



UMC Utrecht

Aangeboren hartafwijking Denk aan de hersenen



Hans Breur
Kindercardioloog





Disclosure belangen spreker

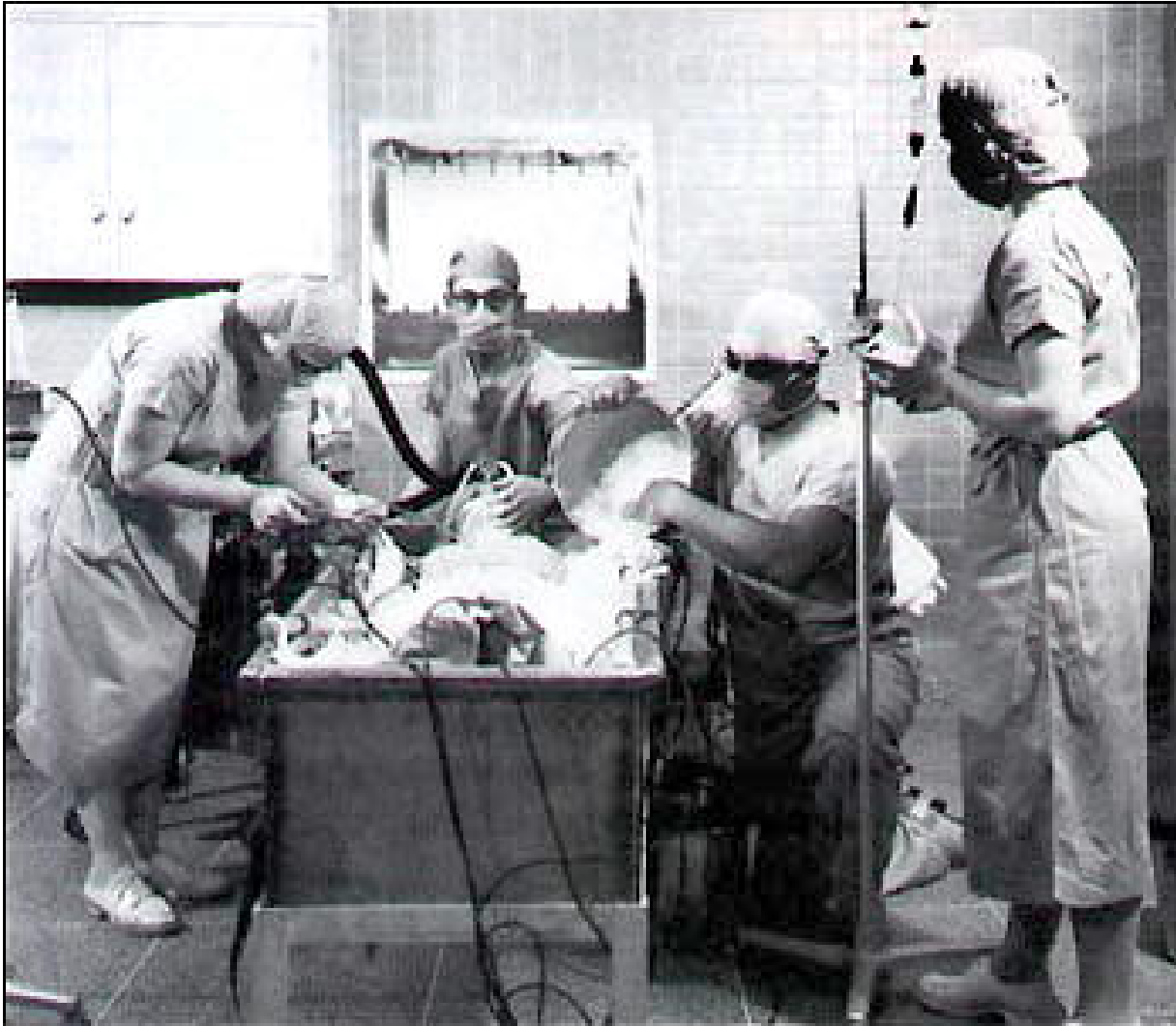
(potentiële) belangenverstrengeling	Geen / Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
<ul style="list-style-type: none"> • Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk ... 	<ul style="list-style-type: none"> •  • 

Overleving met een congenitale hartafwijking

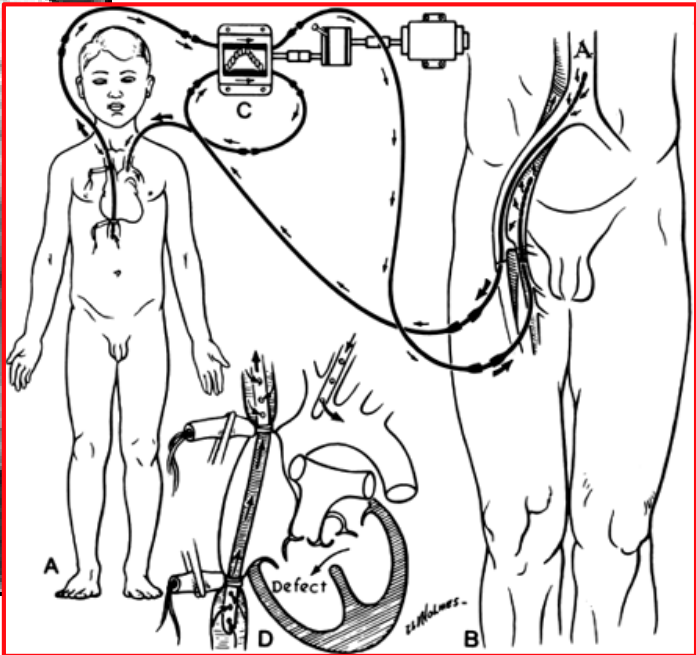
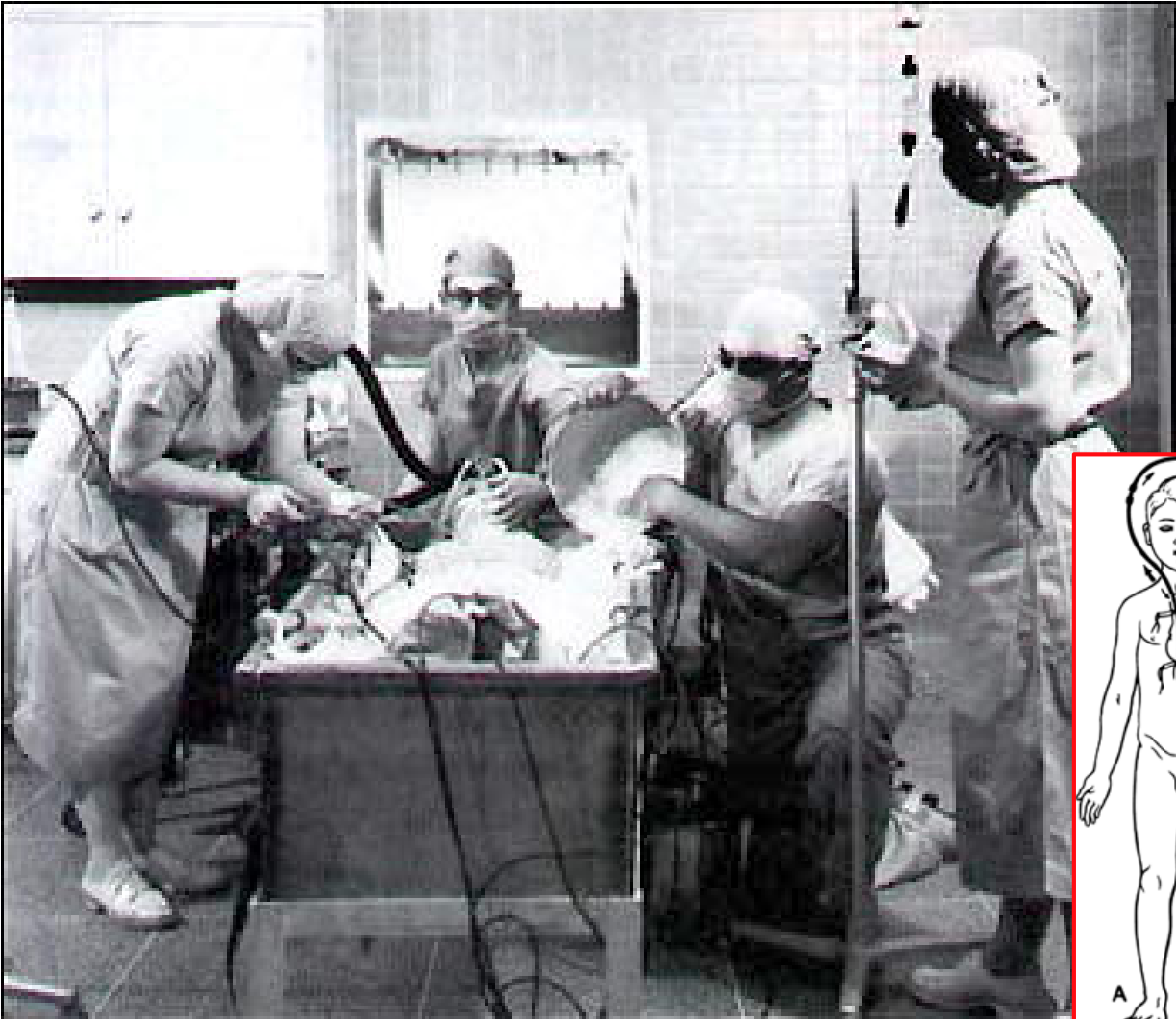
Survival rate in %



Overleving met een congenitale hartafwijking



Overleving met een congenitale hartafwijking

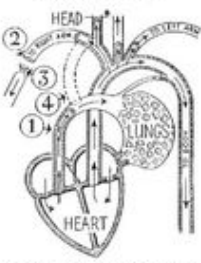




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Overleving met een congenitale hartafwijking

Switching Arteries Sidetracks Blood and Oxygen to Otherwise Starved Lungs



The "Blue" Babies' Blood Lacks Vital Oxygen Because the Artery (1) From the Heart to the Leg is Constricted. By Severing an Artery of the Arm (2), Tying It Off (3) and Attaching It to the Lung Artery (4) the Constriction is By-Passed.

