DIONYSUS

WORLDWIDE COLLABORATION FOR HDFN

Variations & Opportunities in the Management of Hemolytic Disease of the Fetus and Newborn

Postnatal management

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For the **DIONYSUS-investigators**

Sanquin

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Disclosures

DIONYSUS-study is researcher-initiated and not externally funded.

Dutch research group received funding from Momenta Pharmaceuticals to work on biomarkers and data analysis for identification of high-risk HDFN.

Previously…

Considerable variations in antenatal management and IUTs

Far majority born before 37 weeks and 0 days

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This presentation

Exchange transfusions and IVIG

RBC transfusions

Effects of gestational age at birth

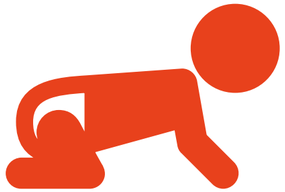
Short-term & Long-term

31 centers, 22 countries

2420 pregnancies

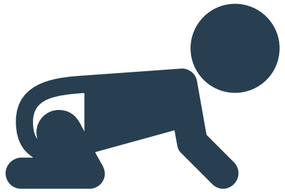
470 (19.2%) missing postnatal
95 (3.9%) perinatal death

Liveborn, antenatal treatment



1017 (55%)

Liveborn, no antenatal treatment

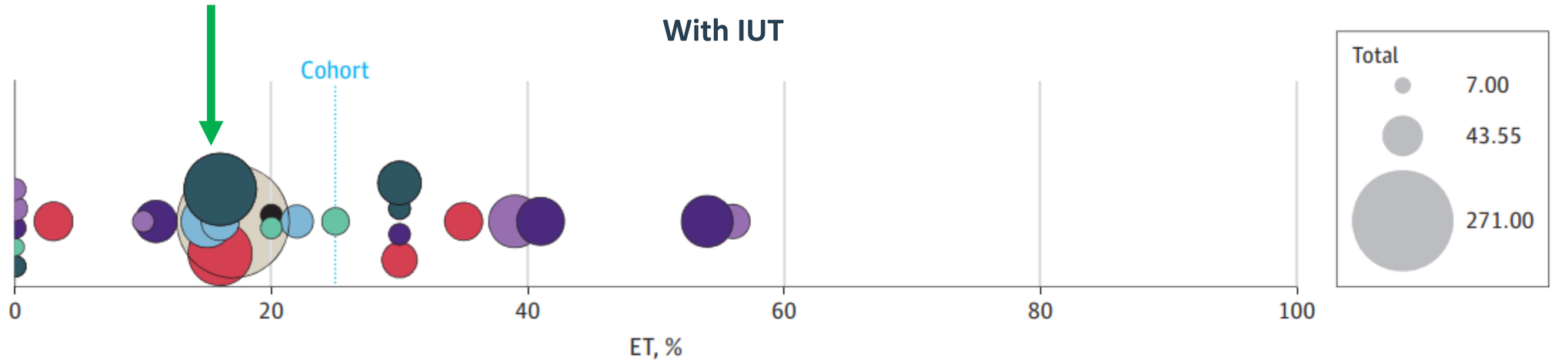


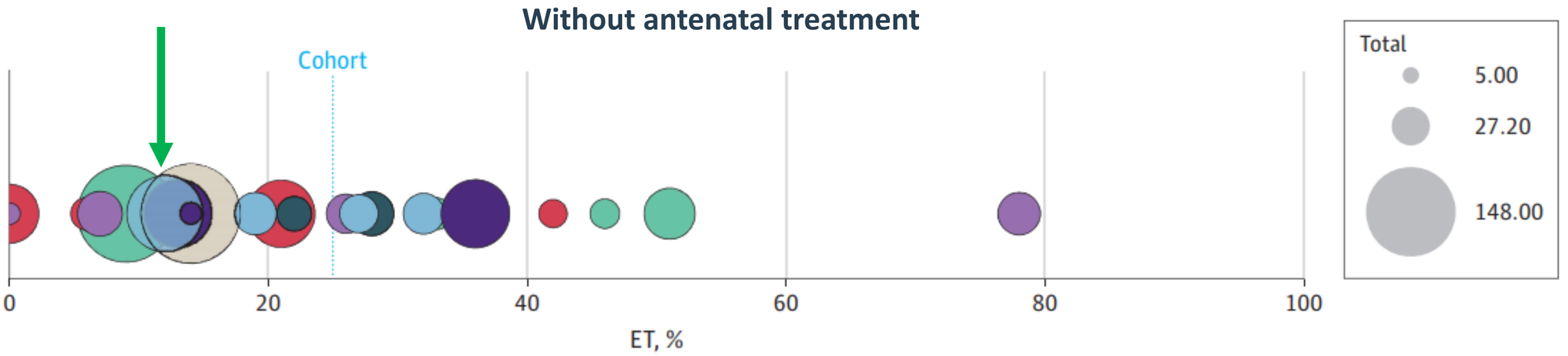
838 (45%)

1 Hyperbilirubinemia - *exchange transfusions*

Phototherapy used in 1743 neonates (94%)
Median duration 4 days (IQR 3-6)

