Prenatal screening and pregnancy outcome
Update: March 2021

Prenatal screening for congenital anomalies

In the Netherlands a national prenatal screening program is implemented. The prenatal screening program includes screening for down-, edwards- and patausyndrome (trisomy 21, trisomy 18 and trisomy 13) through the Non Invasive Prenatal Test (NIPT) or combined test (CT) in the first trimester and screening for structural anomalies through an anomaly scan around 20 weeks of gestation. The anomaly scan is offered free of charge, whereas the CT or NIPT cost around €170.

The prenatal screening program is monitored annually by the regional centers for prenatal screening. The monitoring report (*Monitor 2019, Prenatale screening op down-, edwards- en patausyndroom en het Structureel Echoscopisch Onderzoek*) can be found at the website of the RIVM. In 2019 in Northeast Netherlands (exceeding the Eurocat NNL region), first trimester screening for down-, edwards- and patausyndrome was performed in 7,380 pregnancies through NIPT and in 346 pregnancies through the CT. The uptake was 31,7% for NIPT and 1,5% for the CT. NIPT resulted in 0,5% in a positive result (i.e. indication that fetus is affected with down-, edwards- or patausyndrome). In 4,3% of the CT an increased risk for down-, edwards- or patausyndrome was found. An anomaly scan was performed in 20,874 pregnancies, corresponding with an uptake after counseling of 87,3%. A structural anomaly was suspected in 4,4% of pregnancies.

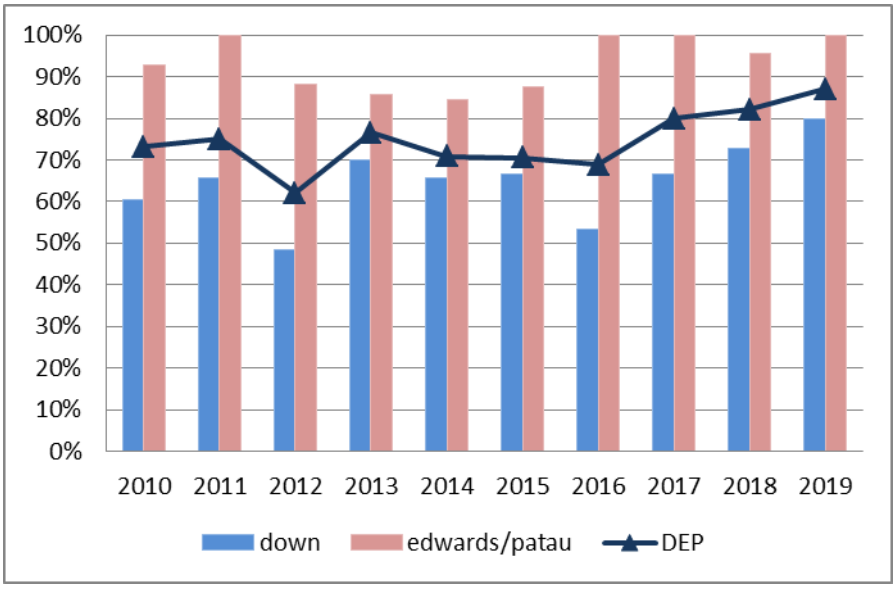
Prenatal diagnosis and pregnancy outcome for down-, edwards- and patausyndrome

In 2010-2019 Eurocat NNL registered 498 cases with down-, edwards- or patausyndrome. Total prevalence in this period was 20,6, 8,0 and 2,5 per 10,000 births respectively. Time trends are reported in chapter 6 of the '*Jaaroverzicht*'.

Prenatal diagnosis

Of these 498 cases, 370 (74,2%) were prenatally diagnosed. The proportion of down-, edwards- and patausyndrome cases that were prenatally diagnosed increased during this 10 year period from 73% in 2010 to 87% in 2019 (p=0,035, figure 1 and supplementary table). Looking at down syndrome and edwards- and patausyndrome separately, a trend was most obviously seen for down syndrome (although not significant), where the proportion of cases with a prenatal diagnosis increased from 61% in 2010 to 80% in 2019. Proportion of prenatally diagnosed cases with edwards- or patausyndrome was high and fluctuated around 90-95% (figure 1 and supplementary table).

