have meconium ileus (MI).
[4] HbH: including 3 children with a mild form of alpha-thalassaemia.
[5] ALD was added to the screening per October 1st, 2023.
[6] MMA: the definition of target disease is still under review: the diagnostic results may change. One of the 29 children referred for MMA had maternal B12 deficiency (counted as 'no target disease'). As the other causes are not recorded unambiguously in Neorah, this is probably a (substantial) underestimate 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.

The detection rates of 2023 are comparable to those of previous years for most conditions (stable since 2019). In 2023, the target values of the positive predictive value (PPV) have been reached for CAH (>60%), CH (>30%), SCD (>90%), bTM (>50%), PKU (>60%), MCADD (>70%), MPS I (>50%), ALD (>90%), SMA (>95%) and for several other metabolic diseases (>30%). For CF (>65%), HbH (>50%), and SCID (>10%) target values were not met. In addition, the signal value of >30% for the other MD with at least 5 referrals (introduced in the monitor for 2022) was not achieved for CPT1, GALT, MMA, and VLCAD. For MMA, the target disease has not yet been clearly defined. This condition is the only one that does not achieve the signal value for specificity: there seem to be many false referrals. The overall PPV (48%) is equal to the 2019-2023 average.

In 2023, the target values for sensitivity were achieved for all conditions except CH and CF, due to one false-negative result for CH and two false-negative results for CF. 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 2023 and the period 2019-2023 (excl. OCTN2)[1]

		2023					2019-2023				
		N	Detection rate (per 1000)	PPV[3] (%)	Sens (%)	Spec (%)	N	Detection rate (per 1000)	PPV[3] (%)	Sens (%)	Spec (%)
CAH		17	0.079	76	100	99.998	87	0.059	60	100	99.996
CH		211	0.500	40	98.8	99.925	1165	0.477	36	97.8	99.914
CF	incl. MI	37	0.134	63	91.7	99.992	176	0.140	70	94.4	99.994
	excl. MI	37	0.134	63	91.7	99.992	165	0.127	68	93.9	99.994
HbP	SCD	31	0.183	100	100	100	156	0.179	99	100	99.999
	HbH	11	0.018	27	100	99.995	42	0.024	48	100	99.997
	bTM	6	0.018	50	100	99.998	34	0.020	50	100	99.998
MD	3-MHM	16	0.030	31	100	99.993	62	0.027	37	100	99.995
	ALD[2,4]	1	0.025		100	100		-	-	-	-
	BIO	7	0.018	43	100	99.998	50	0.020	34	100	99.996
	CPT1[2]	10	0.006	10	100	99.995	*21*	*0.003*	*10*	*100*	*99.997*
	GALK[2]	0	0		-	100	*3*	*0*	*0*	-	*99.999*
	GALT	12	0.012	17	100	99.994	48	0.018	31	100	99.996
	GA-1	3	0.012		100	99.999	12	0.002	17	100	99.999
	IVA	5	0.012	40	100	99.998	25	0.009	32	100	99.998
	MSUD	0	0		-	100	11	0.001	9	100	99.999
	MCADD	18	0.098	89	100	99.999	98	0.106	92	100	99.999
	MMA[2]	31	0.012	6	100	99.982	*106*	*0.012*	*8*	*100*	*99.987*
	MPS I[2]	5	0.030	100	100	100	*13*	*0.021*	*77*	*100*	*99.999*
	PA[2]	1	0.006		100	100	*11*	*0.008*	*55*	*100*	*99.999*
	PKU	14	0.085	100	100	100	70	0.075	91	100	99.999
	TFP/LCHAD	3	0		-	99.998	11	0.002	18	100	99.999
	TYR-1	2	0		-	99.999	22	0.002	9	100	99.998
	VLCAD	12	0.006	8	100	99.993	59	0.019	27	94.1	99.995
SCID[2]		12	0	0	-	99.993	*55*	*0.004*	*4*	*100*	*99.990*
SMA[2]		17	0.104	100	100	100	*27*	*0.102*	*100*	*100*	*100*
Total[2]		482	1.372	48	98.7	99.849	2128[2]	1.181	48	98.3	99.872

[1] The PPV, Sens and Spec of five years combined are also calculated 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 CPT1, MMA and PA (added per 1-10-2019), 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 2023 (excluding ALD). The definition of target disease is still under review for MMA: 8% had a genetic cause for MMA (counted as target disease) and another 8% had another condition (not a target disease) or a maternal condition according to current registration. These outcomes may still change.

[3] The PPV for 2023 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.

[4] ALD is added to the screening per 1 October 2023.