Exchange transfusions in 23.5%

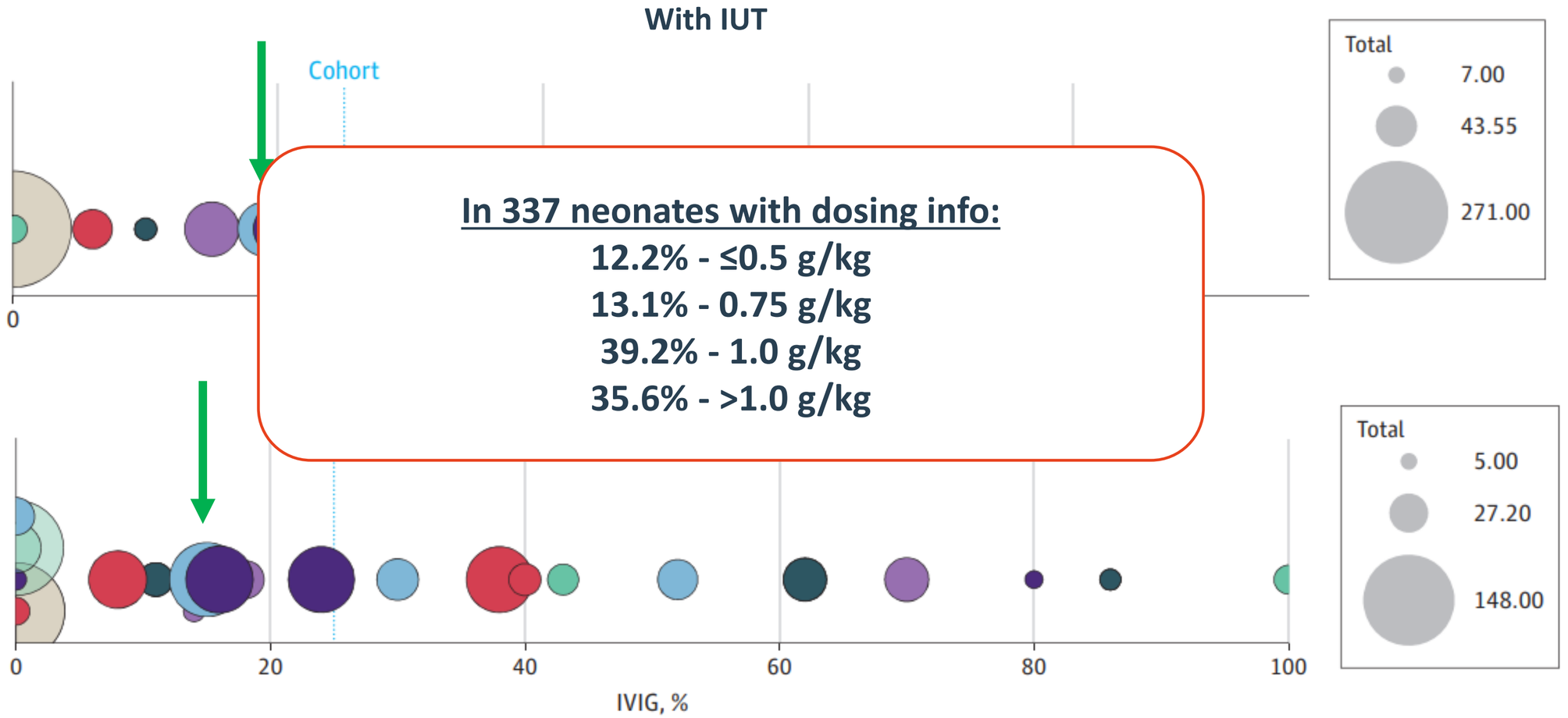




1 Hyperbilirubinemia - *IVIG*

To delay or prevent impending ET

Postnatal IVIG in 24.6%



In 337 neonates with dosing info:

12.2% - ≤0.5 g/kg

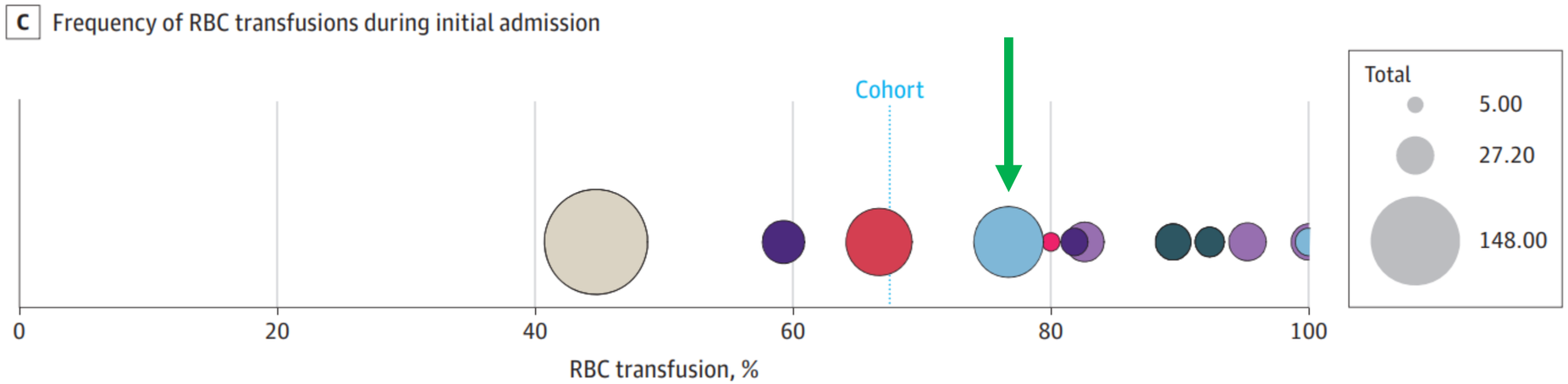
13.1% - 0.75 g/kg

39.2% - 1.0 g/kg

35.6% - >1.0 g/kg

2 Neonatal anemia - *RBC transfusions*

Data on timing and admission available in 465 of 1855 neonates
314 (67%) received 1 or more RBC transfusions during admission



Median **pretransfusion Hb 7.9 g/dL** (IQR 7.1-8.9)
Variations between centers – no consensus on thresholds

Erythropoietin used in 6.4%
Proportions ranging between 0% and 47% among centers

3 Gestational age at birth - Exchange transfusions

Hypothesis: lower risk of severe hyperbilirubinemia in increasing gestational age at birth?

