

## Kliiniline küsimus nr 2

Kas kõik ähvardava enneaegse sünnitusega rasedad tuleb ema tervises seisundi parandamiseks ning vastsündinu parema ravitulemi saavutamiseks tsentraliseerida vastavate ravivõimalustega ja piisava enneaegsete vastsündinute arvuga keskustesse võrreldes mittetsentraliseerimisega?

Kriitilised tulemusnäitajad: raseduse prolongeerimine, emade tervisetulem ja suremus, lapse peamised tulemusnäitajad

## Süsteematilised ülevaated

### *Kokkuvõtte süstemaatilistest ülevaadetest*

Perinataalse regionaliseerimise kohta on mitmeid publikatsioone, mille tulemuste alusel soovitatakse enneaegse sünnituse korral emade ja vastsündinute tulemi parandamiseks suunata kõrge riskiga rasedaid spetsialiseeritud keskustesse, kus on kättesaadav kõrgema etapi neonataalne intensiivravi, kuigi tõenduspõhisus antud teema kohta on piiratud. Enamik andmetest pärinevad retrospektiivsetest kohort-uuringutest ja nende põhjal tehtud süstemaatilistest ülevaadetest.

Kokkuvõttes esitan uuemate (viimased 5 aastat) uuringute kokkuvõtteid ja mõned olulisemad publikatsioonid varasemast perioodist, millele viitavad eelkõige juhendid.

Üks uuematest ülevaateartiklitest on publitseeritud Locatelli et al., 2015 poolt, kus võetakse kokku kõige uuemaid tõenduspõhiseid seisukohti enneaegse sünnituse kohta.

(Locatelli, A., Consonni, S., Ghidini, A., 2015. Preterm labor: approach to decreasing complications of prematurity. *Obstet. Gynecol. Clin. North Am.* 42, 255–274. doi:10.1016/j.ogc.2015.01.004)

Artiklis rõhutatakse, et eksisteerivad ainult kaks interventsiooni, mis vähendavad perinataalset suremust enneaegse sünnituse korral: kortikosteroidide manustamine ja riskirasedate suunamine kõrgema etapi haiglasse, kus on võimalik spetsialiseeritud ravi vastsündinutele.

Mitmete uuringutega on tõestatud, et neonataalsed tulemused on paremad vastsündinutel, kes olid transporditud *in utero* võrreldes nendega, kes olid transporditud pärast sündi, eriti nendel, kes olid sündinud enne 30-nädalat.

Viidatakse Lee et al., 2003 poolt publitseeritud Kanadas läbiviidud kohort-uuringule, mis uuris kolmanda etapi üksuse mõju enneaegsete vastsündinute tervisetulemile erinevates gestatsioonivanustes. Uuringusse oli võetud kokku 2962 enneaegset last sündinud enne 32-nädalat 17ndas keskustes 1 aasta jooksul (1996-1997).

Suremuse (OR 1.7) ja ajusisese hemorraagia risk (OR 2.2) oli oluliselt kõrgem lastel sündinud alla 26-nädalat üksustes, kus puudus III. astme NICU.

Kroonilise kopsuhaiguse risk oli kõrgem lastel sündinud vanuses 27- kuni 29-nädalat üksustes, kus puudus III. astme NICU.

30- kuni 31-nädalal sündinud laste tervisetulem oli sarnane sõltumata üksuse tasemest.

Samuti viidatakse Chung et al., 2011 kohort-uuringule (läbiviidud US-s 1997-2002. aastal), et üksuse aastane maht/suurus tundub olevat kõige olulisem faktor, mis vähendab suremust väga enneaegsetel vastsündinutel, seega mida suurem on üksus, seda paremad on ta ravitulemused.

Viidatakse Lorch et al., 2012 poolt publitseeritud retrospektiivsele kohort-uuringule, mis sai läbi viidud California ja Missouri sünnitusmajades 1995-2005. aastal.

[Type text]

Uuringusse olid kaasatud 23 – 37-nädalal sündinud enneaegsed lapsed, kokku 1 328 132 last. Uuringu eesmärgiks oli aru saada, kas sünnitus kõrgema etapi haiglas III. astme NICUga mõjutab vastsündinute tervisetulemit. Analüüs näitas, et kõrgemas etapis sünnitamine vähendab vastsündinu suremuse riski.

Et garanteerida toimivat ja efektiivset haiglatevahelist kommunikatsiooni, tuleks luua adekvaatne võrgustamine ja adekvaatsed transpordiprotokollid.

<b>Principles</b>	<b>Tools</b>
Communications between professionals	Electronic database, informatics tools, maternal transfer form
24-h availability transport system	Link to territorial emergency facilities (ambulance or helicopter service)
Transport protocols	Clinical guidelines shared between different facilities
Good knowledge of transport system	Meeting and audit of cases in the network
Continuum of care	During transport an adequate level of assistance must be maintained; close monitoring of vital sign and clinical conditions
Back transport to referring hospital when problems are resolved	Good distribution of sanitary resources

Artiklis mainitakse, et kommunikatsioon suunava ja vastuvõtva arsti vahel on essentsiaalne, et rakendada efektiivset ravi. Suboptimaalse ravi põhjusteks enneaegse sünnituse korral on tavaliselt puudulik kommunikatsioon.

Tuakse ka välja ema transpordi vastunäidustusi

- Ebastabiilne ema seisund
- Loote ebastabiilne seisund, mis võib halveneda kiiresti
- Kohene või vältimatu sünnitus

Edasi on esitatud oluliste publikatsioonide kokkuvõtted.

1. Lapcharoensap, W., Gage, S.C., Kan, P., Profit, J., Shaw, G.M., Gould, J.B., Stevenson, D.K., O’Brodivich, H., Lee, H.C., **2015. Hospital variation and risk factors for bronchopulmonary dysplasia in a population-based cohort.** JAMA Pediatr 169, e143676. doi:10.1001/jamapediatrics.2014.3676

Uuringu tähtsus: BPD on tõsine haigestumus madala kaaluga enneaegsete vastsündinute hulgas (alla 1500g). Neonataalse abi deregionaliseerimist seostatakse BPD esinemissageduse kasvuga nendel vastsündinutel. Riskifaktorid on tavaliselt: madal sünnikaal, väike gestatsioonivanus, meessugu, IUGR, prolongeeritud ventilatsioonist tekitatud kahju. Probleemiks on #midlevel low-volume# üksuste suurenev arv.

Antud retrospektiivse kohort-uuringu andmeid koguti 2007-2011. aastatel ja see hõlmas 90% NICUdest Californias. Uuringu eesmärgiks oli hinnata BPD arengu individuaalseid riskifaktoreid ja võrrelda BPD esinemissagedust erineva tasemega NICUde vahel enneaegsetel lastel sündinud vanuses 22- kuni 29-nädalat (VLBW).

NICU tasemed olid defineeritud järmselt: NICU I well newborn nursery, NICU II special care nursery, NICU III ja NICU IV regional. NICU II tegeleb >32-nädalal sündinud

[Type text]

lastega või kehakaalu järgi >1500 g ja seal on võimalik lühike mehhaanilise ventilatsiooni pakkumine alla 24 tundi. NICU III ja IV vahel on erinevus ainult selles, et NICU IV pakub kirurgilist ravi kongenitaalsete malformatsioonidega vastündinutel.

BPD oli defineeritud kui pidev hapniku vajadus vanuses 36-nädalat. Tulemusnäitajateks oli mõõdukas või raske BPD või surm enne 36-nädalat.

Kohort sisaldas 15779 enneaegset vastündinut. Nendest 7081 vastündinul (44.8%) arenes BPD ja nad olid kaasatud analüüsi.

BPD esinemissagedus varieerus NICUde vahel 17.7% - 73.4%-ni (kokku kaasatud 116 NICU).

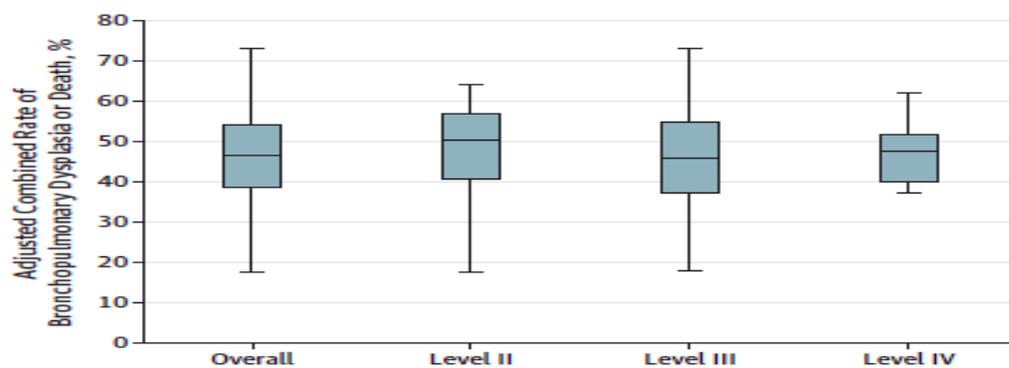
Võrreldes IV astme NICUga risk saada BPD oli kõrgem II astme NICU-s

(OR, 1.23; 95% CI, 1.02-1.49) ja sarnane III astme NICU ga

(OR, 1.04; 95% CI, 0.95-1.14).

Kokkuvõte: BPD esineb ca 45% väikse kaaluga vastündinutel Californias. Väga erinev esinemissagedus erinevate üksuste vahel tähendab, et regionaliseerimine võib vähendada BPD esinemissagedust VLBW hulgas.

**Figure 2. Combined Outcome of Bronchopulmonary Dysplasia or Death Across California Perinatal Quality Care Collaborative Centers Stratified by Academy of Pediatrics Level of Care**



Boxes represent the 25th to 75th percentile. Middle line represents the median. Whiskers extend to the minimum and maximum values found. Risk-adjusted rates are based on a single multivariable logistic regression model that includes all variables listed in Table 2.

2. Jensen, E.A., Lorch, S.A., 2015. Effects of a Birth Hospital's Neonatal Intensive Care Unit Level and Annual Volume of Very Low-Birth-Weight Infant Deliveries on Morbidity and Mortality. JAMA Pediatr 169, e151906. doi:10.1001/jamapediatrics.2015.1906

Uuringu eesmärgiks oli hinnata NICU aastase mahu ja NICU taseme mõju väga madala sünnikaalu vastündinute haigestumisele ja suremusele.

Retrospektiivne kohort-uuring 1999-2009. aastatel California, Missouri ja Pennsylvania piirkondades. Kokku oli analüüsitud 72 431 väga väikese kaaluga enneaegse vastündinu andmeid 10 aastase perioodi jooksul.

Tulemusnäitajateks oli BPD, NEK, retinopaatia, IVH esinemissagedus.

Tulemused: Üksustes, kus sündis vähem kui 10 VLBW vastündinut oli kõige kõrgem suremus (15.3% [95% CI, 14.4%-16.3%]), IVH risk (17.5% [95% CI, 16.5%-18.6%]), NEK (19.3% [95% CI, 18.1%-20.4%]).