Saving our Doomed 'Blue' Babies

By Robert D. Potter

A WOMAN physician's courageous research and imagination, and the skill of one of the world's great surgeons have combined to bring hope that many "blue" babies, hitherto considered doomed to early death, may be saved.

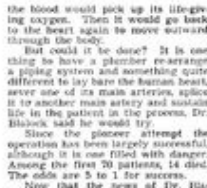
These babies are blue because they are suffering from a lack of oxygen in their blood stream, in a condition known as cyanosis. The artery from their heart to their lungs is so constricted that their blood never gets oxygen to make cheeks rosy.

Their lips are blue. Their toes are blue, and they can walk only a few feet without exhaustion. Doctors used to give them only a few hours to live.

But now medicine can give hope . . . and more . . . for since Nov. 26, 1941, Dr. Blalock, Professor of Surgery at Johns Hopkins University in Baltimore, has been conquering the "blue" baby malady by re-creating an artery from the arm and making it carry blood to the lungs, where it can receive its vital oxygen.

Nearly 70 operations have been performed on "blue" babies. In many cases almost miraculous recovery has come.

It is Dr. Blalock's fingers that wield the knife in the delicate operation that exposes the heart and transplants its vital arteries. But behind the brilliant operation he has perfected are years of painstaking research by Dr. Helen B. Taussig, daughter of the late Prof. F. W. Taussig, world-famous Harvard economist. Dr. Taussig had watched "blue" babies come to her heart clinic at Johns Hopkins Hospital.



Six-Year-Old Mike Schirmer of Baltimore Could Walk Only Five Feet Without Stopping Before His Operation. He Shows His "Ticky Zipper"—the Incision for His Operation.



Little Bonnie Stewart of Florida is Another of the 70 Children Saved by the New Johns Hopkins Surgery.

In many cases she discovered that the artery leading to the lung from the heart was narrowed so that an insufficient supply of blood was reaching the lungs to receive the vital oxygen. Dr. Taussig reasoned that a surgical operation might be able to side-track the constricted artery and sidetrack blood into the lungs. On paper, when the diagram of the ar-

tery would pick up its life-giving oxygen. Then it would go back to the heart again to move outward through the body.

But could it be done? It is one thing to have a plumber re-arrange a piping system and something quite different to lay bare the human heart, sever one of its main arteries, splice it to another main artery and sustain life in the patient in the process. Dr. Blalock said he would try.

Since the pioneer attempt the operation has been largely successful, although it is one filled with danger. Among the first 20 patients, 14 died. The odds are 5 to 1 for success.

Now that the news of Dr. Blalock's operation is known through the country the list of patients grows daily. Blue little Bonnie Stewart of Florida, daughter of a daddy killed on Solapas, near in Baltimore with her grandmother. Today Bonnie walks and plays like other children.

The card of six-year-old Mike Schirmer—the boy with the "ticky zipper"—shows what can be done.

was no hope that Mike could grow up. But then came new hope, for Dr. Maudsley told us about the operation of Dr. Blalock.

"They took him to the operating room and brought him back two hours later. It was a miracle.

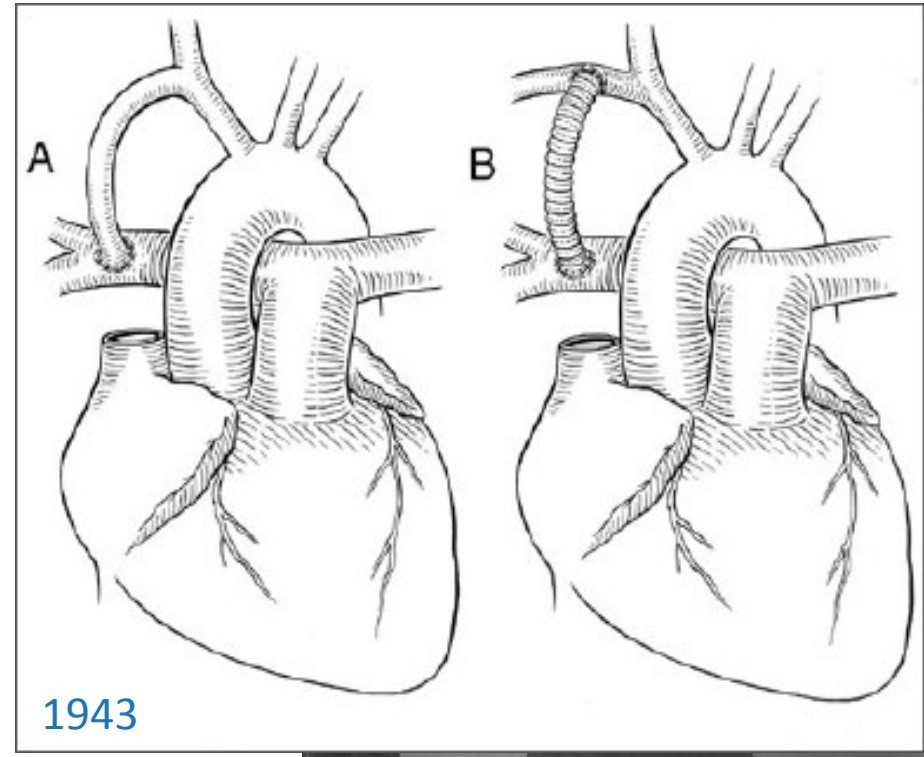
"After only two weeks of convalescence he came home and he has been on the go ever since. If anyone wants anything he'll run and get it. He's up and down stairs 75 times a day. He climbs on bushes and takes just for the joy of jumping off. He swears me out. But I love it."

The Blalock-Taussig operation is not a simple one. It takes from an

branches of the pulmonary artery (to the lungs) are two large blood vessels. One connects the heart and the arm, the other the heart and the head. Dr. Blalock chooses the most convenient—usually the arm artery—and severs it. One end is clamped off and the other closed permanently.

The end nearest the heart is then spliced to the nearest branch of the pulmonary artery. The clamps are removed and the blood that would ordinarily flow to the arm goes into the lung. There it becomes enriched with vital oxygen and the baby's blue lips quickly begin to turn red.