Earlier gestational age at birth

Less transfer of maternal IgG

Potential reduce hemolysis rate?

Later gestational age at birth

Increased fetal maturation

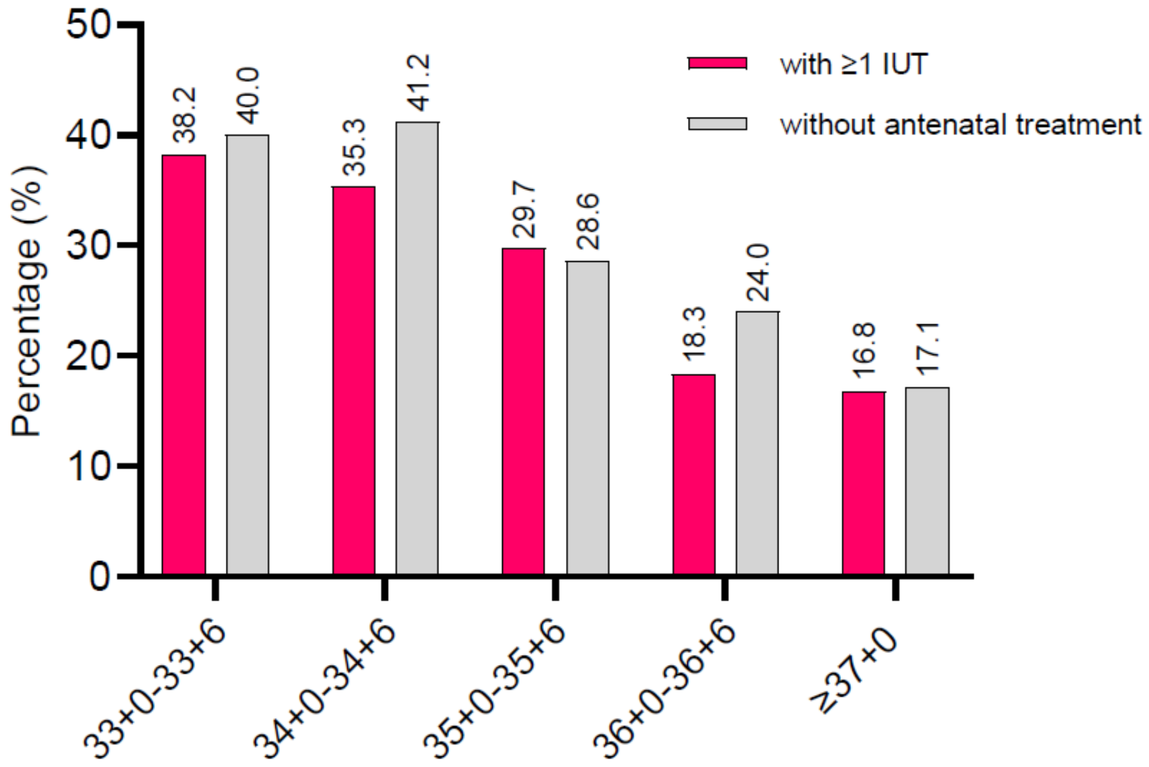
Decreased risk of severe hyperbilirubinemia?

3 Gestational age at birth - Exchange transfusions

Included 990 neonates in a comparative analysis
Baseline characteristics are comparable

Assessed in D- or c-mediated HDFN, born ≥33+0

To prevent confounding and accurately assess an association, we excluded:
Antenatal IVIG = 67
Postnatal IVIG = 236
Severe hydrops = 67
Twin pregnancy = 21