[Type text]

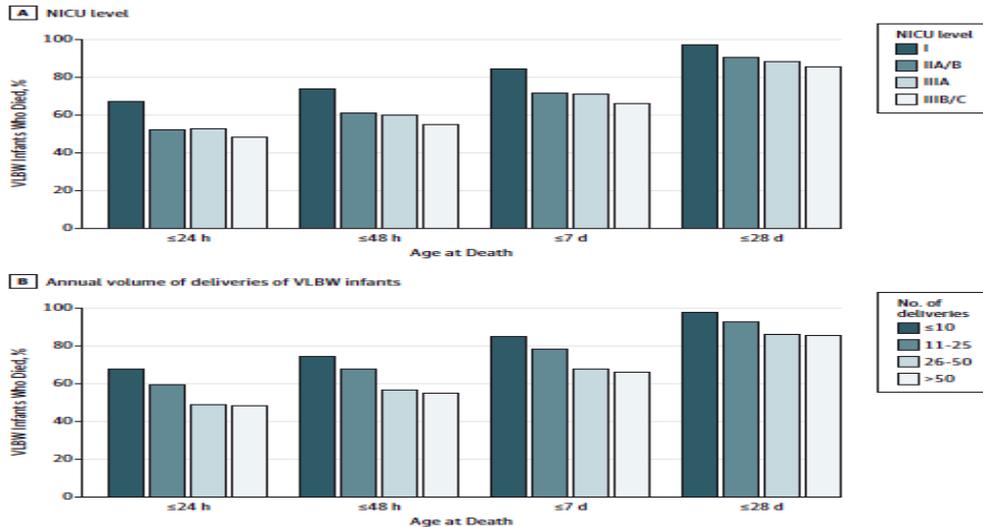
Need tsistused esinesid ka sagedamini vastsndinutel, kes olid sndinud NICU I ja II tasemega vrreldes NICU III ja IV tasemega.

Kokkuvte: Tsistusi esines vhem vastsndinutel, kes sndisid krgema etapi haiglas ja suurema mahuga haiglates.

Jreldati, et ksuse VLBW snnituse maht mjutab vastsndinute suremust ja heaigestumist (IVH, NEK) rohkem kui NICU tase.

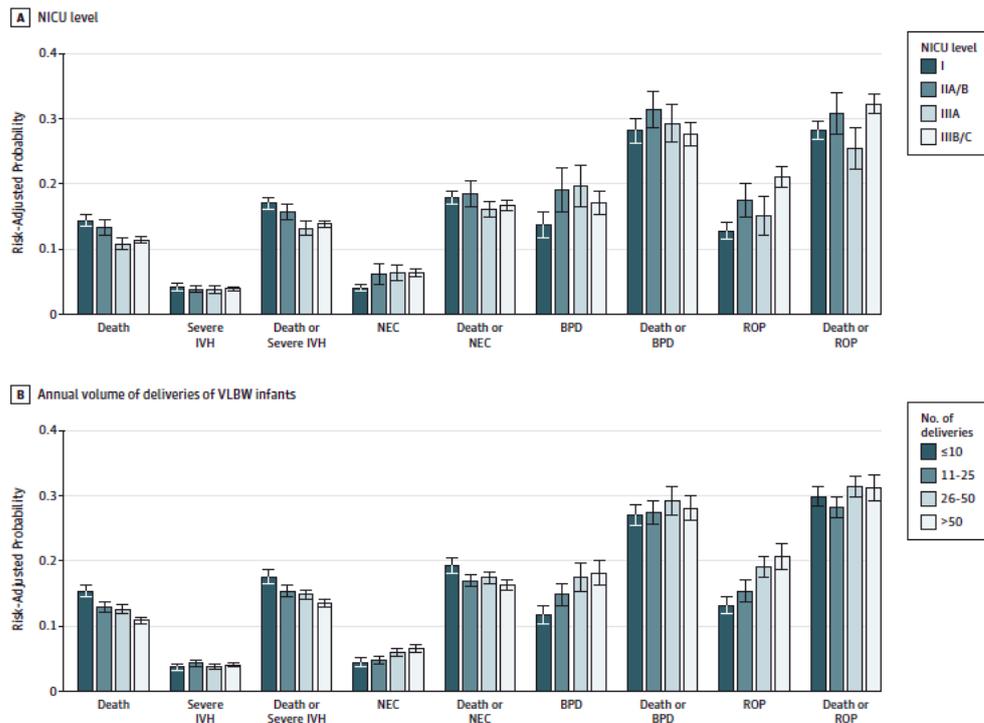
Seega krge riskiga rasedate antenataalne transport nendesse ksustesse (suurem maht ja krgem tase) vib vhendada suremust ja parandada ravitulemusi.

**Figure 1. Percentage of Deaths Occurring Within the First 24 Hours, 48 Hours, 7 Days, and 28 Days by Birth Hospital's Neonatal Intensive Care Unit (NICU) Level (A) and Annual Volume of Very Low-Birth-Weight (VLBW) Infant Deliveries (B)**



[Type text]

Figure 2. Risk-Adjusted Probability of the Individual and Morbidity-Mortality Composite Outcomes by Birth Hospital's Neonatal Intensive Care Unit (NICU) Level (A) and Annual Volume of Very Low-Birth-Weight (VLBW) Infant Deliveries (B)



Probabilities adjusted for birth weight; sex; small for gestational age status; multiple gestation status; maternal age, race, and insurance status; maternal chronic hypertension, renal disease, diabetes mellitus, gestational diabetes and hypertension, abnormal placentation, oligohydramnios, premature rupture of membranes, chorioamnionitis, and precipitous labor; fetal distress; mode of delivery; year; and state. BPD indicates bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; and ROP, retinopathy of prematurity. Error bars indicate 95% CIs.

Table 3. Risk-Adjusted Odds Ratios for Death and Morbidity-Mortality Composite Outcomes After Simultaneous Adjustment for Both NICU Level and Annual Volume of VLBW Infant Deliveries<sup>a</sup>

Hospital Factor	Odds Ratio (95% CI)				
	Death	Death or BPD	Death or Severe IVH	Death or NEC	Death or ROP
<b>NICU level</b>					
I	1.08 (0.90-1.28)	1.38 (1.06-1.79)	1.15 (0.98-1.37)	0.95 (0.81-1.12)	0.73 (0.59-0.90)
IIA/B	1.15 (0.94-1.41)	1.43 (1.13-1.82)	1.15 (0.97-1.36)	1.12 (0.90-1.39)	0.91 (0.71-1.18)
IIIA	0.89 (0.78-1.01)	1.17 (0.92-1.49)	0.90 (0.79-1.04)	0.94 (0.82-1.08)	0.63 (0.49-0.82)
IIIB/C	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
<b>No. of deliveries</b>					
≤10	1.63 (1.35-1.96)	0.71 (0.55-0.91)	1.36 (1.14-1.63)	1.33 (1.12-1.57)	1.14 (0.92-1.41)
11-25	1.25 (1.09-1.44)	0.80 (0.65-0.98)	1.15 (1.01-1.33)	1.06 (0.92-1.21)	0.95 (0.78-1.16)
26-50	1.24 (1.12-1.38)	1.07 (0.88-1.29)	1.15 (1.04-1.28)	1.10 (0.99-1.22)	1.02 (0.88-1.18)
>50	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; ROP, retinopathy of prematurity; VLBW, very low-birth-weight.

<sup>a</sup> Odds ratios are adjusted for birth weight; sex; small for gestational age status; multiple gestation status; maternal age, race, and insurance status; maternal

chronic hypertension, renal disease, and diabetes mellitus; gestational diabetes and hypertension; abnormal placentation; oligohydramnios; premature rupture of membranes; chorioamnionitis; precipitous labor;

diagnosis of fetal distress; mode of delivery; year; state; NICU level; and annual volume of VLBW infant deliveries.

3. Rashidian, A., Omidvari, A.H., Vali, Y., Mortaz, S., Yousefi-Nooraie, R., Jafari, M., Bhutta, Z.A., 2014. The effectiveness of regionalization of perinatal care services--a systematic review. Public Health 128, 872–885. doi:10.1016/j.puhe.2014.08.005

Publikatsioonis selgitatakse, et regionaliseerimise all mõistetakse ratsionaalset meditsiinilise teenuse jaotamist riigis, kus kõigi astme teenused (primaarne, sekundaarne ja tertsiaarne) on hästi kättesaadavad populatsioonile, kuid ka kulu efektiivsed.

[Type text]

WHO Europe 2010 ja USA, American Academy of Pediatrics 2004 soovitusel põhjal efektiivne perinataalne regionaliseerimine hõlmab kolme tasemega üksuseid: I tase (normaalne rasedus ja terve vastündinu), II tase (mõõduka riskiga rasedus) ja III tase on regionaalsed keskused, kuhu suunatakse kõrge riskiga rasedaid.

Antud ülevaate eesmärgiks oli hinnata olemasolevat tõendust perinataalse regionaliseerimise mõjust ema ja vastündinu tervisetulemile. Teiseks eesmärgiks oli uurinda, kas erinevate regionaliseerimise mudelite vahel on erinevus efektiivsus.

Autorid tunnistavad, et tõendusmaterjal on selle teema kohta limiteeritud. Ülevaade oli tehtud populatsiooni uuringute põhjal. Esialgu otsingutega õnnestus valida 53 publikatsiooni ja nendest ainult 8 uuringut (10 publikatsiooni) läbisid kõike kriteeriume ja olid kaastaud analüüsi: USA, Kanada, Prantsusmaa. 3 nendest olid hinnatud kvaliteetsemateks (low risk of bias) ja nendest üks raporteeris olulist neonataalsete surmade langust regionaliseerimise tulemusel. Vähem kvaliteetsemad uuringud (higher risk of bias) samuti raporteerisid tulemi paranemist.

Kokkuvõte: Perinataalse regionaliseerimise rakkendamise programmiid korreleeruvad perinataalse tulemi paranemisega. Paljud riigid raporteerivad perinataalsete tulemuste paranemist regionaliseerimise tulemusel, kuid otsest seost on raske välja tuua eksisteerivate uuringute põhjal (metdoloogilised piirangud). Regionaliseerimisega kaasnevad ka teised faktorid, mis võivad tulemust mõjutada nagu elutaseme tõus populatsioonid, uute ravimeetodite ja ravimite leidmine ja ka suuremad investeringud tervishoidu. Tõendus efektiivsuse kohta on ikkagi nõrk.

Vajalik hinnata regionaliseerimise efektiivsust parma disainiga uuringute põhjal erinevates riikides randomiseeritud kontroll uuringutes.

**Table 2 – The direction of effect observed in the included studies for important outcomes reported in at least two studies.**

Study designs	ITS			CBA	Before-after or controlled after-only studies				
	Usher 1977	North Carolina*	Mandell 1986	McCormick 1985	Hoekstra 1981	North Carolina*	Hein 1986	Bode 2001	Zeitlin 2010
Perinatal mortality	↓	↓	×	×	↓	×	×	×	×
Neonatal mortality	↓	↓	⇓	↓	⇓	×	⇓	↓	×
Low birth weight rate	↓	×	×	↓	⇓	×	⇓	×	×
Still births	↓	×	×	×	↓	×	×	×	×
LBW delivery in level III centers	↑	×	×	↑	×	×	⇓	⇓	⇓
Fetal mortality	×	↓	×	×	×	×	⇓	×	×
Infant mortality	×	×	⇓	×	×	×	×	×	×
Low 5 min Apgar score	×	×	×	×	⇓	⇓	×	×	×
Intra ventricular hemorrhage	×	×	×	×	×	×	×	×	⇓
Motor development, mental status	×	×	×	×	×	↑	×	×	×
Maternal sensitivity or involvement	×	×	×	×	×	⇓	×	×	×

⇓ Decreased significantly; ↓ Decreased, significance level was not noted; ↓ Decreased, not significant; ⇓ Increased significantly; ↑ Increased, significance level was not noted; ↑ Increased, not significant; × Outcome not reported in the study. \* Linked North Carolina papers include Gilling et al., 1981, Siegel et al., 1985 and Siegel et al., 1986.