Nature has provided other blood vessels which take up the blood load



1943



Overleving met een congenitale hartafwijking

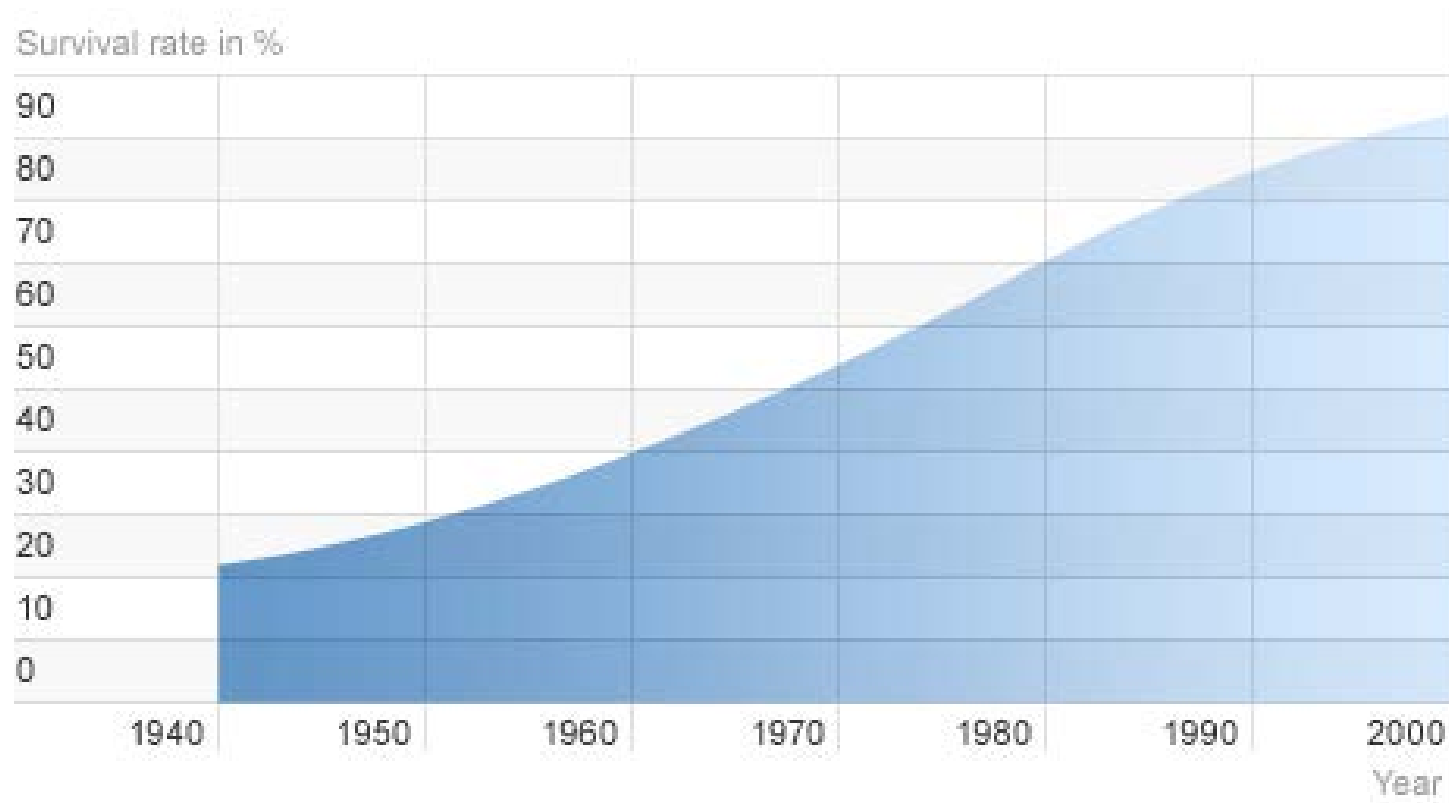


1953
ASD sluiting

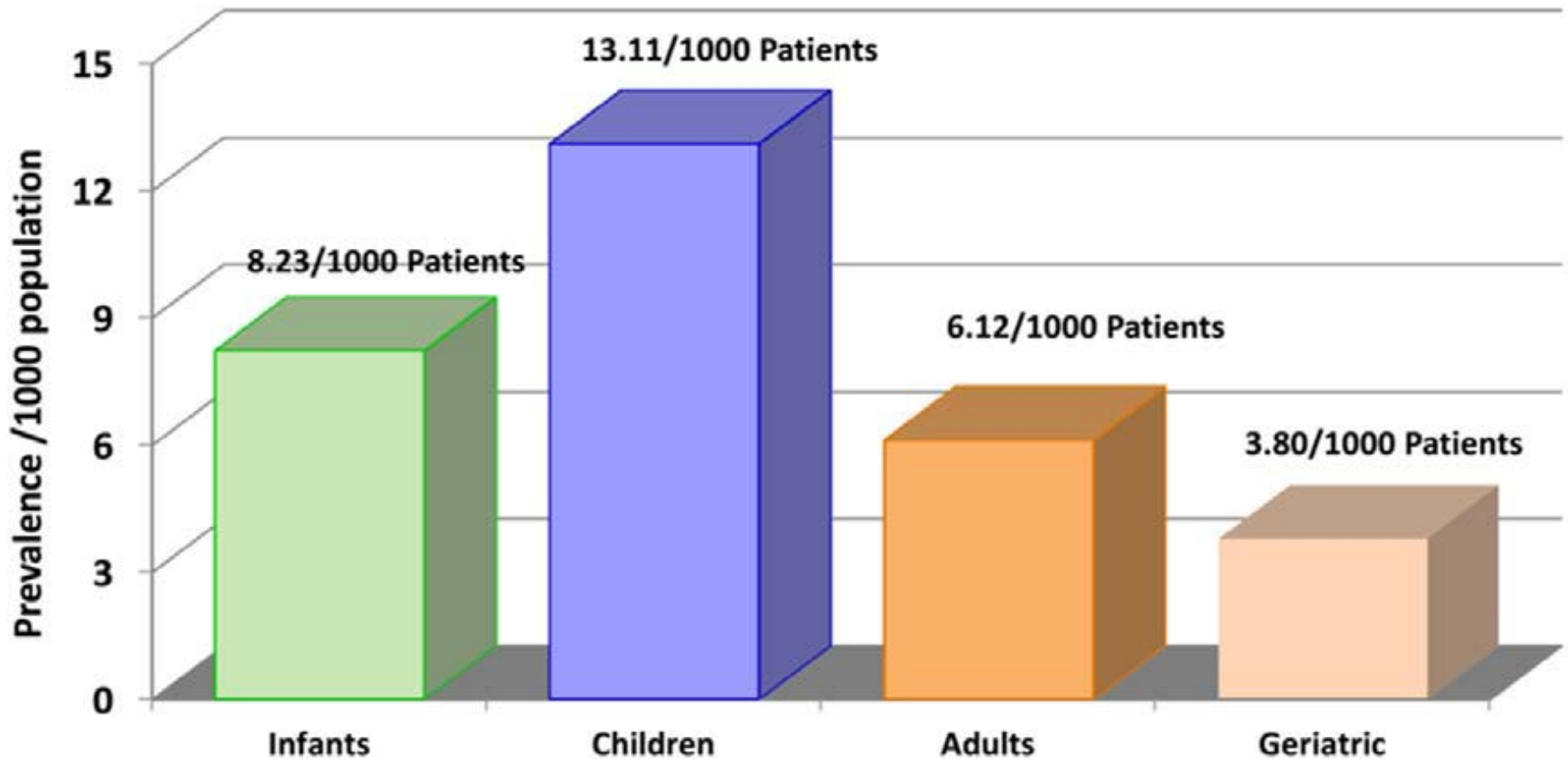


Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE

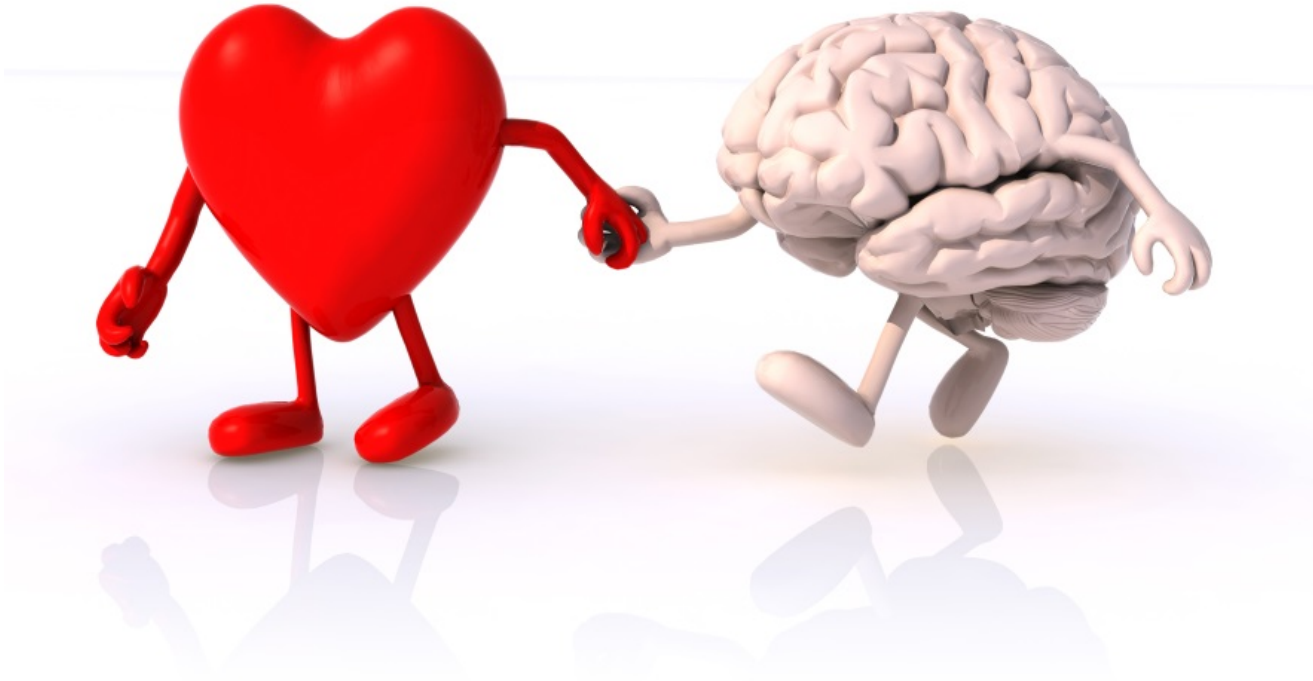
Overleving met een congenitale hartafwijking