Figure 1 Proportion prenatally diagnosed cases with down syndrome and with edwards- or patausyndrome, Eurocat Northern Netherlands 2010-2019.



Total cases down syndrome: 328, total cases edwards syndrome: 128, total cases patausyndrome: 40.

Line shows the proportion prenatally diagnosed cases with down-, edwards- and patausyndrome together (DEP), bars show proportion prenatally diagnosed for down syndrome and edwards/patausyndrome separately.

First positive prenatal test

For the prenatally diagnosed cases we determined what was the first positive prenatal test (defined as first prenatal test whether screening procedure or diagnostic test which indicated a possible congenital anomaly or need for further tests):
1) an increased risk at the CT test or a positive result for NIPT,
2) abnormal findings at ultrasound (US), or
3) positive result at chorionic villus sampling (CVS) or amniocentesis.

In 50% of the prenatally diagnosed down syndrome cases the first positive prenatal test was a positive CT or NIPT, in 44% it was an abnormal finding at US and in 5% it was a positive CVS or amniocentesis. For edwards- and patausyndrome on the other hand, abnormal findings at US accounted for 66%, a positive screening test (CT or NIPT) for 30% and a positive invasive test (CVS or amniocentesis) for 4%.

Table 1 – Prenatal diagnosis, first positive prenatal test and outcome of pregnancy after prenatal diagnosis for down and edwards- and patausyndrome, Eurocat Northern Netherlands 2010-2019

	down syndrome		**edwards/patau syndrome**	
Total cases	**328**	**(100%)**	**168**	**(100%)**
Prenatally diagnosed	**212**	**(64,6%)**	**158**	**(94,0%)**
First positive prenatal test	*(prenatally diagnosed is 100%)*			
• Screening test (CT/NIPT)	107	(50,5%)	47	(29,7%)
• Ultrasound	94	(44,3%)	105	(66,5%)
• CVS or amniocentesis	11	(5,2%)	6	(3,8%)
Outcome of pregnancy <u>after prenatal diagnosis</u> *(prenatally diagnosed is 100%)*				
• Live birth (including postnatal death)	44	(20,8%)	10	(6,3%)
• Fetal death or stillbirth	19	(9,0%)	22	(13,9%)
• Termination of pregnancy	149	(70,3%)	126	(79,7%)

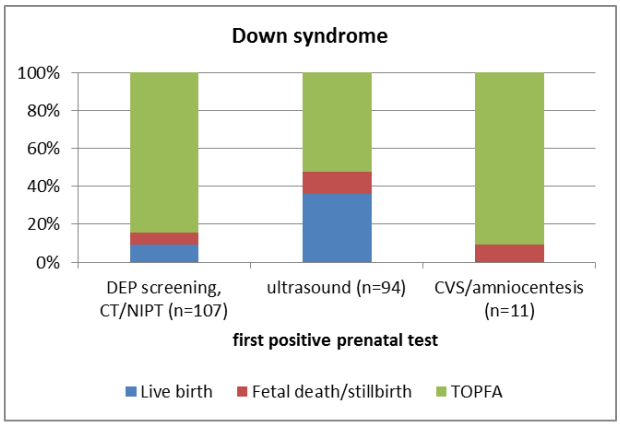
Outcome of pregnancy overall

Overall, 44% (n=151) of the down syndrome cases were live born, 10% (n=33) resulted in a fetal death and 46% (n=151) resulted in a termination of pregnancy. For edwards- and patausyndrome, these proportions were 8% (n=13), 17% (n=29) and 75% (n=126) respectively. The live born cases with edwards- or patausyndrome all died after birth.