4. Marlow, N., Bennett, C., Draper, E.S., Hennessy, E.M., Morgan, A.S., Costeloe, K.L., 2014. **Perinatal outcomes for extremely preterm babies in relation to place of birth in England: the EPICure 2 study.** Arch. Dis. Child. Fetal Neonatal Ed. 99, F181–188. doi:10.1136/archdischild-2013-305555

What this study adds:

- Vastsündinute elulemus on parem spetsialiseeritud haiglate NICUs ja veel paraneb suurema mahuga üksustes.
- Tulemuste paranemine on enamasti saavutatud antenataalse lootesurmade vähenemisega, neonataalse surmade vähenemisega sünnitustoa ja esimese elunädala jooksul.

[Type text]

- Rasedad, kes saavad antenataalset jälgimist spetsialiseeritud keskustes, nendel on väiksem suremus võrreldes nendega, kes saavad jälgimist mittespetsialiseeritud keskustes, antenataalne transfer samuti parandab vastsündinu tulemusi.

Tegemist on polulaptsiooni uuringuga, mille hüpoteesiks on, et sünnitus või antenataalne transport III etappi üksusesse vähendab suremust ja haigestumust.

Üksuste klassifikatsioon: I tase: ainult norm rasedused ja sünnitused, ülejäänud kuuluvad transferile. II tase: transfer enne 27 nädalat. III tase: regionaalne ja kõrge kõrgem.

Mahu järgi klassifikatsioon III taseme üksustes: kõrge aktiivsus ( $\geq 2000$  päeva respiratoorset toetust aastas (cPAP või mehhaniline ventilatsioon)+ rohkem kui 4 arst-konsultanti; keskmine aktiivsus (500-1999 päeva respiratoorset toetust aastas + 1 arst-konsultant; madal aktiivsus: (alla 500 päeva respiratoorset toetust aastas) ja arst-konsultati puudumine.

Neonataalne haiegtumus oli defineeritud kui üks või mitu probleemi esinemist: retinopaatia, mis vajab kirurgilist ravi; mõõdukas või raske BPD, tõsine ajukahjustus (paremhümaalsed infarkt, tsüstilised muutused, hüdrosefaalia); NEK, mis vajab operatsiooni.

Uuringu taust: kogemus ja ressursid võivad mängida olulist rolli sügavalt enneaegse vastsündinute tulemis. Uuring hindas üksuse mõju ja perinataalse transpordi mõju elumusele ja haigestumisele sügavalt enneaegsetel vastsündinutel 22-26 nädalal Inglismaal sündinud 2006 aasta jooksul.

Meetodid: 2760 vastsündinut olid kaasatud analüüsi.

Ravitulemused olid võrreldud III ja II NICU taseme vahel transpordiga või ilma.

Samuti ravitulemused olid võrreldud erineva mahuga III NICU tasemega üksuste vahel.

Tulemused: 56 % sündisid III tasemega NICU ja 34% sündisid II tasemega NICU, 10% olis sündinud I tasemega üksustes, kus puudus NICU.

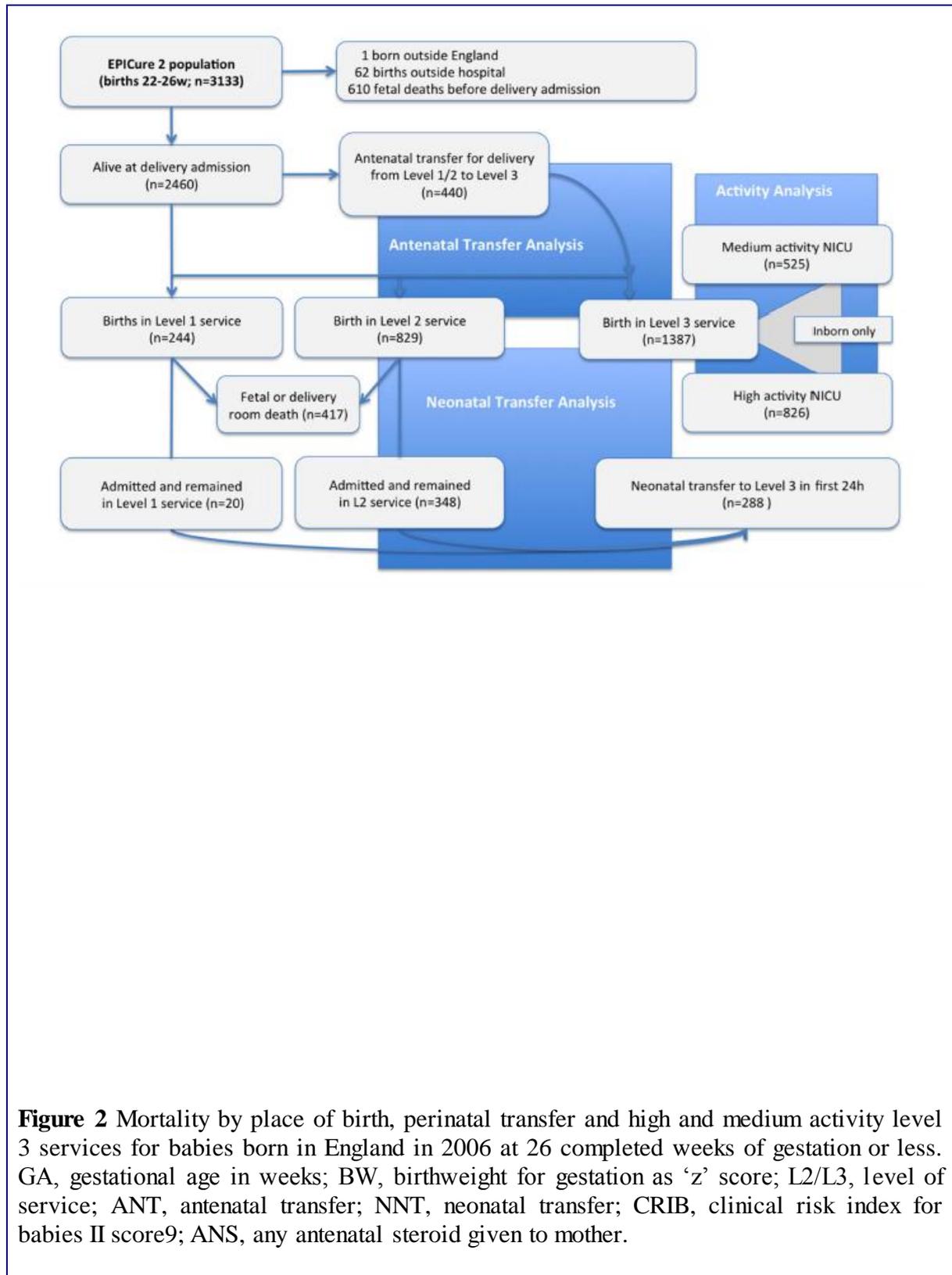
Võrreldes II taseme NICUga, III taseme NICU suremuse risk oli väiksem (aOR 0.73 (95% CI 0.59 to 0.90) aga proportsioon nendest, kes jäid ellu ilma neonataalse haigestumisega oli sama (aOR 1.27 (0.93 to 1.74).

Kui oli rakendatud antenataalne transfer III tasemega üksusesse, siis oli vähem surmasid sünnituse ajal ja üldine perinataalne suremus nende hulgas, kes jäid II astmega üksusesse oli kõrgem (aOR 1.44 (1.09 to 1.90). III etappi üksused, kus olid suuremad mahud, esines vähem surmasid üleüldse (aOR 0.68 (0.52 to 0.89).

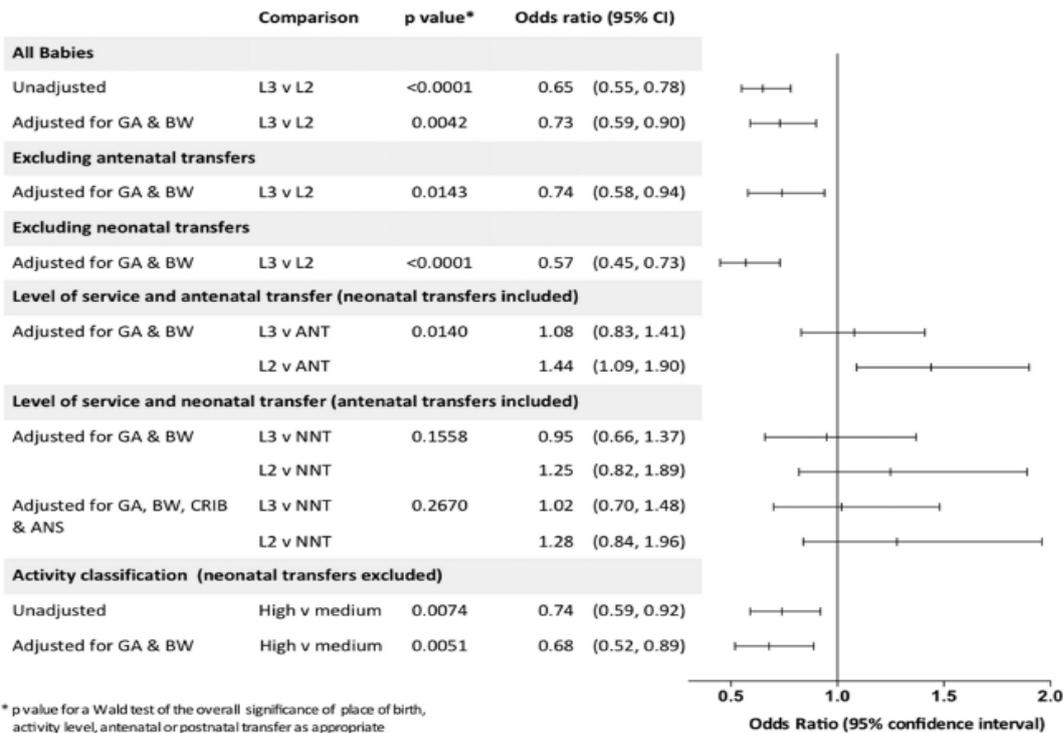
Tulemuste interpretatsioon: vaatamata riiklikule korrale ainult 56% sügavalt enneaegset vastsündinutest sündisid III etappi üksustes. Elulemus oli nende üksustes oluliselt parem eriti siis, kui üksuse maht oli kõrge ja samal ajal ei olnud täheldatud suuremat neonataalset haigestumist.

**Figure 1** Population of births reported to the EPICure 2 study by place of birth and transfer status, indicating the population of babies included in antenatal transfer, neonatal transfer and activity analyses.