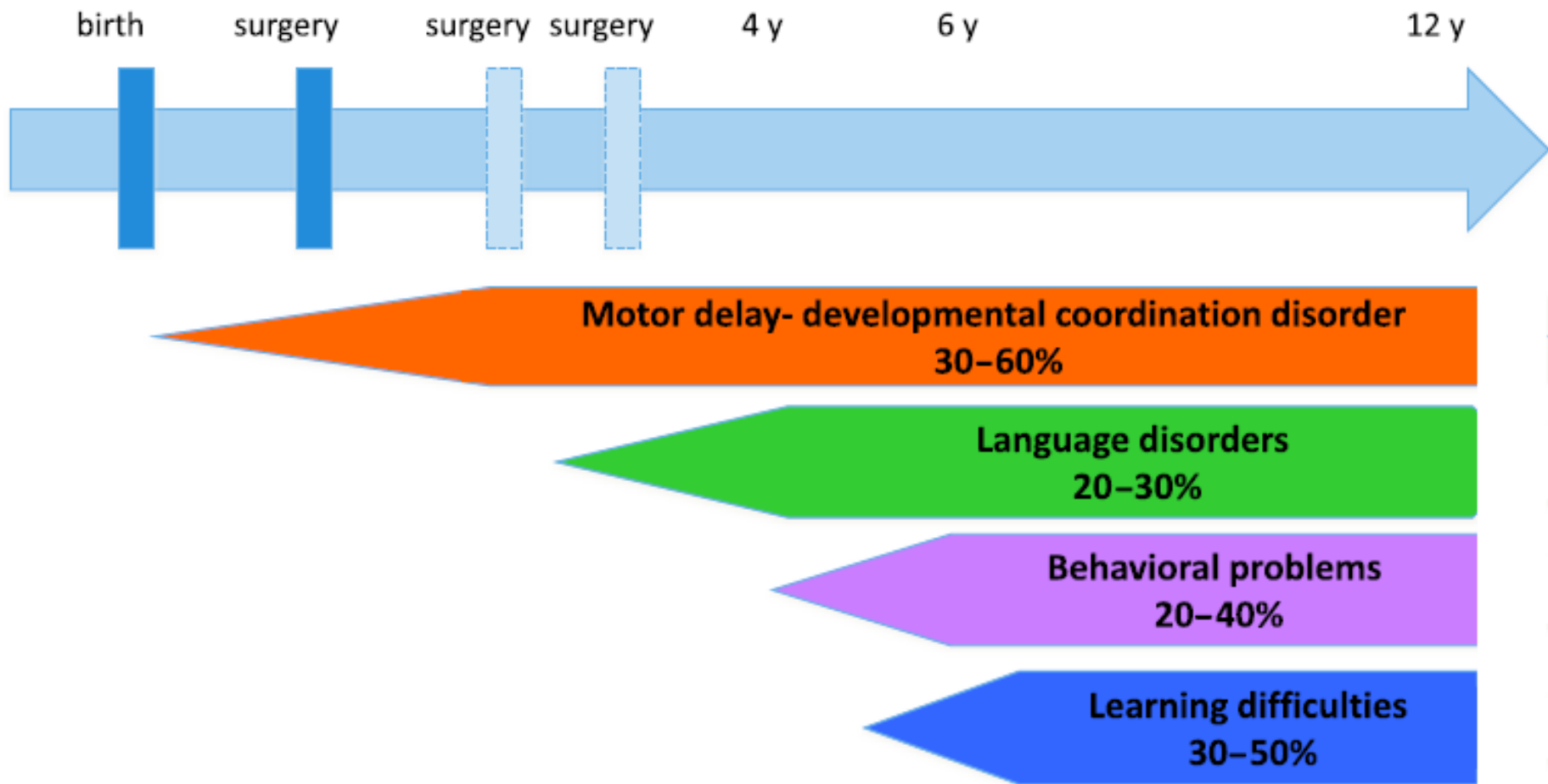


Overleving met een congenitale hartafwijking









Cognitieve ontwikkeling op schoolleeftijd

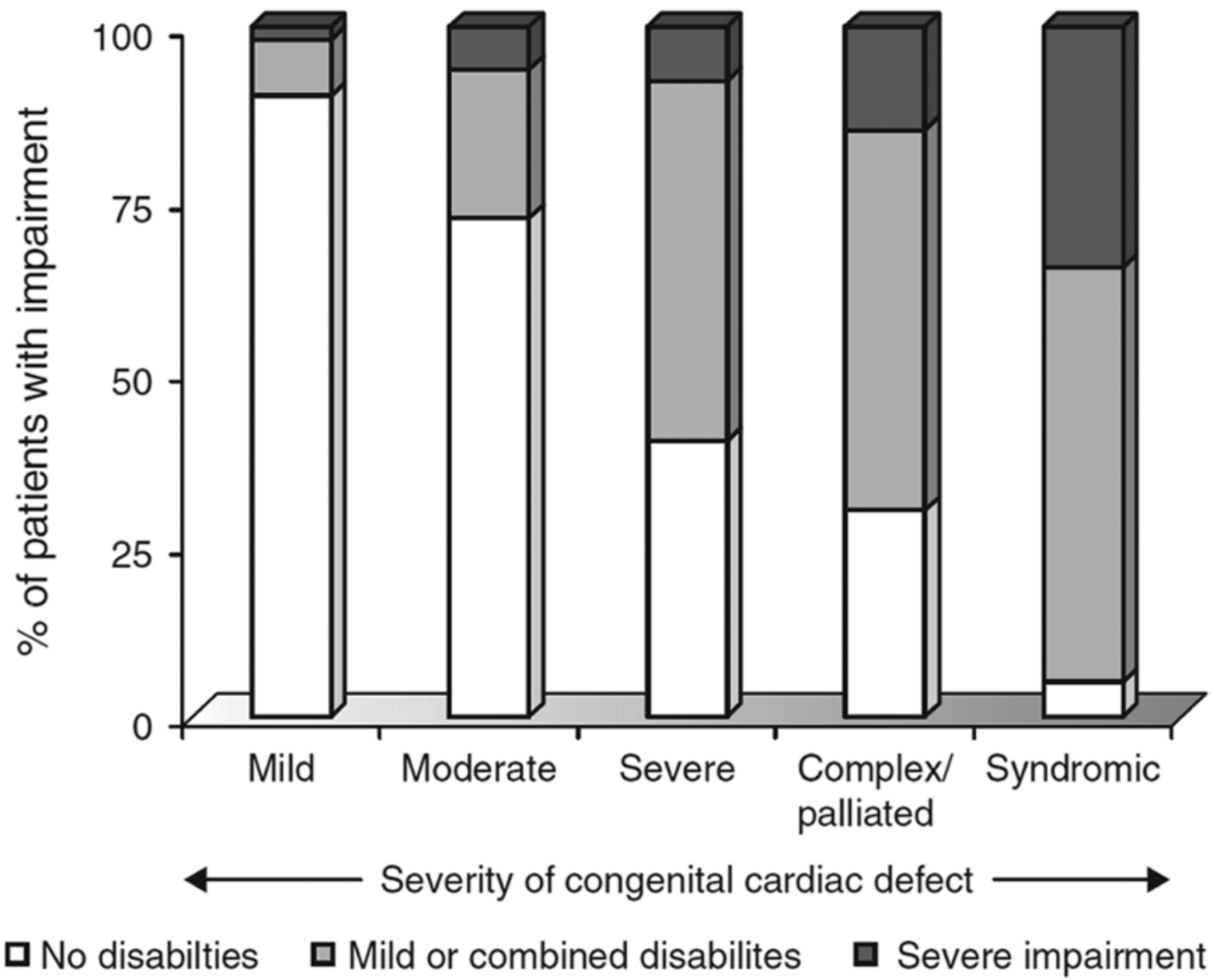
Ontwikkeling	% van de kinderen waarin afwijkend
Zelfredzaamheid	22%
Sociale participatie	13%
Communicatie	17%
Aanpassingsvermogen	15%