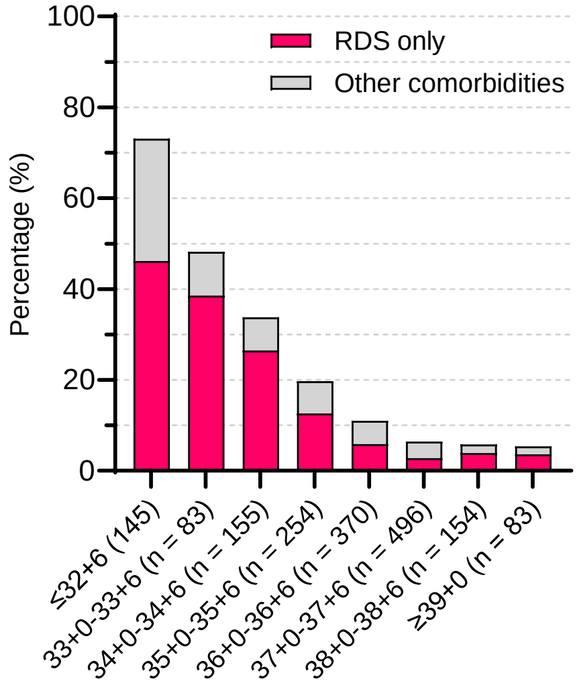


Potential positive clinical effect of waiting for delivery until <u>after 37^{+0} weeks</u> in HDFN

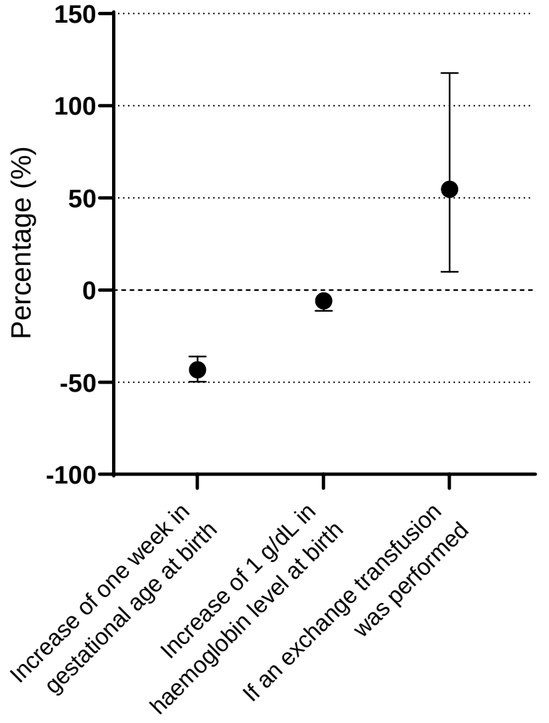
3 Adverse neonatal outcome

Adverse neonatal outcome defined as at least ≥1:
RDS, NEC ≥Bell stage 2A, proven sepsis, severe cerebral injury (e.g. PVL), kernicterus, and neonatal mortality,

Present in 332/1740 neonates (19.1%)