[Type text]



[Type text]



**Table 2** Mortality and morbidity to discharge for babies of women transferred antenatally and for those who delivered in level 2 and level 3 services without transfer for births in England in 2006 between 22 and 26 weeks of gestation

Outcome	Level 2 (n=829)		Antenatal transfer (n=440)		Level 3 (n=947)		p Value*	aOR L3 vs L2	aOR Level 2 v ANT	aOR Level 3 vs ANT
Antenatal death	174	21%	45	10%	163	17%	0.104	0.86 (0.66 to 1.13)	1.52 (1.03 to 2.26)	1.31 (0.89 to 1.93)
Delivery room deathst	143	17%	30	7%	118	12%	0.002	0.53 (0.37 to 0.77)	1.67 (1.02 to 2.72)	0.89 (0.54 to 1.46)
Neonatal unit deaths <7 days	116	14%	50	11%	118	12%	0.005	0.69 (0.51 to 0.94)	1.80 (1.23 to 2.63)	1.25 (0.86 to 1.81)
All early neonatal deaths	259	31%	80	18%	236	25%	0.0001	0.61 (0.47 to 0.79)	1.85 (1.33 to 2.57)	1.12 (0.81 to 1.56)
Late neonatal death (7–28 days)†	56	7%	43	10%	79	8%	0.932	0.94 (0.64 to 1.38)	1.08 (0.69 to 1.68)	1.01 (0.67 to 1.53)
Death 29 days to discharge	35	4%	32	7%	54	6%	0.853	1.08 (0.68 to 1.73)	0.86 (0.50 to 1.46)	0.93 (0.57 to 1.51)
All deaths	524	63%	200	45%	532	56%	0.014	0.75 (0.59 to 0.95)	1.44 (1.09 to 1.90)	1.08 (0.83 to 1.41)
Survival without morbidity	70	8%	65	15%	92	10%	0.086	1.14 (0.80 to 1.61)	0.65 (0.44 to 0.96)	0.74 (0.51 to 1.06)
Survivors only										
No morbidity	70	23%	65	27%	92	22%	0.166	0.99 (0.69 to 1.43)	0.72 (0.48 to 1.08)	0.71 (0.49 to 1.04)
Perinatal factors										
Antenatal steroid (any)	531/824	64%	412/436	95%	656/936	70%	<0.0001	1.15 (0.90 to 1.47)	0.20 (0.12 to 0.31)	0.23 (0.14 to 0.36)
Resuscitation withheld	89/653	14%	12/395	3%	61/784	8%	0.002	0.41 (0.25 to 0.66)	1.25 (0.62 to 2.55)	0.51 (0.24 to 1.09)
Alive with HR>100 at 5 m	463/551	84%	342/379	90%	610/710	86%	0.243	1.16 (0.84 to 1.60)	0.70 (0.46 to 1.06)	0.81 (0.53 to 1.22)
Admitted to NNU	511/829	62%	365/440	83%	664/947	70%	0.014	1.41 (1.09 to 1.81)	0.69 (0.50 to 0.96)	0.98 (0.70 to 1.35)

\* p Value for overall significance of transfer adjusted for gestational age and birthweight for gestation.

†Heterogeneity of effect of antenatal transfer across gestational age for two outcomes (p=0.048 for delivery room and p=0.039 for late neonatal deaths).

ANT, antenatal transfer; aOR, OR adjusted for gestational age and birthweight for gestation based on population alive at start of time period.

**Table 3** Mortality and morbidity to discharge for neonatal unit admissions for babies who were transferred to a level 3 service after admission (NNT) compared with babies who remained in their hospital of birth, for births in England in 2006 between 22 and 26 weeks of gestation

Outcome	Level 2 (n=348) (%)		Neonatal transfer (n=261)		Level 3 (n=1028)		p Value*	aOR L3 vs L2	aOR L2 vs NNT	aOR L3 vs NNT
Neonatal unit deaths <7 days	80	23%	35	21%	166	16%	0.002	0.56 (0.41 to 0.78)	1.50 (0.93 to 2.42)	0.85 (0.55 to 1.30)
Late neonatal death (7–28 days)	34	10	22	14%	122	12%	0.935	0.93 (0.61 to 1.43)	1.01 (0.55 to 1.86)	0.94 (0.56 to 1.58)
Death 29 days to discharge	22	6	13	8%	86	8%	0.831	1.05 (0.63 to 1.76)	1.16 (0.54 to 2.49)	1.22 (0.64 to 2.34)
All deaths	136	39%	70	43%	374	36%	0.156	0.76 (0.58 to 1.00)	1.25 (0.82 to 1.89)	0.95 (0.66 to 1.37)
Survival without morbidity	58	17%	12	7%	157	15%	0.124	1.09 (0.77 to 1.54)	1.76 (0.90 to 3.46)	1.92 (1.02 to 3.60)
Survivors only										
No morbidity	58	27%	12	13%	157	24%	0.172	0.97 (0.67 to 1.40)	1.88 (0.94 to 3.78)	1.83 (0.96 to 3.50)

No heterogeneity was detected for any outcome in the effect of neonatal transfer at different gestational ages.

\* p Value for overall significance of transfer adjusted for gestational age and birthweight for gestation.

aOR, OR adjusted for gestational age and birthweight for gestation based on population alive at start of time period; NNT, neonatal transfer.

[Type text]

**Table 4** Mortality and morbidity to discharge for babies cared for in level 3 services categorised by medium and high-activity levels (see text)

Outcome	High activity (n=826)		Medium activity (n=525)		aOR high vs medium activity	p Value*
Antenatal death	121	15%	85	16%	0.92 (0.66 to 1.27)	0.600
Delivery room deaths*	82	10%	65	12%	0.78 (0.49 to 1.22)	0.274
Neonatal unit deaths <7 days	94	11%	68	13%	0.82 (0.58 to 1.17)	0.275
All early neonatal deaths	176	21%	133	25%	0.78 (0.58 to 1.06)	0.119
Late neonatal death (7–28 days)*	69	8%	50	10%	0.72 (0.47 to 1.08)	0.115
Death 29 days to discharge	49	6%	35	7%	0.65 (0.40 to 1.06)	0.086
All deaths	415	50%	303	58%	0.68 (0.52 to 0.89)	0.005
Survival without neonatal morbidity	86	10%	65	12%	0.79 (0.55 to 1.14)	0.205
Survivors only						
No neonatal morbidity	86	21%	65	29%	0.69 (0.47 to 1.02)	0.063

No heterogeneity (of effect of throughput level) was found across gestational age for any outcome.

\*Test for significance of effect of throughput, adjusted for gestational age and birthweight for gestation; further adjustment for antenatal transfer did not materially change the ORs or CIs for any of the outcomes.

aOR, OR adjusted for gestational age and birthweight for gestation based on population alive at start of time period.

5. Watson, S.I., Arulampalam, W., Petrou, S., Marlow, N., Morgan, A.S., Draper, E.S., Santhakumaran, S., Modi, N., Neonatal Data Analysis Unit and the NESCOP Group, 2014. **The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: retrospective population-based cohort study.** *BMJ Open* 4, e004856. doi:10.1136/bmjopen-2014-004856

Uuringu eesmärgiks oli uurida neonataalse üksuse taseme ja suuruse mõju vastsündinute haigestumisele ja suremusele väga enneaegsete laste hulgas. See on retrospektiivne populatsiooni uuring. 165 NHS üksust osalesid andmete kogumises uuringu jaoks: 26.7% III etapp, 49% II etapp (saadavad ära <27näd), 23.6% I etapp. 23.6% olid klassifitseeritud suurema mahuga üksusteks, nendest 78% olid III etappi üksused.

20556 vastsündinut sündinud enne 33 rasedusnädalat olid kaasatud analüüsi (17 995 sündinud 27–32 nädalal; 2559 sündinud <27 nädalal).

9466 (46.1%) olid sündinud III etapi üksuses ja 9541 (46.4%) olid sündinud suure mahuga üksustes. Suure mahuga üksuste cut off oli ca 3480 ravipäeva aastas vastsündinutele sündinud enne 33 nädalat.

Andmete kogumise periood oli 1 jaanuar 2009 kuini 31 detsember 2011(3 aastat).

Tulemusnäitajad olid: neonataalne suremus, haiglasine haigestumus, NEK op ravi, retinopaatia op ravi, BPD.

Tulemused: Vastsündinute hulgas, kes sündisid enne 33 nädalat ja kes said ravi suure mahuga NICU-s neonataalne suremus langes (OR) 0.70, 95% CI 0.53 to 0.92) ja igasugune haiglasine suremus kokku samuti langes (OR) 0.68,

95% CI 0.54 to 0.85). Suremuse langus oli eriti suur vastsündinute grupis, kes sündisid enne 27 nädalat ja said ravi suure mahuga NICU-s (OR 0.51, 95% CI 0.33 to 0.79). Samuti vastsündinute grupis vanuses alla 27 nädalat oli täheldatav suremuse langus III etapi üksustus võrreldes mitte III etappi üksustega.

Järeldus: Suure mahuga üksused võivad vähendada haiglasest suremust eriti väga enneaegsetel vastsündinutel. Seega need sündinud peaksid toimuma suure mahuga üksustes.

**Table 2** presents the estimated adjusted ORs associated with admission to either tertiary or high-volume neonatal care at the hospital of birth.

The standard logistic regressions did not reveal a statistically significant difference in the OR of mortality for very preterm infants admitted to tertiary-level care at the hospital of birth compared with their counterparts admitted to non-tertiary-level care. However, when considering only infants born at  $\leq 26+6$  weeks gestation, we found a reduction in the OR of

[Type text]

neonatal mortality (OR 0.65, 95% CI 0.46 to 0.91, p=0.012), but not any in-hospital mortality.

For infants admitted to a high-volume neonatal unit at the hospital of birth, a reduced OR of neonatal mortality was observed for those born at  $\leq 32+6$  weeks gestation (OR 0.73, 95% CI 0.56 to 0.95, p=0.018) and at  $\leq 26+6$  weeks gestation (OR 0.62, 95% CI 0.44 to 0.87, p=0.006), but this was not replicated for infants born at 27+0 to 32+6 weeks gestation. Those infants born at  $\leq 26+6$  weeks gestation were also at reduced OR of any in-hospital mortality (0.71, 95% CI 0.52 to 0.97, p=0.033) and increased OR of BPD (OR 1.59, 95% CI 1.18 to 2.14, p=0.002) compared with their counterparts admitted to a non-high-volume neonatal unit at the hospital of birth. There were no other statistically significant differences observed for the morbidity outcomes.

**Table 2** Adjusted ORs for outcomes associated with admission to either tertiary or high-volume neonatal care at the hospital of birth using a 'standard' logistic regression model

Outcome	Tertiary neonatal unit			High-volume neonatal unit†		
	(1) $\leq 32+6$ weeks	(2) $\leq 26+6$ weeks	(3) 27 <sup>+</sup> 0–32 <sup>+</sup> 6 weeks	(4) $\leq 32+6$ weeks	(5) $\leq 26+6$ weeks	(6) 27 <sup>+</sup> 0–32 <sup>+</sup> 6 weeks
Neonatal mortality	0.77 (0.59 to 1.00)	0.65* (0.46 to 0.91)	0.92 (0.69 to 1.22)	0.73* (0.56 to 0.95)	0.62** (0.44 to 0.87)	0.86 (0.65 to 1.14)
Any in-hospital mortality	0.91 (0.72 to 1.15)	0.78 (0.57 to 1.06)	1.06 (0.83 to 1.36)	0.83 (0.65 to 1.05)	0.71* (0.52 to 0.97)	0.96 (0.75 to 1.24)
BPD	1.23** (1.07 to 1.40)	1.50** (1.11 to 2.01)	1.17 (0.99 to 1.39)	1.11 (0.97 to 1.28)	1.59** (1.18 to 2.14)	1.02 (0.86 to 1.22)
Treatment for ROP	1.26 (0.91 to 1.75)	1.09 (0.76 to 1.57)	1.52 (0.91 to 2.55)	0.95 (0.68 to 1.32)	0.81 (0.56 to 1.17)	1.22 (0.71 to 2.09)
Surgery for NEC	1.05 (0.76 to 1.44)	0.89 (0.58 to 1.36)	1.17 (0.80 to 1.70)	1.05 (0.76 to 1.45)	0.94 (0.62 to 1.45)	1.11 (0.76 to 1.61)
PMA at discharge >40 weeks	1.17 (0.97 to 1.41)	1.09 (0.87 to 1.37)	1.19 (0.97 to 1.47)	1.13 (0.94 to 1.37)	1.11 (0.89 to 1.38)	1.11 (0.90 to 1.37)

Values are ORs (95% CI).