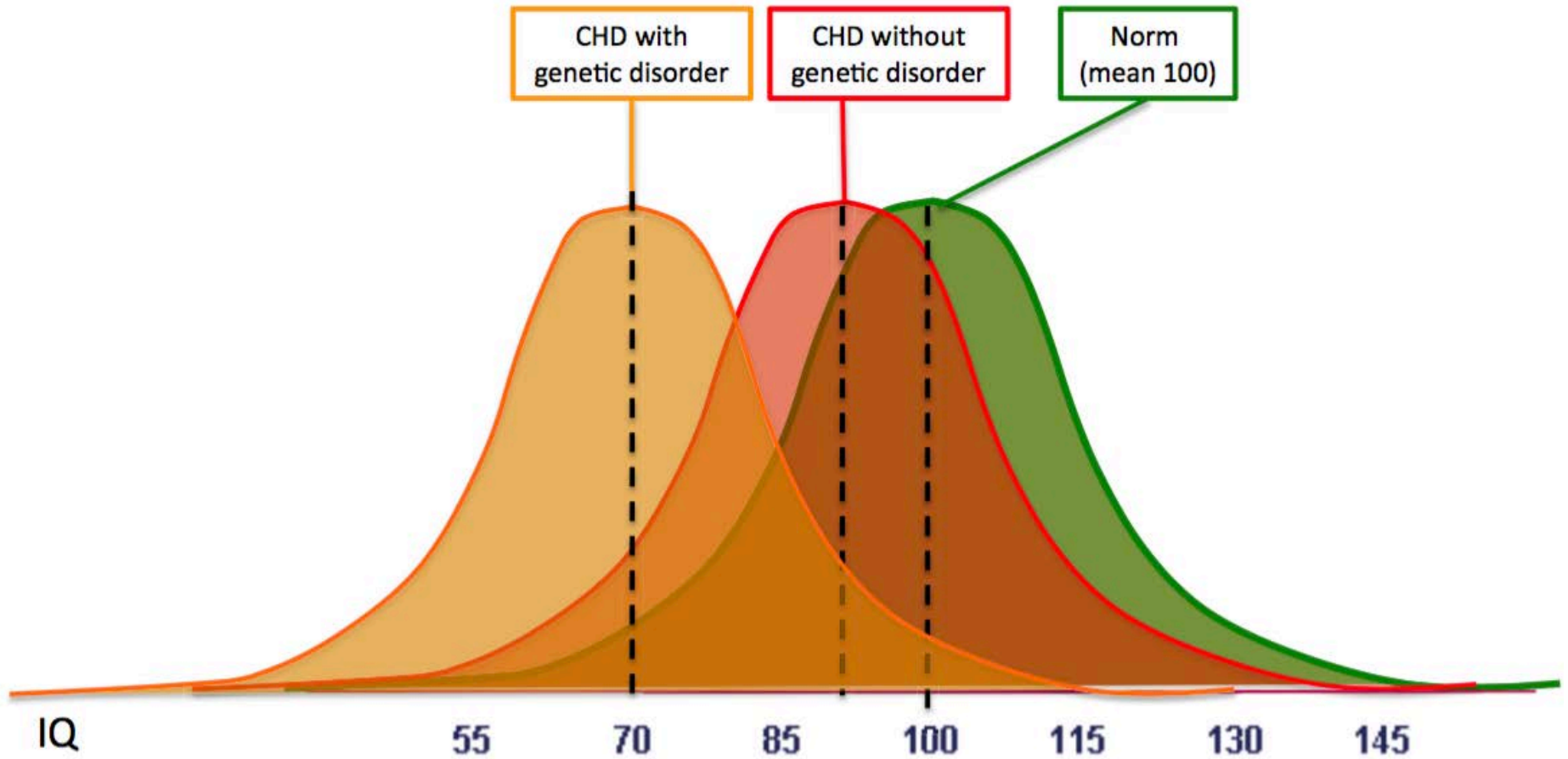
Neurologische ontwikkeling in adolescenten

	Patients (<i>n</i> =59), mean (SD)	Comparison children (<i>n</i> =40), mean (SD)	<i>p</i>
Wechsler Intelligence scale for children			
Full scale IQ	103.10 (16.49)	112.68 (10.43)	0.001
Verbal comprehension	109.14 (18.83)	115.21 (15.96)	0.11
Perceptual reasoning	103.66 (14.77)	113.82 (8.83)	<0.001
Working memory	93.42 (13.64)	103.76 (12.19)	<0.001
Processing speed	101.46 (14.19)	105.39 (11.20)	0.15





Cognitieve ontwikkeling



Andere populaties met neonatale problemen

Table 1
Overview of major outcome categories in the largest at-risk population

	HIE	Very Preterms	CHD
Prevalence	1–6/1000	10/1000	6/1000
Cerebral palsy	30% TH: 20%	5%–10%	2%
IQ <70	30%	10%–20%	10%–20%
Mild deficits	~ 50%	~ 50%	~ 30%–50%

Abbreviations: HIE, hypoxic-ischemic encephalopathy; TH, therapeutic hypothermia.



Factoren die invloed hebben op neurologische ontwikkeling

Patiënt gebonden (innate)

Type hartafwijking

Genetische aandoening

Prematuriteit

Prenatale hersenontwikkeling

Familie omgeving

Procedure gebonden (modifiable)

Operatie(s)

Cardiopulmonale bypass

(Post)operatieve complicaties

ECMO, reanimatie

Hersenschade

Factoren die invloed hebben op neurologische ontwikkeling

Patiënt gebonden (innate)

Type hartafwijking

Genetische aandoening

Prematuriteit

Prenatale hersenontwikkeling

Familie omgeving

Procedure gebonden (modifiable)

Operatie(s)