Multivariate logistic regression analysis

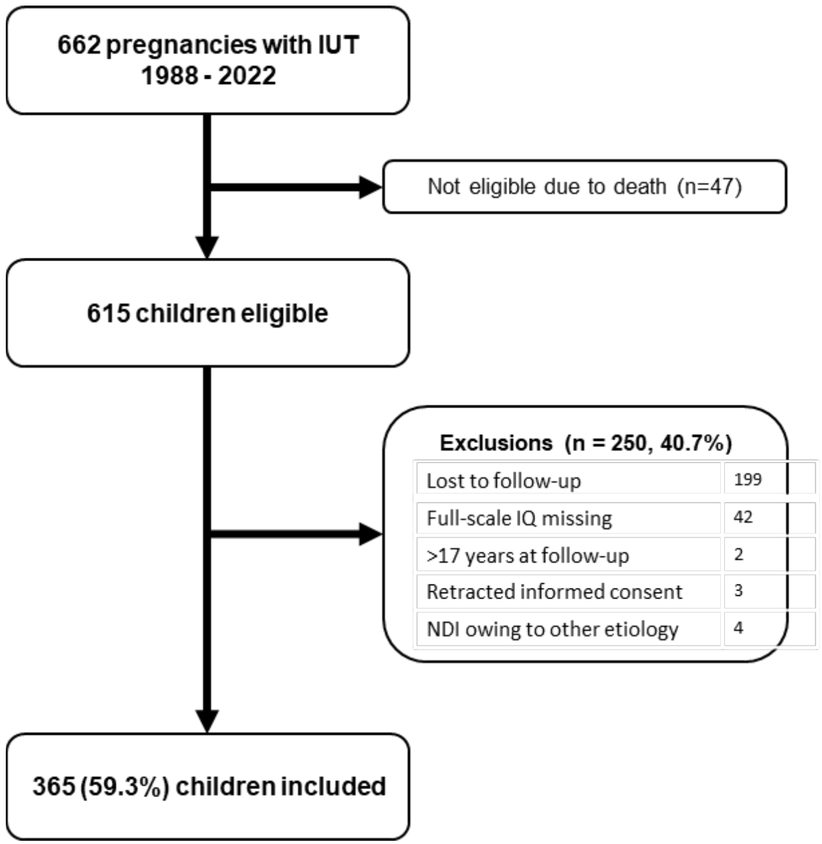


Every additional week at birth: 43% decrease in likelihood
Increase of 1 g/dL in Hb at birth: 5,9% decrease in likelihood
Need for exchange transfusion: 1.55x increase in likelihood

IUT treatment, number IUTs and severe hydrops at first IUT and birthweight not associated

4 Long-term neurodevelopment

- Insufficient data in DIONYSUS database
  - Cases with IUT between 1988-2022 at the LUMC



Full-scale IQ score

Neurodevelopmental impairment: at least ≥1:
cerebral palsy ≥GMFCS level II, severe cognitive developmental delay (<2 standard deviations), hearing loss or deafness and bilateral blindness

Associated factors

4 Long-term neurodevelopment – IQ

Median 101 [IQR 91-110]
IQ <85: 14.6%
IQ <70: 2.5%

Multivariate linear regression analysis
GA at first IUT
Hb at first IUT
Severe hydrops
GA at birth
Maternal education level

Only maternal education level was significantly associated with full-scale IQ score

4 Long-term neurodevelopment - NDI

Neurodevelopmental impairment: at least ≥1:
cerebral palsy ≥GMFCS level II, severe cognitive developmental delay (<2 standard deviations), hearing loss or deafness and bilateral blindness

5% (18/363)

Severe cognitive developmental delay (6)
CP (5)
Deafness (2)
CP + severe cognitive delay (2)
CP + deafness (1)
Hearing loss (1)
CP + severe cognitive delay + hearing loss (1)

Multivariate logistic regression:
GA at first IUT
Presence of severe hydrops
GA at birth

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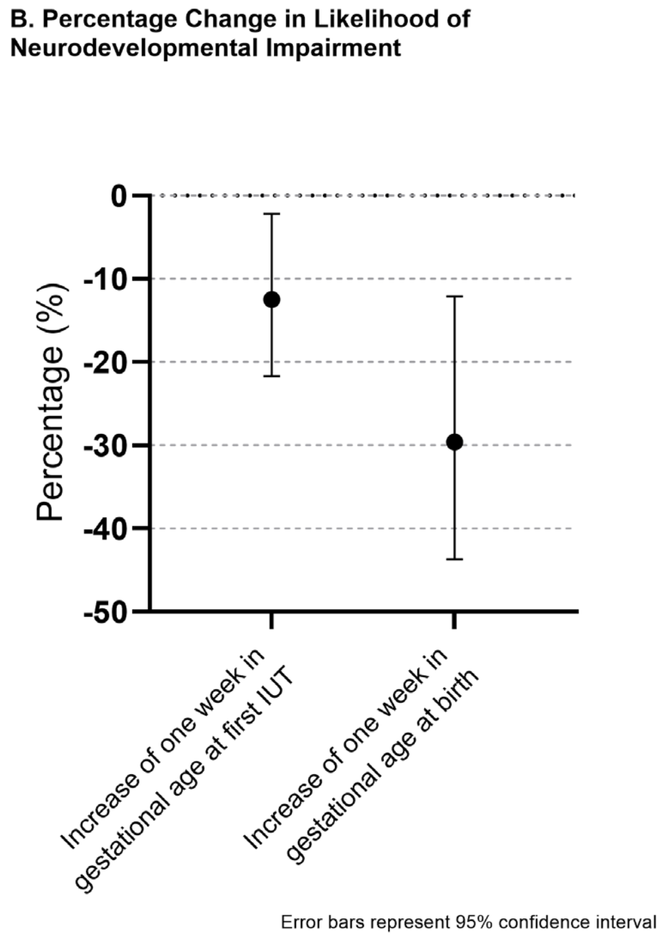