Models are adjusted for gestational age, gestational age squared, birthweight z-score, use of antenatal steroids, gender, infant year of birth and deprivation.

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

†High volume was defined as being in the top quartile of units by number of care days provided to infants born at  $\leq 32+6$  weeks gestation.

BPD, bronchopulmonary dysplasia; NEC, necrotising enterocolitis; PMA, postmenstrual age; ROP, retinopathy of prematurity.

**Table 4** shows the estimated ORs using the instrumental variables logistic regressions.

We found no significant differences in neonatal mortality between infants admitted to either tertiary or non-tertiary neonatal care at the hospital of birth. We did find an increased OR of treatment for ROP for very preterm infants born at 27+0–32+6 weeks gestation born in a hospital with a tertiary-level unit (OR 2.17, 95% CI 1.06 to 4.47, p=0.035). In contrast to the effect of tertiary-level care, admission to a high-volume neonatal unit at the hospital of birth significantly reduced the OR of neonatal mortality (OR 0.70, 95% CI 0.53 to 0.92, p=0.011) and any in-hospital mortality (OR 0.68, 95% CI 0.54 to 0.85, p=0.001) in very preterm infants. These effects were most acute among infants born at  $\leq 26+6$  weeks gestation. In terms of morbidity, the only significant effect was found for BPD (OR 1.78, 95% CI 1.12 to 2.81, p=0.014) for infants born at  $\leq 26+6$  weeks gestation and admitted to high-volume neonatal care at the hospital of birth.

**Table 4** Adjusted ORs for outcomes associated with admission to either tertiary or high-volume neonatal care at the hospital of birth using an instrumental variable logistic regression model

Outcome	Tertiary neonatal unit			High-volume neonatal unit†		
	(1) $\leq 32+6$ weeks	(2) $\leq 26+6$ weeks	(3) 27 <sup>+</sup> 0–32 <sup>+</sup> 6 weeks	(4) $\leq 32+6$ weeks	(5) $\leq 26+6$ weeks	(6) 27 <sup>+</sup> 0–32 <sup>+</sup> 6 weeks
Neonatal mortality	0.87 (0.66 to 1.15)	1.01 (0.63 to 1.61)	0.82 (0.58 to 1.14)	0.70* (0.53 to 0.92)	0.54** (0.33 to 0.87)	0.80 (0.56 to 1.13)
Any in-hospital mortality	0.85 (0.68 to 1.06)	0.95 (0.62 to 1.44)	0.84 (0.64 to 1.10)	0.68** (0.54 to 0.85)	0.51** (0.33 to 0.79)	0.80 (0.60 to 1.07)
BPD	1.19 (0.95 to 1.49)	1.04 (0.66 to 1.64)	1.17 (0.91 to 1.51)	1.05 (0.85 to 1.29)	1.78** (1.12 to 2.81)	0.96 (0.75 to 1.22)
Treatment for ROP	1.91* (1.16 to 3.14)	1.57 (0.83 to 2.96)	2.17* (1.06 to 4.47)	1.02 (0.60 to 1.73)	0.58 (0.29 to 1.15)	1.84 (0.83 to 4.05)
Surgery for NEC	1.17 (0.72 to 1.90)	0.81 (0.40 to 1.66)	1.34 (0.76 to 2.38)	1.26 (0.76 to 2.07)	1.11 (0.54 to 2.28)	1.35 (0.75 to 2.43)
PMA at discharge >40 <sup>+</sup> weeks	0.95 (0.73 to 1.22)	0.83 (0.60 to 1.13)	0.97 (0.72 to 1.31)	0.92 (0.72 to 1.17)	1.04 (0.78 to 1.40)	0.86 (0.67 to 1.14)

Values are ORs (95% CI).

Models are adjusted for gestational age, gestational age squared, birthweight z-score, use of antenatal steroids, gender, infant year of birth and deprivation.

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001. †High volume was defined as being in the top quartile of units by number of care days provided to infants born at  $\leq 32+6$  weeks gestation.

BPD, bronchopulmonary dysplasia; NEC, necrotising enterocolitis; PMA, postmenstrual age; ROP, retinopathy of prematurity.

[Type text]

Kõige olulisem uuringu leid oli OR langus erakordselt enneaegsetel vastsündinutel alla 27 nädal, kes said ravi suure mahuga üksustes. Analüüs oli tehtud eraldi gruppidele  $\leq 26+6$  ja 27 kuni 32+6 ja statiiliselt oluline OR langus suuremuses oli ainult esimes grupis.

Mis puudutas haigestumist, siis ROP ravi vajasid rohkem vastsündinuid vanuses 27+6–32+6 III etappi üksutes. Kuigi nende vastsündinute arv oli väga väike (86/17 995; 0.5%), nii et see ei pruugi olla kliiniliselt oluline.

Sama tulemust sai Chung et al., 2011 oma uuringus, kui võrdlesid üksuste taseme ja mahtu mõju vastsündinute tulemile eraldi USA-s ja leidsid, et mahul on suurem tähtsus.

Antud uuring samuti leidis OR langust suuremuses, kui analüüsiti VLBW ravitud arvu aastas: mida suurem arv, seda väiksem suurem, nagu Phibbs et al., 2007 poolt tehtud analüüsis.

6. Rautava, L., Eskelinen, J., Häkkinen, U., Lehtonen, L., PERFECT Preterm Infant Study Group, 2013. **5-year morbidity among very preterm infants in relation to level of hospital care.** JAMA Pediatr 167, 40–46. doi:10.1001/jamapediatrics.2013.415

Kohort uuring läbiviidud Soomes, mille eesmärgiks oli võrrelda laste tervisetulemit 5 aasta vanuselt nendel, kes sündisid väga enneaegselt.

Uuringu eesmärgiks oli võrrelda erinevate tasemega üksuste mõju nende laste tulevasele tervisele. Kuna Soomes eksisteerib praktika, kus III etapis sündinud ja stabiilseid lapsed viiakse üle II etappi haigaltesse elukoha järgi, siis sooviti aru saada kas esineb erinevus III ja II etapi vahel ja ka nende vahel kes olid sündinud III etapis ja üle viidud II etappi.

Uuringusse olid kaasatud kõik ellu jäänud 5 aastased lapsed, kes sündisid enneaegselt enne 32 nädalat või kaaluga alla 1500 g III või II etappi haiglates, kokku 2168 last. Lisaks oli analüüsitud ajaliste laste andmed N 238857, kes sündisid samal perioodil : alatest jaanuar 2000 kuni 31 detsember 2004.

Lapsed jägati kolme gruppi ja nende diagnoosid olid võrreldud omavahel: need, kes sündisid ja said ravi III etapis (grupp III), sündinud III etapis, kuid üle viidud II etappi (grupp III/II), sündinud ja ravitud II etappis (grupp II).

Tulemused:

Grupp III/II suurenenud retinopaatiate (OR, 2.43 [95% CI, 1.66-3.56]) ja astma (1.41 [1.09-1.81]) esinemissagedus .

Gruppi III/II esines vähem viraalseid infektsioone (0.75 [0.59-0.95]) võrreldes gruppiga III.

Gruppi II esines rohkem epilepsiat (odds ratio, 2.71 [95% CI, 1.29-5.70]) ja hüperkineerilist häiret (2.19 [1.13-4.25]) võrreldes gruppiga III.

Teiste diagnooside vahel erinevust ei leitud.

Järeldus: Suurem astma ja retinopaatia esinemissagedus lastel, kes olid üle viidud III etapist II etappi vajaks analüüsi, et aru saada ravi erinevustest erinevate üksuste vahel.

**Table 1. Assignment of Study Groups by Hospital Level<sup>a</sup>**

Birth Hospital	Place of Treatment During the Initial Hospitalization	Study Group
Level III (n = 1771)	Level III hospital (n = 686)	Group III
	Transferred from level III to level II hospitals (n = 761)	Group III/II
	Transferred from level III to level I hospitals (n = 324)	
Level II (n = 397)	Level II hospitals (n = 397)	Group II

**Table 4. Adjusted ORs for the Comparison of Postdischarge Diagnoses Between the Study Groups<sup>a</sup>**

	OR (95% CI)	
	Group III/II (n = 1084)	Group II (n = 394)
Diagnoses likely to be influenced by the level of neonatal care		
Disorders of speech	1.38 (0.99-1.92)	1.06 (0.66-1.73)
Specific developmental disorder of motor function	1.34 (0.95-1.87)	1.01 (0.60-1.68)
Mixed specific developmental disorders	0.72 (0.49-1.06)	1.60 (0.98-2.60)
Retinopathy of prematurity	2.43 (1.66-3.56)	0.45 (0.18-1.10)
Strabismus, disorders of refraction and accommodation, amblyopia ex anopsia	0.78 (0.60-1.00)	0.90 (0.63-1.27)
Epilepsy	1.44 (0.76-2.72)	2.71 (1.29-5.70)
Cerebral palsy	1.11 (0.71-1.74)	1.52 (0.84-2.76)
Hyperkinetic disorders	0.53 (0.28-1.00)	2.19 (1.13-4.25)
Asthma	1.41 (1.09-1.81)	1.36 (0.97-1.91)
Respiratory infections	1.07 (0.87-1.32)	0.94 (0.72-1.22)
Any of the diagnosis influenced by the level of neonatal care	1.18 (0.93-1.50)	0.97 (0.73-1.30)
Diagnoses overrepresented in preterm infants but not likely to be influenced by the level of neonatal care		
Gastroenteritis or unspecified viral infections	0.75 (0.59-0.95)	0.95 (0.70-1.30)
Pyelonephritis or urinary tract infection	0.73 (0.45-1.19)	0.99 (0.55-1.79)
Inguinal hernia	1.09 (0.82-1.44)	1.14 (0.77-1.67)
Functional intestinal diseases	1.11 (0.71-1.71)	1.16 (0.64-2.10)
Any of the abovementioned diagnoses	1.00 (0.77-1.29)	1.08 (0.78-1.50)

Transfer III etapist II etappi tundub olevat seotud suurenenud riskiga retinopaatiatele ja astmale väga enneaegsetel vastündinutel. Lisaks epilepsia ja hüperkineetiliste häirete suurem esinemissagedus II etapis ravitud lastel võrreldes III etapiga paneb üle vaatama ravi meetodeid, mis on kasutuses II etapis eriti hapniku kasutamine ravis ja toitumisprintsipiibid Soomes.