TIMELINESS OF DIAGNOSTICS

The timeliness of diagnostics (based on date of first contact with peadiatrician) is calculated using data from all referred children. Timeliness has improved for all conditions compared to 2022, and the target values are met in 2023 for CAH, CH, SCID, and SMA (table 7).

Table 7
Timeliness of diagnostics among children born in 2019-2023

Screening	2019	2020	2021	2022	2023	Target value
CAH	86	90	73	83	94	≥90% <15 days
CH	86	88	80	81	90	≥90% <15 days
CF all referrals	58	77	72	72	89	≥90% <30 days
excl. MI	53	74	70	70	89	≥90% <30 days
HbP[1]	100	81	82	77	79	≥90% ≤6,0 weeks[2]
MD (excl. OCTN2)	91	89	88	84	86	≥90% <10 days (most MD), <14 d (PA/MMA), <30 d (MPS I)
SCID			90	86	92	≥90% <15 days if TREC ≤2, <30 days if TREC >2 - ≤10, <15 days from aterme date for preterm children
SMA				100	100	≥90% <15 days

[1] All children referred for HPLC patterns matching with sickle cell disease, HbH-disease and beta-thalassemia.
[2] The target value has been changed to ≥90% ≤6.0 weeks since 1-1-2020 (this was ≥90% ≤12.0 weeks).

COSTS

The costs of the screening programme (excluding diagnostics) were about 27.1 million euro in 2023 (source: Final bill NBS, RIVM-CvB, excluding the costs for Caribbean Netherlands). Screening costs per child are approximately 165 euro. Compared to last year, there is a cost increase of approximately 13% per child screened (figure 4). This increase is mainly explained by SMA (added per 1 June 2022) being included in the costs for a full year for the first time, and by substantial indexation of the rates for blood collection and laboratory analyses due to high inflation. Furthermore, organisational costs increased due to qualitative and quantitative catching up in the areas of ICT/ information provision, privacy/GDPR, contract management and electronic quality management system.

Total costs increased less (11% relative to 24.5 million in 2022) due to the decrease in the number of births in 2023. Over the past 5 years, screening costs have increased by almost 60%.

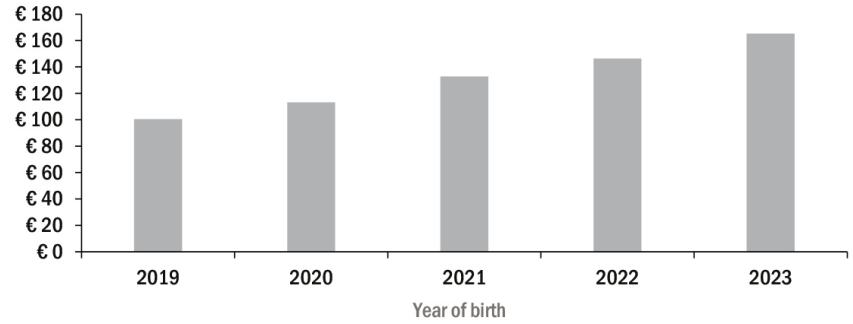


Figure 4
Costs of the screening programme per screened child according to year of birth (2019-2023)

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 2023 11.2% 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 2023 (Figure 5).

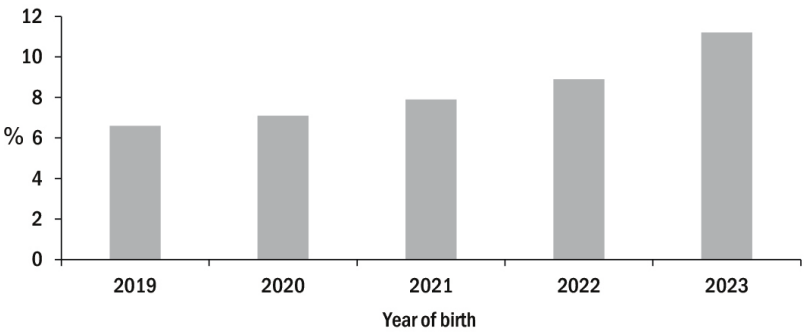


Figure 5
Objection of parents against the storage of NBS remnants for non-identifiable scientific research, by year of birth (2019-2023)

January 2025

AUTHORS
Kitty van der Ploeg
Olmo van der Mast
Paul Verkerk

PROJECT NUMBER
060.51605

REPORT NUMBER
TNO 2025 R10106

COMMISSIONED BY
RIVM – Centre for population screening

TNO.NL

TNO – CHILD HEALTH

Sylviusweg 71
2333 BE Leiden

Post office box 3005
2301 DA Leiden

www.tno.nl/en
www.tno.nl/first1000days

T +31 88 866 90 00