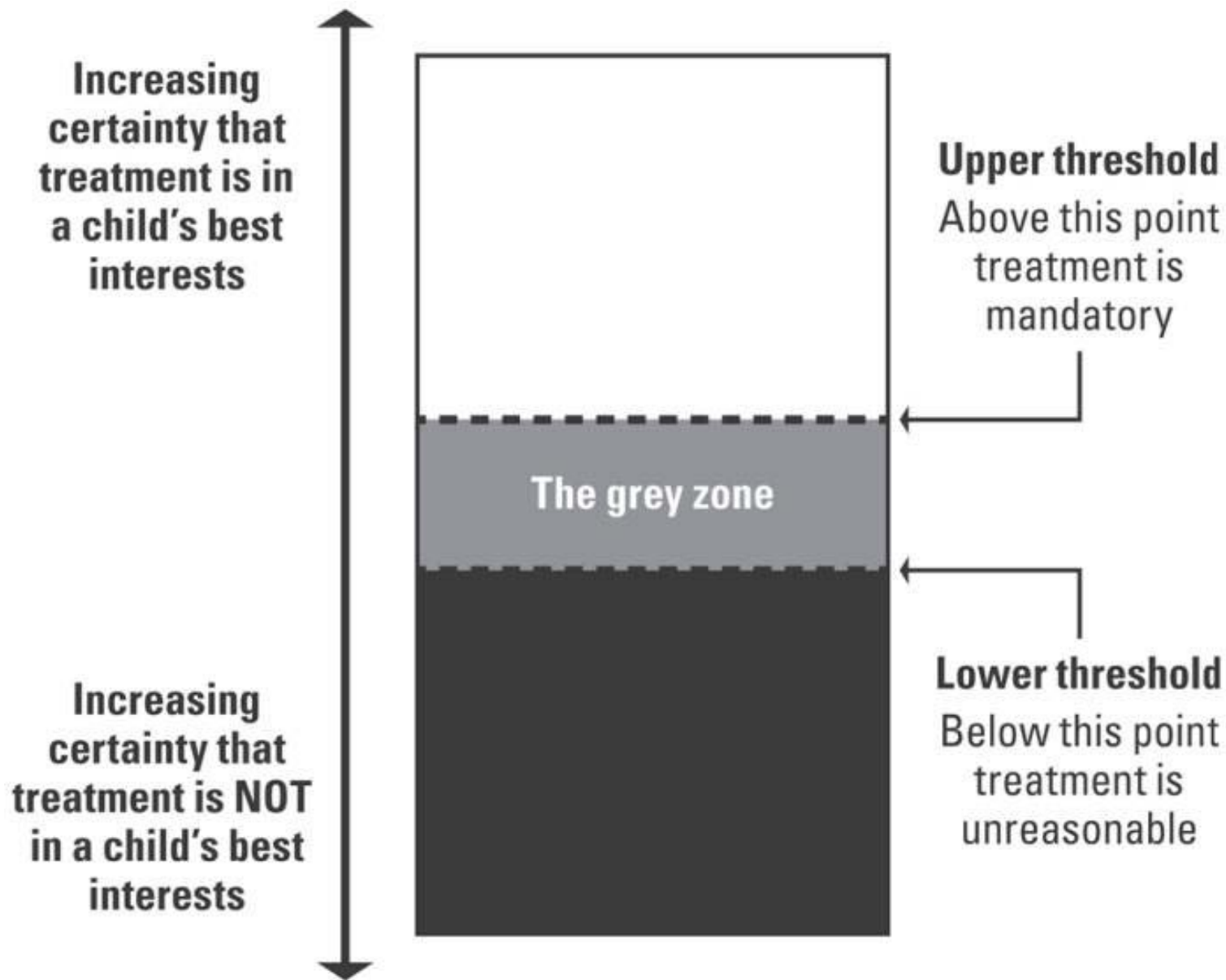


What is the limit of viability?