7. Lasswell, S.M., Barfield, W.D., Rochat, R.W., Blackmon, L., 2010. **Perinatal regionalization for very low-birth-weight and very preterm infants: a meta-analysis.** JAMA 304, 992–1000. doi:10.1001/jama.2010.1226

US-s vaatamata perinataalsele regionaliseerimisele ja soovitustele, mõnes osariigis suur protsent VLBW vastündinutes sünnivad madala astmega üksustes. Metaanalüüsi eesmärgiks oli analüüsida haigla taseme mõju VLBW ja VPT vastündinu suremusele.

Otsingud olid teostatud 1976-2010(30 aastat) perioodi kohta.

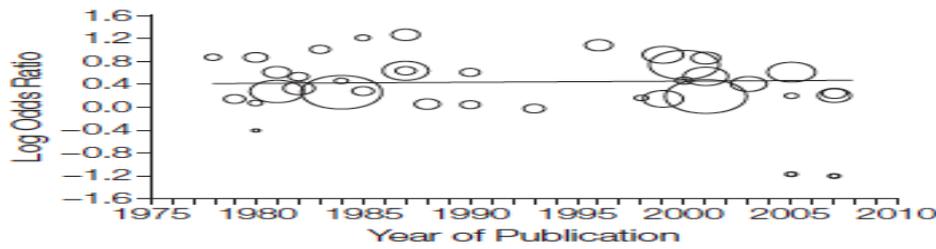
41 publikatsiooni olid kaasatud(randomized controlled trial, cohort, and case-control studies measuring neonatal or pre-discharge mortality among live-born infants alla 1500 g or alla 32 weeks gestation delivered at a level III vs lower-level facility).

VLBW vastündinute grupis esines kõrgem suremus, nendel kes sündisid väljaspool III etappi (38% vs 23%; adjusted OR, 1.62; 95% confidence interval [CI], 1.44-1.83), analoogselt kõrgem suremus esines ka VPT vastündinu grupis (15% vs 17%; adjusted OR, 1.55; 95% CI, 1.21-1.98)

Metaregressioon publikatsiooni aastja järgi ei muutnud tulemusi. (slope, 0.00; P=.87).

Järeldus: VLBW ja VPT vastündinutel, sünd väljaspoolt III etappi haiglat toob kõrget suremusriksi.

**Figure 2. Meta-regression of Association Between Hospital Level of Birth and Neonatal/Predischarge Mortality by Year of Publication**



Each circle in the plot represents a study, and the circumference of each circle is proportional to study population size. These data represent change in published evidence over time, not actual outcome measures at a given time. Because each study includes its own unique range of birth dates (eTable), calculation of change by infant birth date was not possible.

**Figure 3. Meta-analysis Results of Adequate- and High-Quality Publications on Very Low-Birth-Weight (VLBW) Infants, Stratified by Level of Adjustment for Confounding**

Source	Level Comparison	Deaths/Live Births, No.		Adjusted Odds Ratio (95% CI)	Z Value	Favors Lower Level Hospitals	Favors Level III Hospitals	P Value
		Lower Levels	Level III					
<b>Adjustment for Confounding: Case Mix</b>								
Paneth et al. <sup>50</sup> 1982	II vs III	602/1083	423/869	1.32 (1.08-1.62)	2.68			.01
Gortmaker et al. <sup>37</sup> 1985 <sup>a</sup>	I and II vs III	708/2717	508/2382	1.30 (1.14-1.48)	3.95			<.001
Sanderson et al. <sup>18</sup> 2000	II + vs III	15/88	292/2038	1.23 (0.70-2.17)	0.71			.48
Bode et al. <sup>32</sup> 2001 <sup>b</sup>	II vs III	929/2266	2517/14479	2.06 (1.82-2.33)	11.39			<.001
Kamath et al. <sup>16</sup> 2008	I and II vs III	757	1459	1.85 (2.31-1.22)	5.44			<.001
Combined estimate <sup>c</sup>		2254/6154	3740/19768	1.56 (1.22-1.98)	3.61			<.001
Test for heterogeneity: $Q=31.56$ ; $P<.001$								
<b>Adjustment for Confounding: Extensive</b>								
Verloove-Vanhorick et al. <sup>22</sup> 1988	II vs III	83/359	125/482	1.90 (1.11-3.24)	2.36			.02
Cifuentes et al. <sup>13</sup> 2002	II vs III	1414	2472	2.37 (1.65-3.40)	4.68			<.001
Bacak et al. <sup>29</sup> 2005	I and II vs III	232/545	570/1127	1.50 (1.11-2.02)	2.66			.01
Howell et al. <sup>15</sup> 2008	I and II vs III/IV	1626/11781		1.23 (0.89-1.70)	1.25			.21
Combined estimate <sup>c</sup>		315/904	695/1609	1.66 (1.24-2.23)	3.42			<.001
Test for heterogeneity: $Q=7.60$ ; $P=.06$								
Overall: all adequate- and high-quality VLBW studies <sup>c</sup>		2569/7058	4435/21377	1.60 (1.33-1.92)	4.96			<.001
Test for heterogeneity: $Q=39$ ; $P<.001$								

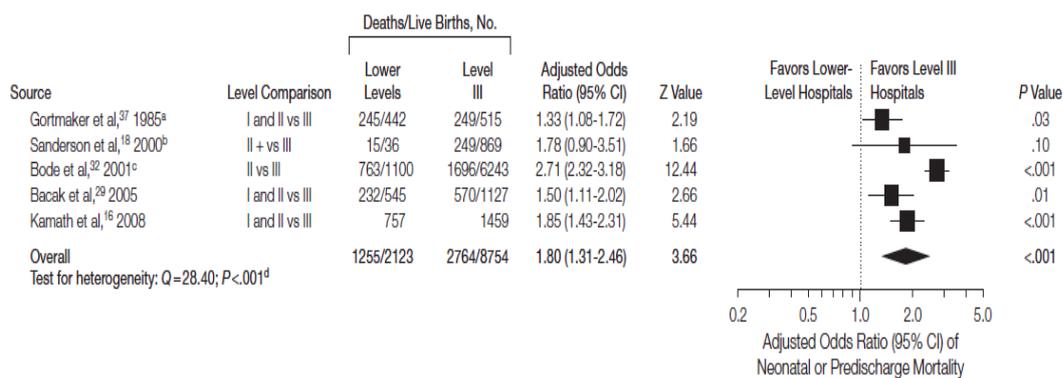
Case mix indicates adjustment for demographic and/or socioeconomic status variables; extensive indicates adjustment for case mix plus maternal/perinatal risk factors and infant illness severity. CI indicates confidence interval. Size of data markers indicates size of study population.

<sup>a</sup>Included data are for urban populations and combine reported black/white race strata and birth weight strata (750-1000 g and 1001-1500 g).

<sup>b</sup>Included data combine reported birth date interval strata (1980-1984, 1985-1989, and 1990-1994) and birth weight strata (500-1000 g and 1001-1500 g).

<sup>c</sup>Raw death counts are not reported in Cifuentes et al.<sup>13</sup> and Kamath et al.<sup>16</sup> and are not stratified by hospital level in Howell et al.<sup>15</sup> These studies are not included in combined death/birth counts.

**Figure 4.** Meta-analysis Results of Adequate- and High-Quality Publications on Extremely Low-Birth-Weight Infants



CI indicates confidence interval. Size of data markers indicates size of study population.

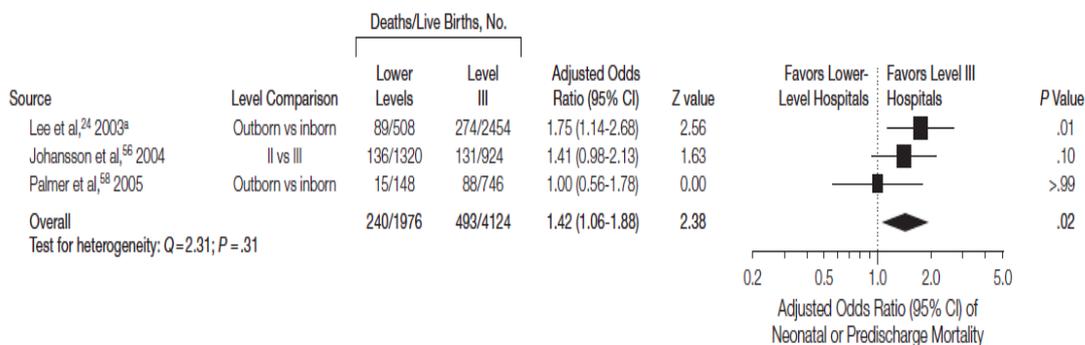
<sup>a</sup>Included data are for urban populations and combine reported black/white race strata.

<sup>b</sup>Included data combine reported birth weight strata (500-749 g and 750-1000 g).

<sup>c</sup>Included data combine reported birth date interval strata (1980-1984, 1985-1989, and 1990-1994).

<sup>d</sup>The study by Kamath et al.<sup>16</sup> does not report raw death count data and is not included in combined death/birth counts.

**Figure 5.** Meta-analysis Results of Adequate- and High-Quality Publications on Very Preterm Infants



CI indicates confidence interval. Size of data markers indicates size of study population. Inborn infants are those born in a level III hospital; outborn infants are those born in a lower-level hospital then transferred to a level III hospital.

<sup>a</sup>Included data combine reported gestational age strata (<26 weeks, 27-29 weeks, and 30-31 weeks).

## 8. Euroopa projekt MOSAIC

'Models of OrganiSing Access to Intensive Care for very preterm births,' finanseeritud European Commission poolt viis läbi kohort uuringu enneaegsetest sünitustest 22 kuni 31 nädalal kümnes Euroopa regioonis (7222 väga enneaegset vastündinut) ja perinataalse abi organiseerimisest erinevates euroopa regioonites (428 sünitumaja ja 290 NICU).

Põhieesmärgiks oli hinnata väga enneaegsete vastündinute ravi regionaliseerimist Euroopas. Uuringu tulemusena ilmus mitu publikatsiooni. Nendest esitan olulisemad, mis puudutavad just regionaliseerimise teemat.

Projekt MOSAIC pakub kõrge kvaliteediga empiirilisi andmeid Euroopa väga väikeste enneaegsete ravi kohta. Väga enneaegsetel lastel on parem elulemus ja madalam haigestumus, kui nad sünnivad haiglates kus on NICU ja paljud riigid on arendanud III etappi üksusi, kus need lapsed peaksid sündima. Väga enneaegsete laste ravi analüüs enamuses Euroopa riikides ei ole võimalik, kuna puuduvad võrreldavad andmed. Samuti on

[Type text]

olemas andmed halvade tulemuste kohta, kui väga enneaegsed lapsed sünnivad üksustes, kus puudub neonataalne intensiivne ravi kohapeal ja uuringud ka näitavad halvemaid tulemusi väikese mahuga üksustes.

Uuring näitas, et perinataalse abi organisatsioon varieerus riigiti ja erinevused avaldasid ka mõju kindla populatsiooni tervisetulemile. Antud analüüs tõi välja erinevused väga enneaegsete vastsündinute suremuses, neroloogilises haigestumuses, respiratoorses haigestumuses erinevates 10 euroopa regioonides, samuti erinevused ravimeetodite kasutamises nagu kesrilõige, antenataalsed kortikosteroidide manustamine ja mehhaaniline ventilatsioon.

MOSAIC uuringu tulemused püstitasid küsimusi, tänu millele oli algatatud EPICE projekt. Tänu EPICE uuringule loodetakse saada detailsemat informatsiooni ravimeetoditest ja hinnata kuidas on kasutatud tõenduspühised ravimeetodid erinevates Euroopa regioonides.