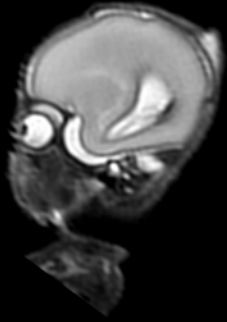
Cardiopulmonale bypass

(Post)operatieve complicaties

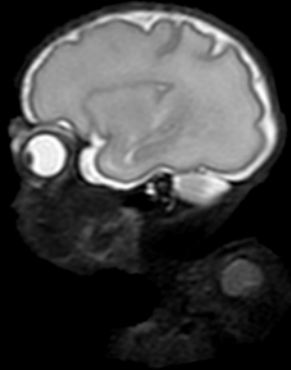
ECMO, reanimatie

Hersenschade

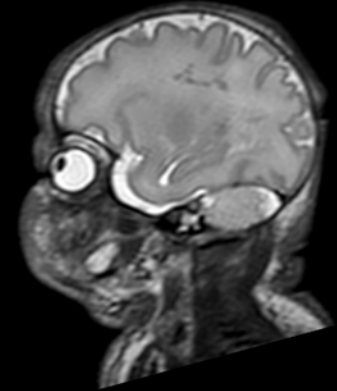




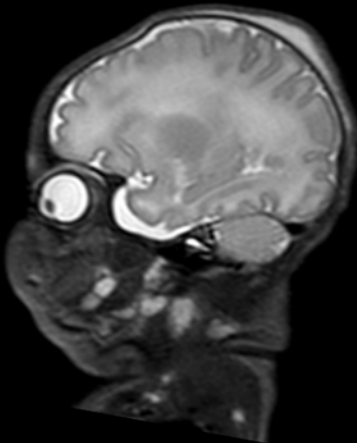
25 weken



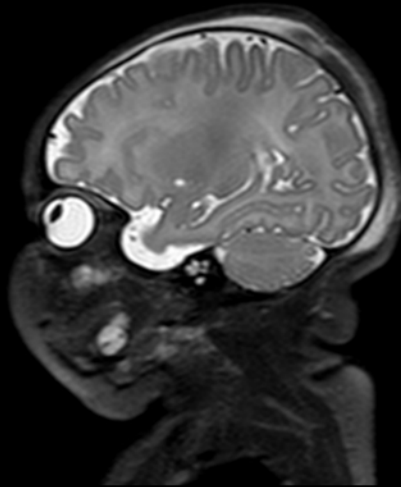
30 weken



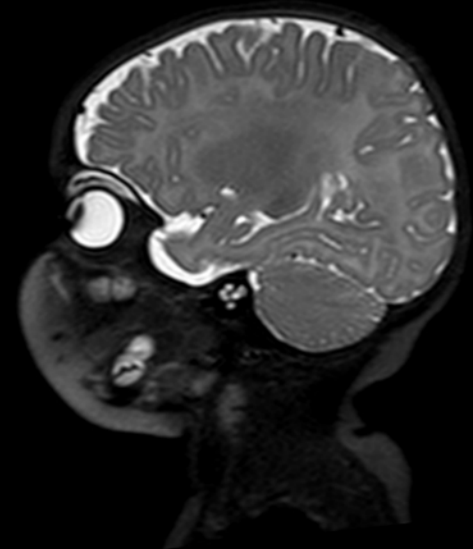
33 weken



36 weken

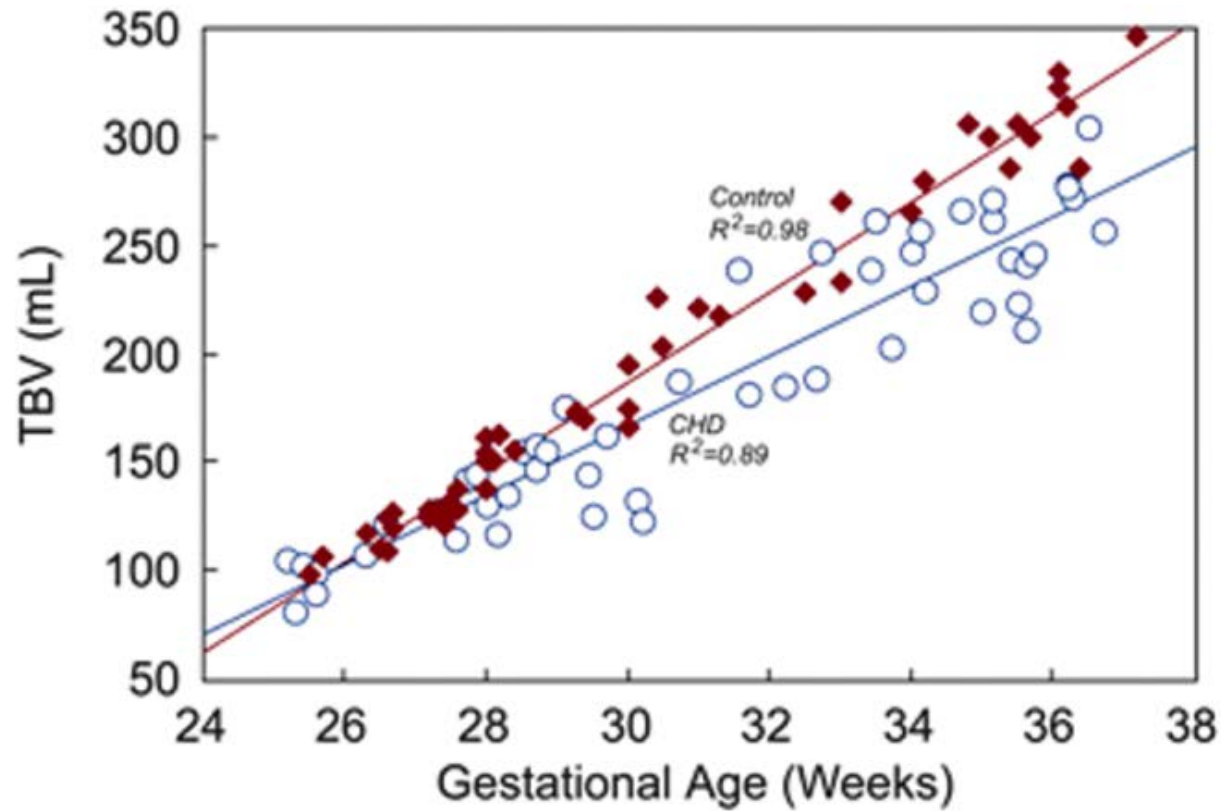
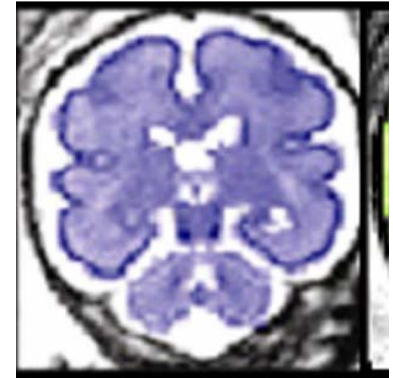


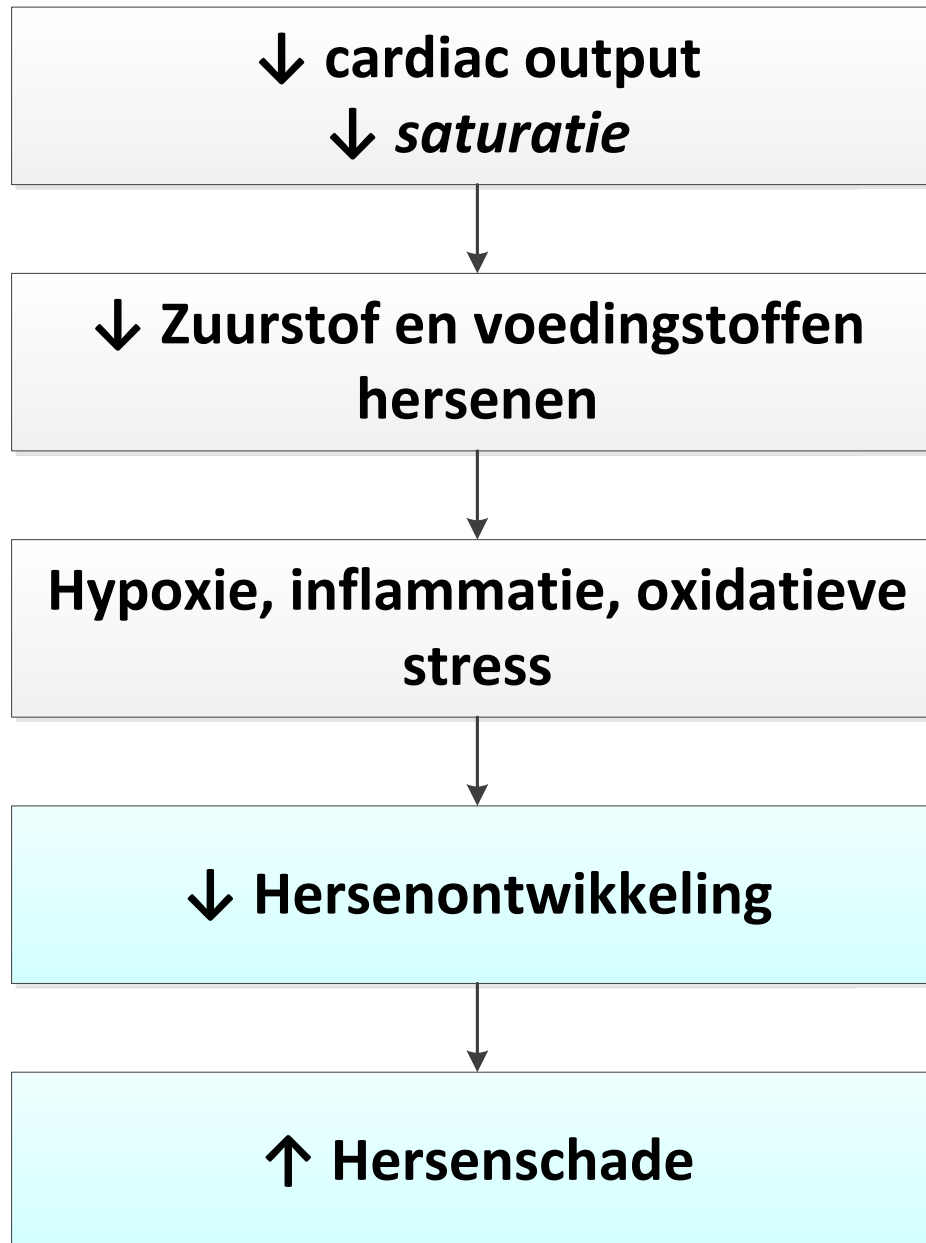
Uitgerekende datum



3 maanden

Foetale hersenontwikkeling







Congenital Heart Disease **Life Span**

PREVENTING COLLATERAL DAMAGE



Wilhelmina Kinderziekenhuis

Child health, science for life





Beeldvorming

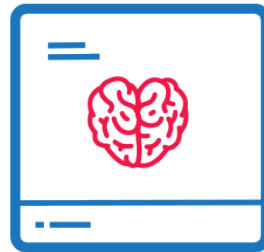


Crucial trial



Follow-up





Beeldvorming hersenen



1. Hartafwijking waarvoor een operatie nodig is in de eerste levensweken

- Hypoplastisch linker/rechter hart (HLHS, HRHS, DILV, tricuspidalis atresie, ongebalanceerd AVSD)
- Transpositie van de grote vaten
- Afwijking aortaboog (HLHC, IAA, HAA, CoA)
- TAPVC
- *Tetralogie van Fallot*
- *Truncus arteriosus*



2. Beeldvorming hersenen



MRI



**Hersenenbewaking
(EEG + NIRS)**





Foetale
MRI

Postnatale
MRI

Postop
MRI

20 weken
Diagnose

40 weken
Geboorte

Neonatale
OK

Follow
Up



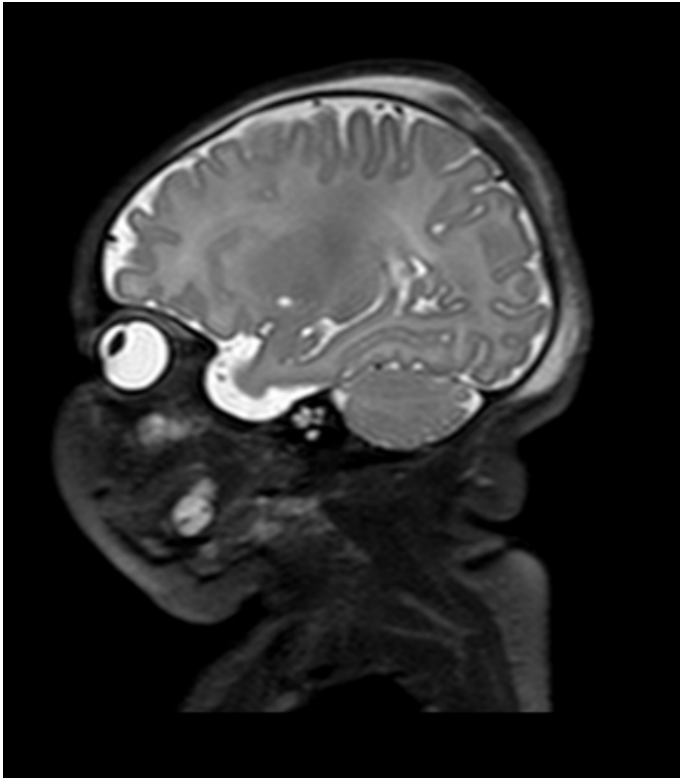
Foetale MRI:

- Hersenontwikkeling?
- Aangeboren afwijkingen?



Neonatale MRI

- Hersenontwikkeling?
- Hersenschade?