Outcome of pregnancy after prenatal diagnosis

After prenatal diagnosis of down syndrome, termination of pregnancy occurred in 70% of the cases, fetal death or stillbirth occurred in 9% and in 21% there was a live birth (of which 3% died after birth). For edwards- and patausyndrome the proportions were 80% terminations, 14% fetal deaths and stillbirths and 6% live births (all died after birth).

When the CT or NIPT provided a positive test result followed by a prenatal diagnosis, pregnancy termination occurred in 84% of the down syndrome cases and in 9% the outcome of pregnancy was a live birth. When the ultrasound was the first positive test (an ultrasound finding followed by a prenatal diagnosis), termination of pregnancy occurred in 52% of the down syndrome cases and in 36% there was a live birth. Pregnancy outcome was therefore related to the type of screening test. After a positive CT or NIPT, followed by prenatal diagnosis of edwards- or patausyndrome, termination of pregnancy occurred in 96% of the cases. When the ultrasound was the first positive test (an ultrasound finding followed by a prenatal diagnosis), termination of pregnancy occurred in 71% of the cases and in 19% there the pregnancy ended in a fetal death or stillbirth (figure 2a and figure 2b)



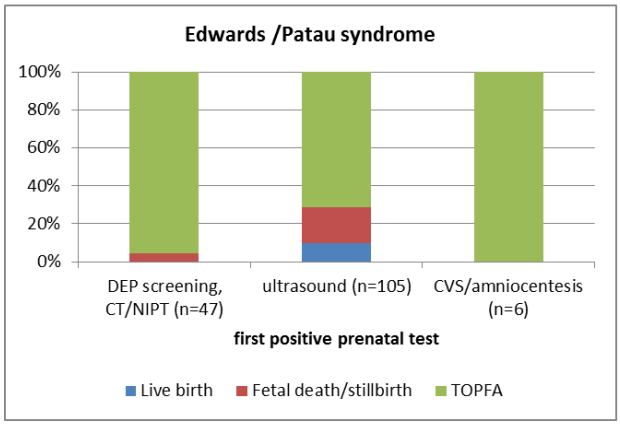


Figure 2 Pregnancy outcome after a first positive prenatal test, followed by prenatal diagnosis for down syndrome and edwards/patausyndrome, Eurocat Northern Netherlands 2010-2019

Prenatal diagnosis and pregnancy outcome for structural anomalies (NTD, severe heart defects and abdominal wall defects)

In 2010-2019 Eurocat NNL registered 149 cases with non-chromosomal neural tube defects (NTD), 268 cases with non-chromosomal severe heart defects and 80 cases with non-chromosomal abdominal wall defects. Total prevalence in this period was 9,0, 16,7 and 5,0 per 10,000 births respectively. Time trends are reported in chapter 6 of the '*Jaaroverzicht*'.

Prenatal diagnosis

Prenatal diagnosis occurred in 97% (n=145) of the cases with NTD's and in 94% (n=75) of the cases with an abdominal wall defect. For severe CHD the proportion prenatally diagnosed was 61% (n=164) and fluctuated between 44% in 2010 and 77% in 2019, with peak in 2013 of 80%. (See supplementary table)

First positive prenatal test

For the prenatally diagnosed cases we determined the first positive prenatal test (defined as first prenatal test whether screening procedure or diagnostic test which indicated a possible congenital anomaly or need for further tests) and at what time in pregnancy this ultrasound was performed (before 14 weeks, 14-22 weeks or after 22 weeks).

In 32% of the prenatally diagnosed NTD cases an ultrasound in the first trimester, before 14 weeks, was the first positive prenatal test, 66% the NTD was detected at ultrasound between 14 and 22 weeks. For severe CHD the vast majority was detected in the second trimester of pregnancy, whereas for abdominal wall defects about half were detected in the first trimester and half in the second trimester, see table 2.