Perinataalse abi organisatsioon varieerus väga riigiti. III astme üksuste arv varieerus riigiti alatest 2.3 :10 000 sünnitust Portugalis kuni 0.2 :10 000 sünnitust Poolas. Väga enneaegsete sünnituste arv III astme üksustes samuti varieerus alatest 93 kuni 63% ni. Erinevad meetodid olid kasutatud, et saavutada perinataalse abi regionaliseerimist: suur osa arv sünnitustest spetsialiseeritud keskustes, suur osa arv in utero tranferit, suur osa arv kõrgriksi raseduste suunamise keskustesse.

Optimaalse perinataalse abi regionaliseerimise konsensus ei ole ja regionaliseerimine võib olla saavutatud erineval viisil organiseerides obstetrist abi.

Mis puudutab juhiseid III etappi üksuse kohata, siis varieeruvus oli samuti suur. 36% oli vähem kui 50 väga enneaegsete vastsündinut aastast, 22% ventileerisid vähem kui 50 last aastast, 28% oli vähem kui 6 kuvöösi. II taseme NICUd olid vähem spetsialiseeritud, kuid 57% pakus mehhaanilist ventilatsiooni ja 20% kõrgsegdeuslikku ventilatsiooni ja 17% olid neontaalse kirurgia võimalused. 69% III NICU ja 36% I ja II NICU omasid spetsialiseeritud pediaatrit kohapeal. 22% vastsündinutest alla 28 nädalat olid ravitus üksustes, kus raviri vähem kui 50 väga enneaegset vastsündinut aasta. (varieeruvus oli 2% kuni 54%) .

9. Richardson, D.K., Reed, K., Cutler, J.C., Boardman, R.C., Goodman, K., Moynihan, T., Driscoll, J., Raye, J.R., **1995. Perinatal regionalization versus hospital competition: the Hartford example.** Pediatrics 96, 417–423.

Selles case study publikatsioonis on esitatud regionaliseerimise raskused ja kasu 1990tel US-s. Perinataalabi regionaliseerimise alguses tekkis mure, et piiramata võistus haiglate vahel tõstab perinataalse abi hinda. Seega oli tehtud turu analüüsi ja haiglate resurside jagamise analüüs konsultantide poolt. Regionaliseerimise tulemusel areneb meditsiiniline teenus väiksema kuluga, haiglatevaheline võitlus aga võib häirida süsteemi efektiivsuse.

Perinataalne regionaliseerimine kaasaegses meditsiinis võimaldab kõrge kvaliteediga teenust madalama hinnaga. Mitmed uuringud ja analüüsid tõestavad regionaliseerimise efektiivsust ja tõhusust. Haiglate vaheline konkurents ja NICU üksuste proliferatsioon ohustavad süsteemi efektiivsust ja kulu tõhusust.

**TABLE 3. Consultants' Recommendations**

---

**Regulatory and public policy**  
 Cooperation in preference to competition  
 Legal definition of level II and III  
 Availability of data  
 Public support for regional leadership costs

**Insurers/payors**  
 Eliminate barriers to transfers, referrals  
 Incentives for collaboration  
 Reimbursement rate should support:  
     Regional leadership costs  
     Transport overhead  
     Outreach costs

Incentives for preventive and prenatal care

**Hospitals and providers**  
 No new NICU beds  
 Greater use of back transfer  
 Better utilization of level I and II hospitals  
 Sustain regional cooperation  
 Continue joint obstetric and pediatric residencies  
 Dempsey—continue regional leadership  
 Hartford  
     Define new mission—multispecialty  
     Potential need for cardiac/ECMO beds

---

**NICU, neonatal intensive care unit; ECMO, extracorporeal membrane oxygenation.**

**TABLE 4. Effects of Competition on Regionalization**

---

Advantages	Disadvantages
Responsiveness to community providers Improved outreach More responsive transport teams Shorter travel time for patients Hospital support for NICU mission Staffing Equipment	Redundant facilities—increased costs Smaller NICUs—inefficiencies of size Limited subspecialty backup (surgical, genetics, etc) Dispersion of high-risk patients Limits trials of new technologies Reduces training opportunities Fragments neonatal follow-up Hampers statistical reporting Impairs quality assurance efforts Financial stress on perinatal center “Cream skimming” by peripheral hospitals Rising overhead to maintain transport/outreach

---

**TABLE 5. Effects of Managed Care on Regionalization**

---

Advantages	Disadvantages
Centralization/consolidation of obstetrics and pediatrics Coordination of pediatric care Concentration of research and education Cost efficiencies Standardization of practice Promotion of convalescent transfers Reduced length of stay Efficient use of subspecialty services	Potential overbuilding of perinatal facilities Redirection of referral patterns Inconvenience/restricted access Cost shifting Avoid regional leadership costs (outreach/transport) Avoid regional training costs (MDs, NNPs) Exclusion from infant follow-up Inhibition of convalescent transfers Restrictions on data availability

---

[Type text]

<b>Viited MOSAIC uuringu publikatsioonidele.</b> <b>Kokkuvõtte (abstract või kokkuvõtlikum info)</b>	<b>Viide kirjandusallikale</b>
<p>Survival and quality of life are improved for very preterm babies when delivery occurs in a maternity unit with on-site neonatal intensive care (level III unit). We investigated the impact of distance on the probability of delivering in such a unit for births before 32 weeks of gestation from 9 European regions with diverse perinatal health systems (the MOSAIC cohort). We analysed distances between women's homes, and the nearest level III in population quartiles, adjusting for maternal and pregnancy characteristics. Living farther away from a level III reduced access to specialised care everywhere; in some regions women residing in the fourth quartile were half as likely to deliver in level III units as those in the first. To improve regionalized perinatal care the spatial location of level III units should be taken into account.</p>	<p>Pilkington, H., Blondel, B., Papiernik, E., Cuttini, M., Charreire, H., Maier, R.F., Petrou, S., Combier, E., Künzel, W., Bréart, G., Zeitlin, J., MOSAIC group, 2010. <b>Distribution of maternity units and spatial access to specialised care for women delivering before 32 weeks of gestation in Europe.</b> Health Place 16, 531–538. doi:10.1016/j.healthplace.2009.12.011</p>
<p>OBJECTIVE: To study the impact of the organisation of obstetric services on the regionalisation of care for very preterm births. DESIGN: Cohort study. SETTING: Ten European regions covering 490 000 live births. POPULATION: All children born in 2003 between 24 and 31 weeks of gestation. METHOD: The rate of specialised maternity units per 10 000 total births, the proportion of total births in specialised units and the proportion of very preterm births by referral status in specialised units were compared. MAIN OUTCOME MEASURE: Birth in a specialised maternity unit (level III unit or unit with a large neonatal unit (at least 50 annual very preterm admissions)). RESULTS: The organisation of obstetric care varied in these regions with respect to the supply of level III units (from 2.3 per 10 000 births in the Portuguese region to 0.2 in the Polish region), their characteristics (annual number of deliveries, 24 hour presence of a trained obstetrician) and the proportion of all births (term and preterm) that occur in these units. The proportion of very preterm births in level III units ranged from 93 to 63% in the regions. Different approaches were used to obtain a high level of regionalisation: high proportions of total deliveries</p>	<p>Blondel, B., Papiernik, E., Delmas, D., Künzel, W., Weber, T., Maier, R.F., Kollée, L., Zeitlin, J., Mosaic Research Group*, 2009. <b>Organisation of obstetric services for very preterm births in Europe: results from the MOSAIC project.</b> BJOG 116, 1364–1372. doi:10.1111/j.1471-0528.2009.02239.x</p>

[Type text]

<p>in specialised units, high proportions of in utero transfers or high proportions of high-risk women who were referred to a specialised unit during pregnancy.</p> <p>CONCLUSION: Consensus does not exist on the optimal characteristics of specialised units but regionalisation may be achieved in different models of organisation of obstetric services.</p>	
<p>OBJECTIVES: We sought to compare guidelines for level III units in 10 European regions and analyze the characteristics of neonatal units that care for very preterm infants.</p> <p>METHODS: The MOSAIC (Models of Organising Access to Intensive Care for Very Preterm Births) project combined a prospective cohort study on all births between 22 and 31 completed weeks of gestation in 10 European regions and a survey of neonatal unit characteristics. Units that admitted &gt; or = 5 infants at &lt; 32 weeks of gestation were included in the analysis (N = 111). Place of hospitalization of infants who were admitted to neonatal care was analyzed by using the cohort data (N = 4947). National or regional guidelines for level III units were reviewed.</p> <p>RESULTS: Six of 9 guidelines for level III units included minimum size criteria, based on number of intensive care beds (6 guidelines), neonatal admissions (2), ventilated patients (1), obstetric intensive care beds (1), and deliveries (2). The characteristics of level III units varied, and many were small or unspecialized by recommended criteria: 36% had fewer than 50 very preterm annual admissions, 22% ventilated fewer than 50 infants annually, and 28% had fewer than 6 intensive care beds. Level II units were less specialized, but some provided mechanical ventilation (57%) or high-frequency ventilation (20%) or had neonatal surgery facilities (17%). Sixty-nine percent of level III and 36% of level I or II units had continuous medical coverage by a qualified pediatrician. Twenty-two percent of infants who were &lt; 28 weeks of gestation were treated in units that admitted fewer than 50 very preterm infants annually (range: 2% -54% across the study regions).</p> <p>CONCLUSIONS: No consensus exists in Europe about size or other criteria for NICUs. A better understanding of the characteristics associated with high-quality neonatal care is needed, given the high proportion of very preterm infants who are cared for in units that are considered small or less specialized</p>	<p>Van Reempts, P., Gortner, L., Milligan, D., Cuttini, M., Petrou, S., Agostino, R., Field, D., den Ouden, L., Børch, K., Mazela, J., Carrapato, M., Zeitlin, J., MOSAIC Research Group, 2007. <b>Characteristics of neonatal units that care for very preterm infants in Europe: results from the MOSAIC study.</b> <i>Pediatrics</i> 120, e815–825. doi:10.1542/peds.2006-3122</p>