**Aantal kinderen
N=45**

**Foetaal
N=14**

Voor start MRI N=10
Postnataal N=12
Logistiek N=7
Weigering N=2

**Postnataal
N=34**

Overleden N=2
SpoedOK N=3
Instabiel N=4
Logistiek N=4

**Postoperatief
N=37**

Overleden N=7
Logistiek N=1

**MRI afwijkingen 54%
Matig-Ernstig 32%**

Witte stof schade	32%
Infarct basale kernen	9%
Infarct cortex	9%
Sinustrombose	3%
Cerebellumbloeding	9%
IVH	21%
Subdurale bloeding	41%

**MRI afwijkingen 78%
Matig-Ernstig 70%**

Witte stof schade	59%
Infarct basale kernen	19%
Infarct cortex	11%
Sinustrombose	16%
Cerebellumbloeding	11%
IVH	22%
Subdurale bloeding	46%



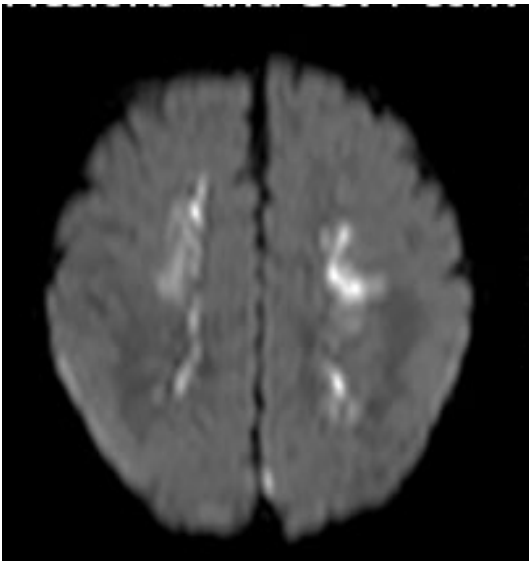
Radiologie



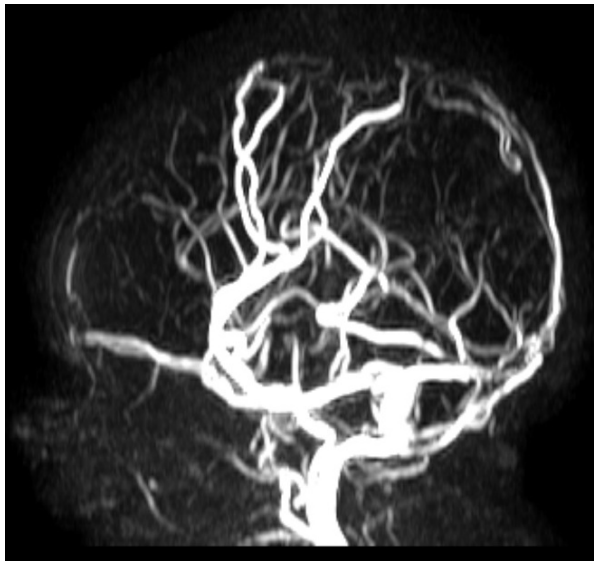
PICU



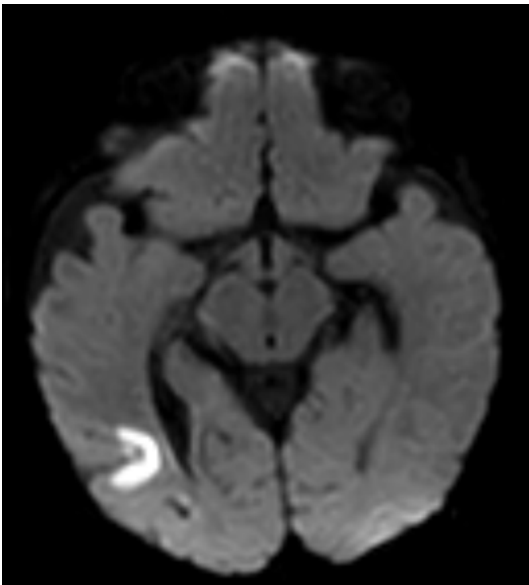
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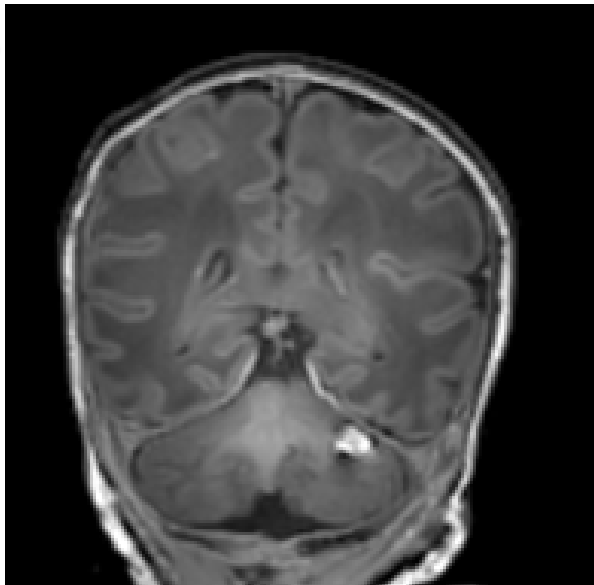
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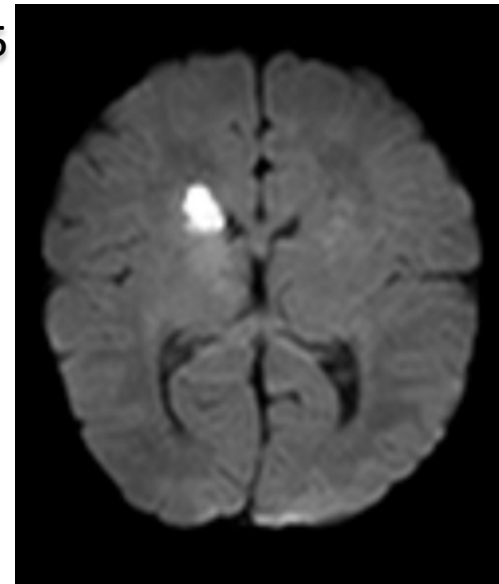
3



4



5





Foetale
MRI

Postnatale
MRI

Postop
MRI

20 weken
Diagnose

40 weken
Geboorte

Neonatale
OK

Follow
Up

EEG +
NIRS

EEG +
NIRS



Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE

EEG: Electroencephalographie (hersensimpje)

> Functie van de hersenen

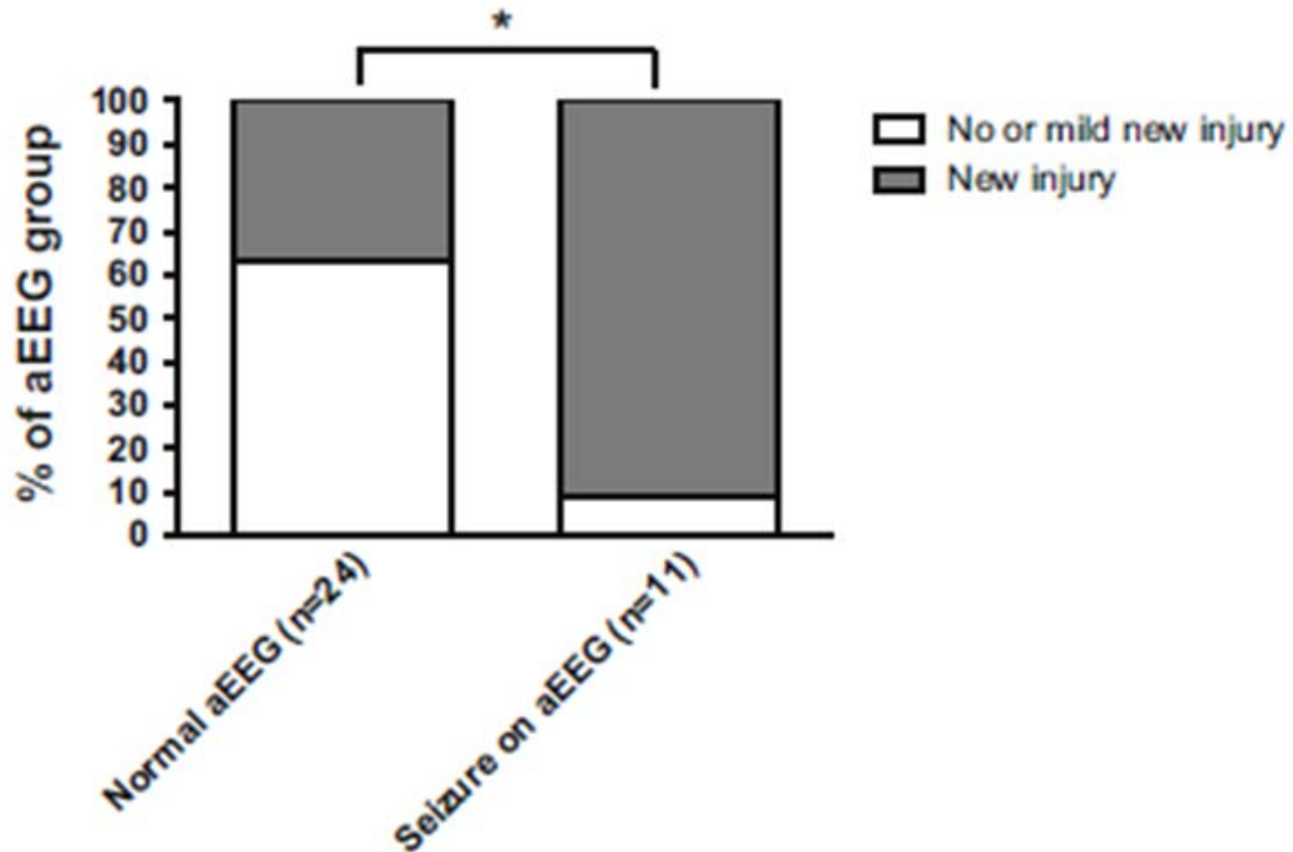


NIRS: Near-infrared spectroscopy

> Regionale zuurstof saturatie hersenen



EEG onderzoek in neonaten met een congenitale hartafwijking





Beeldvorming



Crucial trial



Follow-up





Follow-up



Follow-up



- Uitgebreid motorisch en neurocognitief onderzoek bij alle mijlpalen
 - Voor school (2 jaar)
 - Voor groep 3 (5 jaar)
 - Voor middelbare school (11 jaar)
 - Einde middelbare school (18 jaar)
- Vergelijking met referentie cohort (YoUth Cohort)
- Interventies op jonge leeftijd