Table 2 – Prenatal diagnosis, first positive prenatal test and outcome of pregnancy after prenatal diagnosis for neural tube defects, severe heart defects and abdominal wall defects, Eurocat Northern Netherlands 2010-2019

	Neural tube defects		**Severe heart defects***		**Abdominal wall defects**	
Total cases	**149**		**268**		**80**	
Prenatally diagnosed	**145**	**(97,3%)**	**164**	**(61,2%)**	**75**	**(93,8%)**
First positive prenatal test	*(prenatally diagnosed is 100%)*					
• Ultrasound < 14 weeks	46	(31,7%)	14	(8,5%)	37	(49,3%)
• Ultrasound 14-21 weeks	96	(66,2%)	140	(85,4%)	36	(48,0%)
• Ultrasound > 22 weeks	3	(2,1%)	8	(4,9%)	2	(2,7%)
Outcome of pregnancy after prenatal diagnosis	*(prenatally diagnosed is 100%)*					
• Live birth (including postnatal death)	20	(13,8%)	116	(70,7%)	35	(46,7%)
• Fetal death or stillbirth	6	(4,1%)	13	(7,9%)	9	(12,0%)
• Termination of pregnancy	119	(82,1%)	35	(21,3%)	31	(41,3%)

** severe heart defects include ICD10 codes Q200 persistent ductus arteriosus, Q201 double outlet right ventricle, Q203 complete transposition of great vessels, Q204 single ventricle, Q212 atrioventricular septal defect, Q213 tetralogy of Fallot, Q220 pulmonary valve atresia, Q224 tricuspid atresia, Q225 Ebstein's anomaly, Q226 hypoplastic right heart syndrome, Q230 congenital stenosis of aortic valve, Q232 congenital mitral stenosis, Q233 congenital mitral insufficiency, Q234 hypoplastic left heart syndrome, Q251 coarctatio of aorta,Q252 atresia of aorta, Q262 total anomalous pulmonary venous connection*

Outcome of pregnancy after prenatal diagnosis

After a prenatal diagnosis of NTD, termination of pregnancy occurred in 82% of the cases, a fetal death or stillbirth occurred in 4% and in 14% there was a live birth (of which 30% (6/20) died after birth). For severe CHD termination of pregnancy occurred in 21% and 71% ended in a live birth. For abdominal wall defects 41 % were termination of pregnancy and about half were live births.
For all three anomalies, termination of pregnancy occurred more frequently when the detection of the anomaly was early in pregnancy, than when the anomaly was detected in the second trimester of pregnancy. This is most likely related to the severity of the anomaly.

Supplementary tables

Number of cases and proportion prenatally diagnosed for down-, edwards- and patausyndrome per birth year, Eurocat Northern Netherland 2010-2019

Year of birth	Down syndrome		Edwards- and patausyndrome	
	Total (100%)	prenatally diagnosed	Total (100%)	prenatally diagnosed
2010	43	60,5%	28	92,9%
2011	38	65,8%	14	100%
2012	33	48,5%	17	88,2%
2013	20	70,0%	14	85,7%
2014	35	65,7%	13	84,6%
2015	36	66,7%	8	87,5%
2016	30	53,3%	15	100%
2017	30	66,7%	20	100%
2018	33	72,7%	23	95,7%
2019	30	80,0%	16	100%
Total	330	64,6%	168	6,0%

Number of cases and proportion prenatally diagnosed for non-chromosomal neural tube defects (NTD), severe congenital heart defects (CHD) and abdominal wall defects per birth year, Eurocat Northern Netherland 2010-2019

Year of birth	NTD		Severe CHD		Abdominal wall defects	
	Total (100%)	prenatally diagnosed	Total (100%)	prenatally diagnosed	Total (100%)	prenatally diagnosed
2010	21	95,2%	32	43,8%	5	80%
2011	19	100%	25	56,0%	7	100%
2012	9	100%	27	59,3%	8	88%
2013	15	86,7%	30	80,0%	6	100%
2014	12	100%	33	45,5%	10	100%
2015	20	100%	22	72,7%	8	100%
2016	20	100%	19	52,6%	10	90%
2017	8	100%	31	61,3%	8	75%
2018	12	100%	27	70,4%	9	100%
2019	13	92,3%	22	77,3%	9	100%
Total	149	97,3%	268	61,2%	80	94%