[Type text]

by many recommendations.	
<p><b>OBJECTIVES:</b> Advances in perinatal medicine increased survival after very preterm birth in all countries, but comparative population-based data on these births are not readily available. This analysis contrasts the rates and short-term outcome of live births before 32 weeks of gestation in 10 European regions.</p> <p><b>METHODS:</b> The Models of Organizing Access to Intensive Care for Very Preterm Births (MOSAIC) study collected prospective data on all very preterm births in 10 European regions covering 494,463 total live births in 2003. The analysis sample was live births between 24 and 31 weeks of gestation without lethal congenital anomalies (N = 4908). Outcomes were rates of preterm birth, in-hospital mortality, intraventricular hemorrhage grades III and IV or cystic periventricular leukomalacia and bronchopulmonary dysplasia. Mortality and morbidity rates were standardized for gestational age and gender.</p> <p><b>RESULTS:</b> Live births between 24 and 31 weeks of gestation were 9.9 per 1000 total live births with a range from 7.6 to 13.0 in the MOSAIC regions. Standardized mortality was doubled in high versus low mortality regions (18%-20% vs 7%-9%) and differed for infants &lt; or = 28 weeks of gestation as well as 28 to 31 weeks of gestation. Morbidity among survivors also varied (intraventricular hemorrhage/periventricular leukomalacia ranged from 2.6% to &lt; or = 10% and bronchopulmonary dysplasia from 10.5% to 21.5%) but differed from mortality rankings. A total of 85.2 very preterm infants per 10,000 total live births were discharged from the hospital alive with a range from 64.1 to 117.1; the range was 10 to 31 per 10,000 live births for infants discharged with a diagnosis of neurologic or respiratory morbidity.</p> <p><b>CONCLUSIONS:</b> Very preterm mortality and morbidity differed between European regions, raising questions about variability in treatment provided to these infants. Comparative follow-up studies are necessary to evaluate the impact of these differences on rates of cerebral palsy and other disabilities associated with preterm birth.</p>	<p>Zeitlin, J., Draper, E.S., Kollée, L., Milligan, D., Boerch, K., Agostino, R., Gortner, L., Van Reempts, P., Chabernaud, J.-L., Gadzinowski, J., Bréart, G., Papiernik, E., MOSAIC research group, 2008.</p> <p><b>Differences in rates and short-term outcome of live births before 32 weeks of gestation in Europe in 2003: results from the MOSAIC cohort.</b> Pediatrics 121, e936-944. doi:10.1542/peds.2007-1620</p>
<p><b>OBJECTIVE:</b> To investigate the variation in the survival rate and the mortality rates for very preterm infants across Europe.</p> <p><b>DESIGN:</b> A prospective birth cohort of very preterm infants for 10 geographically defined European regions during 2003, followed to discharge home from hospital.</p> <p><b>PARTICIPANTS:</b> All deliveries from 22 + 0 to 31 + 6 weeks' gestation.</p> <p><b>MAIN OUTCOME MEASURE:</b> All outcomes of pregnancy by gestational age group, including termination of pregnancy for congenital anomalies and other reasons,</p>	<p>Draper, E.S., Zeitlin, J., Fenton, A.C., Weber, T., Gerrits, J., Martens, G., Misselwitz, B., Breart, G., MOSAIC research group, 2009. <b>Investigating the variations in survival rates for very preterm infants in 10 European regions: the MOSAIC birth cohort.</b></p>

[Type text]

anteartum stillbirth, intrapartum stillbirth, labour ward death, death after admission to a neonatal intensive care unit (NICU) and survival to discharge.

**RESULTS:** Overall the proportion of this very preterm cohort who survived to discharge from neonatal care was 89.5%, varying from 93.2% to 74.8% across the regions. Less than 2% of infants <24 weeks' gestation and approximately half of the infants from 24 to 27 weeks' gestation survived to discharge home from the NICU. However large variations were seen in the timing of the deaths by region. Among all fetuses alive at onset of labour of 24-27 weeks' gestation, between 84.0% and 98.9% were born alive and between 64.6% and 97.8% were admitted to the NICU. For babies <24 weeks' gestation, between 0% and 79.6% of babies alive at onset of labour were admitted to neonatal intensive care.

**CONCLUSIONS:** There are wide variations in the survival rates to discharge from neonatal intensive care for very preterm deliveries and in the timing of death across the MOSAIC regions. In order to directly compare international statistics for mortality in very preterm infants, data collection needs to be standardised. We believe that the standard point of comparison should be using all those infants alive at the onset of labour as the denominator for comparisons of mortality rates for very preterm infants analysing the cohort by gestational age band.

Arch. Dis. Child. Fetal Neonatal Ed. 94, F158–163.  
doi:10.1136/adc.2008.141531

## Ravijuhendid

Kokkuvõte ravijuhendites leiduvast

Mis puudutav ravijuhiseid, siis regionaliserrimis soovitusi annavad kolm juhust:

1. European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants – 2013 Update

- **Women at high risk of very preterm birth should be transferred to perinatal centres with experience in management of RDS (C).**

- (C evidence) A body of evidence including studies rated as 2+, directly applicable to the target population and demonstratin consistency of results or

[Type text]

Extrapolated evidence from studies rated as 2++

- Preterm babies at risk of RDS should be born in centres where appropriate skills are available for stabilization and ongoing respiratory support, including intubation and mechanical ventilation (MV) if indicated. Long-term health outcomes for extremely preterm babies are better if they receive their initial neonatal care in tertiary units. (viide eelnevalt esitatud Soome uuringule (Rautava et al., 2013)

2. Queensland clinical guideline. Perinatal care at the threshold of viability 2014.

- **Survival rates are higher in centres that deliver a high volume of very low birth weight babies and provide the highest level of neonatal care**

Viited:

FIGO Committee for the Study of Ethical Aspects of Human Reproduction and Women's Health. Ethical issues in obstetrics and gynecology. London: FIGO; 2009.

Lasswell SM, Barfield WD, Rochat RW, Blackmon L. Perinatal regionalization for very low-birth-weight and very preterm infants: a meta-analysis. JAMA. 2010; 304(9):992-1000.

- **Inborn babies have a better prognosis than outborn babies**

Viited:

ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists: Number 38, September 2002. Perinatal care at the threshold of viability. Obstet Gynecol. 2002; 100(3):617-24.

Berger TM, Bernet V, El Alama S, Fauchere JC, Hosli I, Irion O, et al. Perinatal care at the limit of viability between 22 and 26 completed weeks of gestation in Switzerland. 2011 revision of the Swiss recommendations. Swiss Med Wkly. 2011; 141:w13280

- **Aim to achieve in-utero transfer unless transfer puts the mother's life at risk—this may require a higher level of acceptance of the risk of birth en route**

3. Guidelines for perinatal care. American Academy of Pediatrics and the the American College of Obstetricians and Gynaecologists. 7th edition. 2012

## Maternal and Neonatal Interhospital Transfer ↩

The primary goal of regionalized perinatal care is for women and neonates at high risk to receive care in facilities that provide the required level of specialized care. Neonates born to women transported during the antepartum period have better survival rates and decreased risks of long-term sequelae than those transferred after birth. Delivery in a center providing high level neonatal care offers availability of pediatric subspecialists for early diagnosis and treatment of life-threatening conditions. Antepartum transport avoids separation of mother and infant in the immediate postpartum period, allows mothers to communicate directly with neonatal intensive care unit (NICU) health care providers, and supports the goal of family-centered health care. Because all hospitals cannot provide all levels of perinatal and neonatal care, interhospital transport of pregnant women and neonates is an essential component of a regionalized perinatal health care system.

All attempts should be made to ensure that women and infants at high risk receive care in a facility that provides the required level of specialized obstetric and newborn care. If a woman is receiving obstetric care in a hospital with a low level of NICU care and she is found to be at risk of adverse outcome or premature delivery, transfer of care to a hospital with a high level of NICU care is indicated, whenever safely possible. Delivery hospitals that do not have a level III or level IV NICU should develop affiliation(s) with facilities that provide higher levels of care. Formal transfer agreements should be in place that clearly outline the responsibilities of each facility. The American Academy of Pediatrics has developed general guidance based on neonatal gestational age and potential complications to help determine the most optimal level of NICU care for a given gestational age and estimated fetal weight (see [Table 1-3](#) in Chapter 1).

**Table 1-3. Definitions, Capabilities, and Health Care Provider Types: Neonatal Levels of Care\*** ↩9↩13↩14↩78

Level of Care	Capabilities	Health Care Provider Types <sup>†</sup>
Level I well newborn nursery	Provide neonatal resuscitation at every delivery Evaluate and provide postnatal care to stable term newborn infants Stabilize and provide care for infants born at 35–37 weeks of gestation who remain physiologically stable Stabilize newborn infants who are ill and those born before 35 weeks of gestation until transfer to a higher level of care	Pediatricians, family physicians, nurse practitioners, and other advanced practice registered nurses

(continued)

**Table 1-3. Definitions, Capabilities, and Health Care Provider Types: Neonatal Levels of Care\* (continued)**

Level of Care	Capabilities	Health Care Provider Types†
Level II special care nursery	<p>Level I capabilities plus:</p> <p>Provide care for infants born at 32 weeks of gestation or later and weigh 1,500 g or more who have physiologic immaturity or who are moderately ill with problems that are expected to resolve rapidly and are not anticipated to need sub-specialty services on an urgent basis</p> <p>Provide care for infants convalescing after intensive care</p> <p>Provide mechanical ventilation for brief duration (less than 24 hours) or continuous positive airway pressure or both</p> <p>Stabilize infants born before 32 weeks of gestation and weigh less than 1,500 g until transfer to a neonatal intensive care facility</p>	<p>Level I health care providers plus:</p> <p>Pediatric hospitalists, neonatologists, and neonatal nurse practitioners</p>

Level III neonatal intensive care unit	<p>Level II capabilities plus:</p> <p>Provide sustained life support</p> <p>Provide comprehensive care for infants born before 32 weeks of gestation and weigh less than 1,500 g and infants born at all gestational ages and birth weights with critical illness</p> <p>Provide prompt and readily available access to a full range of pediatric medical subspecialists, pediatric surgical specialists, pediatric anesthesiologists, and pediatric ophthalmologists</p> <p>Provide a full range of respiratory support that may include conventional ventilation and/or high-frequency ventilation and inhaled nitric oxide</p> <p>Perform advanced imaging, with interpretation on an urgent basis, including computed tomography, magnetic resonance imaging, and echocardiography</p>	<p>Level II health care providers plus:</p> <p>Pediatric medical subspecialists‡, pediatric anesthesiologists‡, pediatric surgeons, and pediatric ophthalmologists‡</p>
--	--	---

**Table 1-3. Definitions, Capabilities, and Health Care Provider Types: Neonatal Levels of Care\* (continued)**

Level of Care	Capabilities	Health Care Provider Types†
Level IV regional neonatal intensive care unit	<p>Level III capabilities plus:</p> <p>Located within an institution with the capability to provide surgical repair of complex congenital or acquired conditions</p> <p>Maintain a full range of pediatric medical subspecialists, pediatric surgical subspecialists, and pediatric anesthesiologists at the site</p> <p>Facilitate transport and provide outreach education</p>	<p>Level III health care providers plus:</p> <p>Pediatric surgical subspecialists</p>

[Type text]

Otsingu strateegia	
Andmebaas	Medline (PUBMED)
Otsingustrateegia	Key words:antibiotics, premature birth, premature labor,pretermrupture of membranes,chorionamnionitis, GBS.  MESH1:("Intensive Care Units, Neonatal"[Mesh] AND "Premature Birth"[Mesh]) AND "Delivery of Health Care"[Mesh]  MESH 2:"Perinatal Care"[Mesh] AND "Evidence-Based Practice"[Mesh] AND ((Randomized ControlledTrial[ptyp] OR systematic[sb] OR Meta-Analysis[ptyp]) AND "2010/12/10"[PDat] : "2015/12/08"[PDat])
Tulemustearv	14(MESHterminitega) 49
Filtrid	none
Ajalinepiirang	10years
Muudpiirangud	English language

Andmebaas	Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE)
Otsingustrateegia	Key words: Perinatal Care/og[Organization & Administration] Regional Medical Programs/ or Regional Health Planning/ Referral and Consultation"/ or "Transportation of Patients"/ Patient Transfer/ or Perinatal Care/ or in-utero transport.mp. Perinatal Care/og[Organization & Administration]
Tulemustearv	45
Filtrid	none
Ajalinepiirand	10years
Muudpiirangud	English language

Lisaks oluliste allikate viidete kontroll.

[Type text]