Follow-up



- **Relatie hersenschade op MRI – kliniek**
- Flexibel follow-up programma





Beeldvorming



Crucial trial



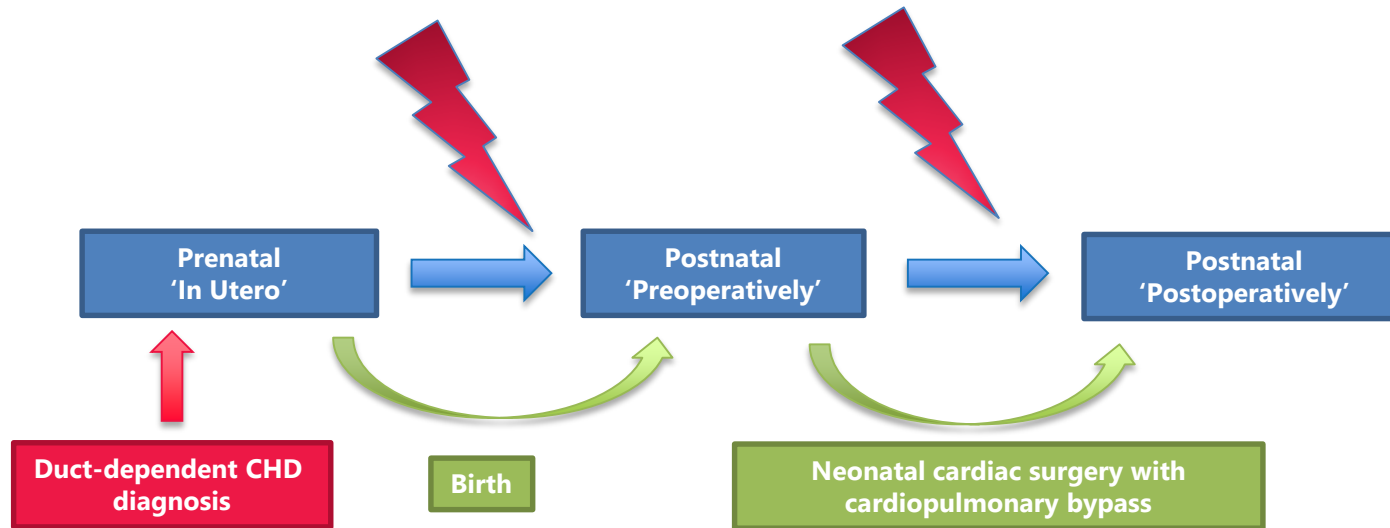
Follow-up





Crucial trial

Crucial trial



INTERVENTION



Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE

Introduction

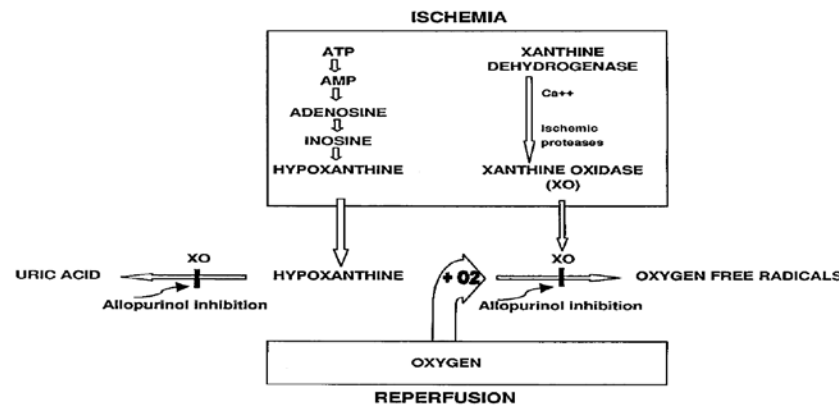


Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE



INTERVENTION

- Allopurinol
 - Xanthine oxidase inhibitor
 - Prevents formation toxic oxygen free radicals
 - Scavenger of free radicals
 - Proradical chelator
 - Anti-inflammatory
 - Neuroprotective effects
 - Cardiovascular protective properties



Boda D. Pren Neon Med 1999

Torrance HL. Pediatrics 2009

Kaandorp JJ. Arch Dis 2005

Gunes T. Pediatr Neurol 2007

Van Bel F. Pediatrics 1998

Benders MJNL. Arch Dis 2006

Kaandorp JJ. Arch Dis 2012

Derks JB. Pediatr Res 2010

Allison BJ. FASEB J 2016

Clancy RR. Pediatrics 2001



Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE

Study design



Congenital Heart
Disease **Life Span**
PREVENTING COLLATERAL DAMAGE



INTERVENTION

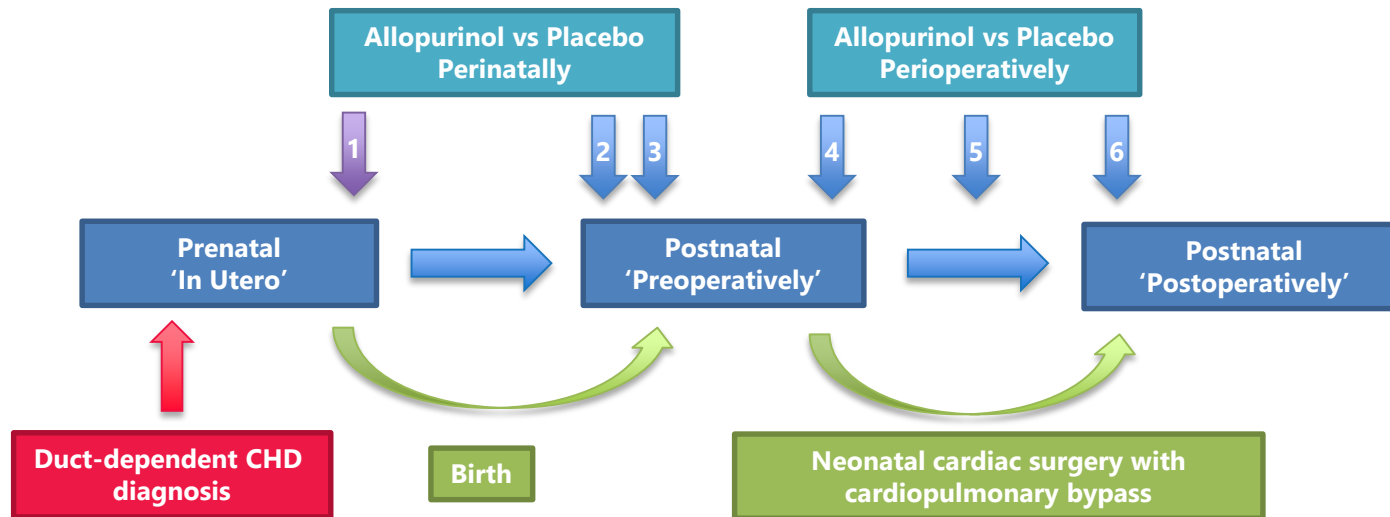
- Prospective, randomized, double blind, placebo-controlled, multicentre trial (phase III)
 - CAHAL Amsterdam/Leiden
 - EMC Rotterdam
 - UMC Groningen
 - UMC Utrecht



Congenital Heart
Disease **Life Span**
PREVENTING COLLATERAL DAMAGE

Study medication

Antenatal diagnosis



INTERVENTION



Congenital Heart
Disease Life Span
PREVENTING COLLATERAL DAMAGE

Conclusie

- Hersenschade komt frequent voor bij ernstige aangeboren hartafwijkingen
- Hersenschade geeft NIET altijd ontwikkelingsproblemen
- Ernstige hersenschade is op jonge leeftijd zichtbaar
- Minder ernstige hersenschade uit zich pas veel later en subtieler (complexe executieve functies)
- Gelukkig is het IQ van ouders meer voorspellend voor IQ van het kind dan de hartafwijking





Bedankt!

**Wilhelmina
Kinderziekenhuis**

- **Kinderhartcentrum**
- **Kinder-IC**
- **Neonatologie**
- **Obstetrie**
- **Radiologie**
- **Kinderbewegingscentrum**
- **Medische Psychologie**