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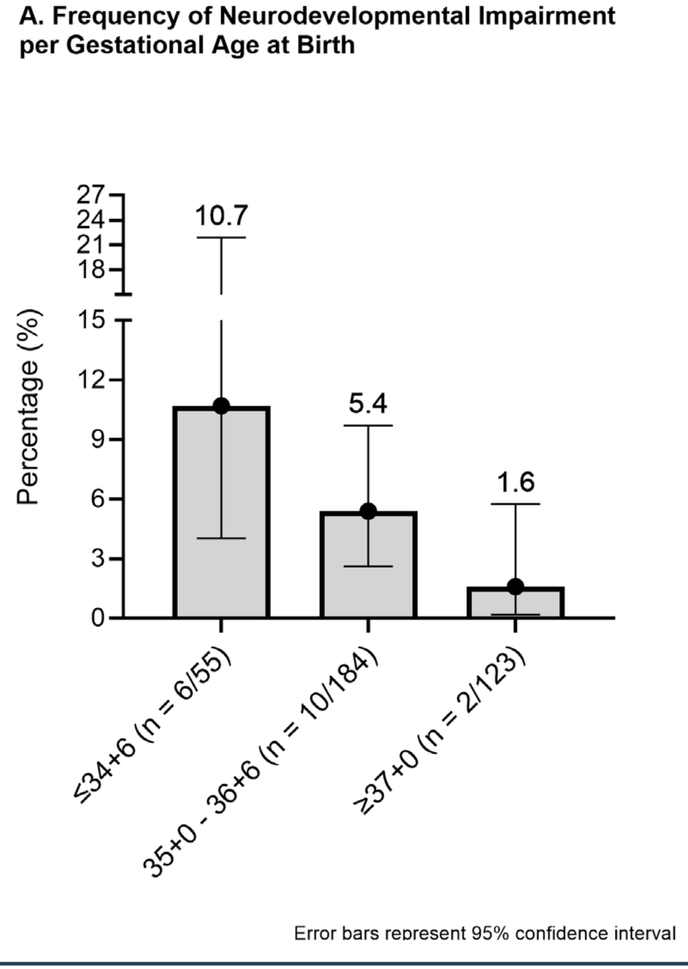
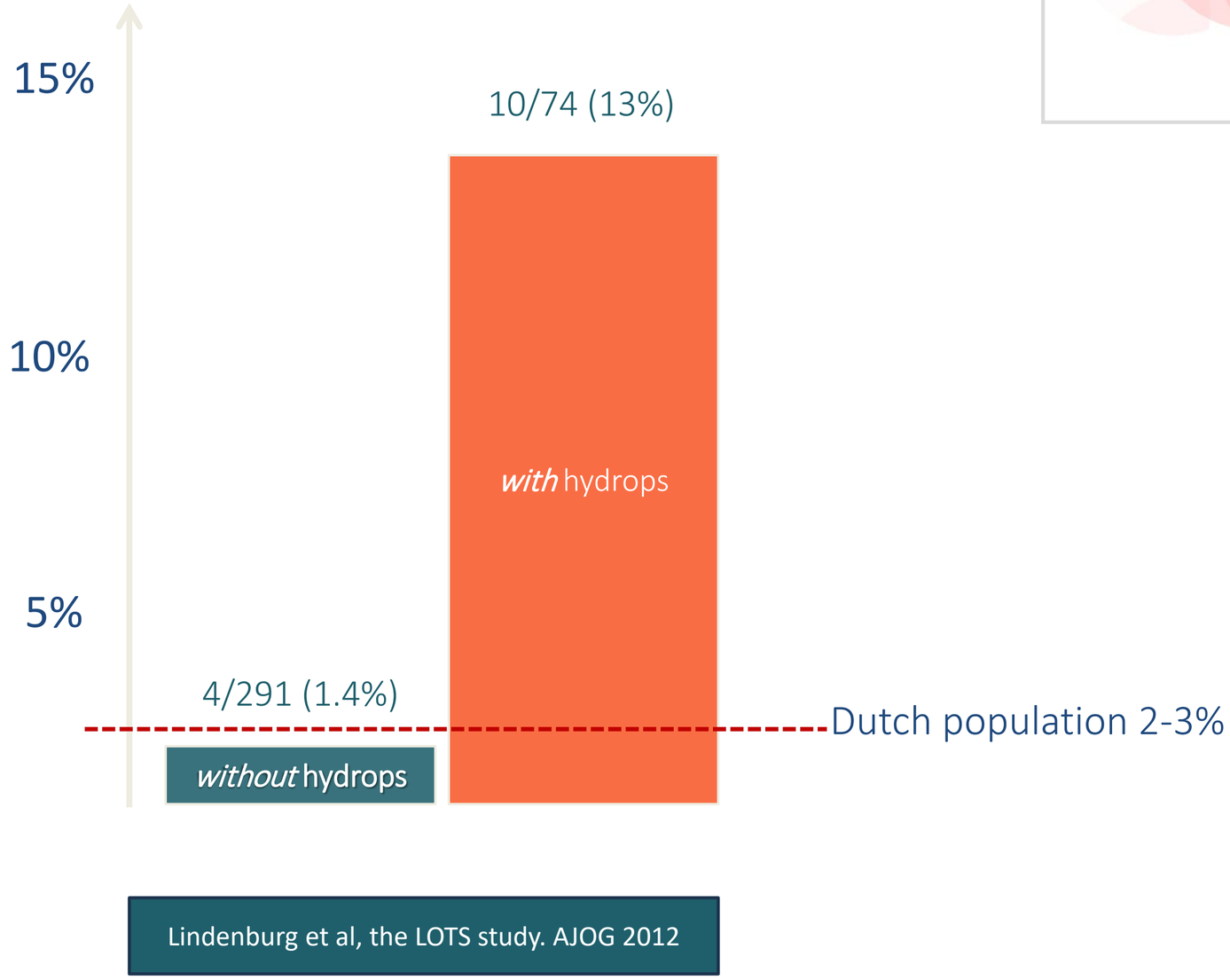


Risk factors NDI



Lindenburg et al, the LOTS study. AJOG 2012

To conclude

Considerable variation between centers in:

Exchange transfusions

IVIG

RBC transfusions

Beneficial effect of waiting for delivery ≥37 weeks and 0 days

Exchange transfusion frequency

Adverse neonatal outcome

Long-term neurodevelopmental impairment

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WORLDWIDE COLLABORATION FOR HDFN

Thank you to the participating centers!

Birmingham Women's and Children's Hospital NHS Foundation Trust

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Hospital de la Mujer, La Paz, Bolivia

Hospital La Paz Madrid, Spain

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University Medical Center Ljubljana, Slovenia