John D. Lantos MD,
Children's Mercy Bioethics Center
Kansas City, Missouri, USA

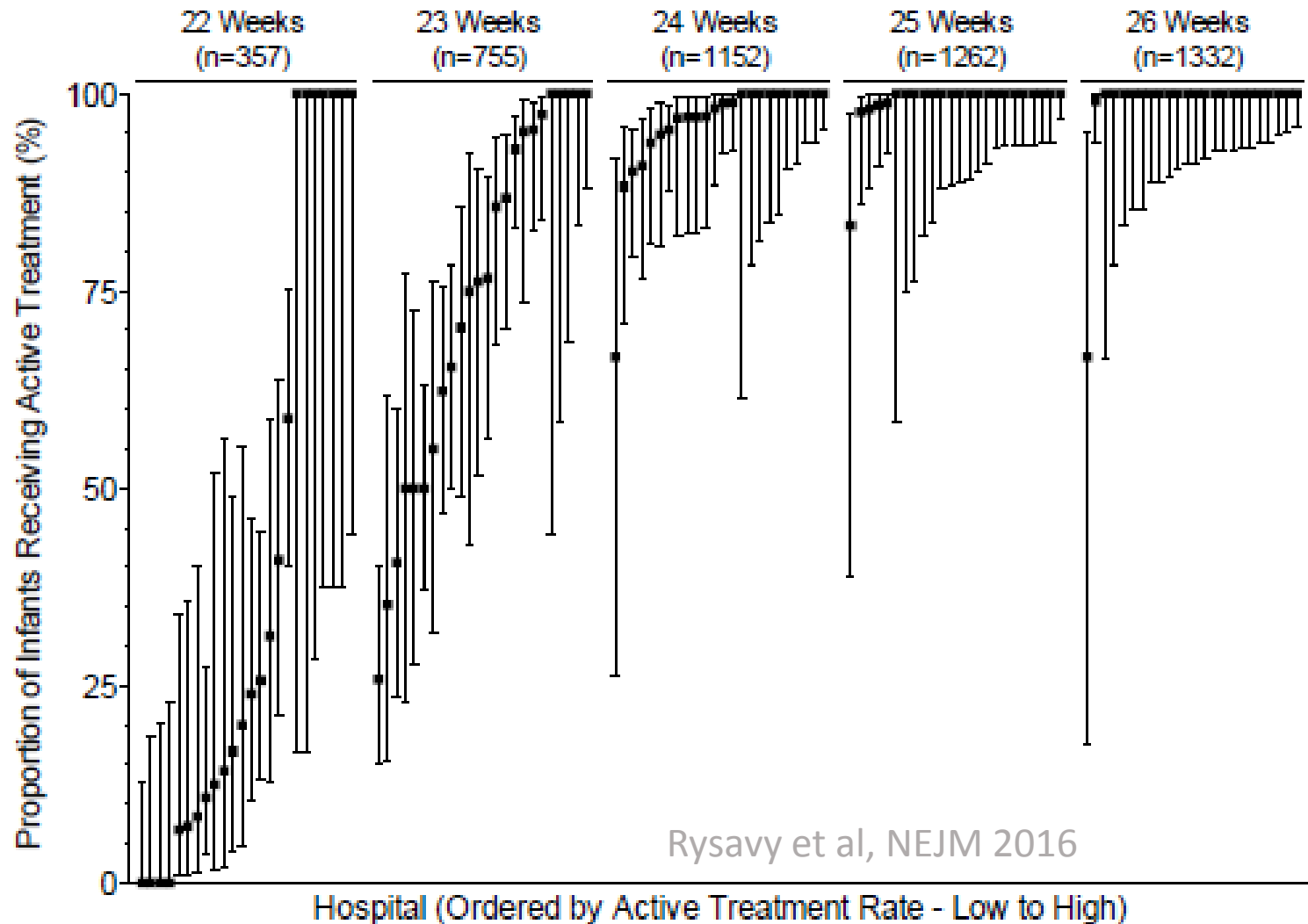
Limit of viability – always a central question

- Neonatology was founded to push the limits
 - Relentlessly progressive
 - Now the field seems to have lost its energy
 - No longer saving tinier and tinier babies.
-
- Central message of this talk – limit of viability is 22 weeks. But many people don't like that!



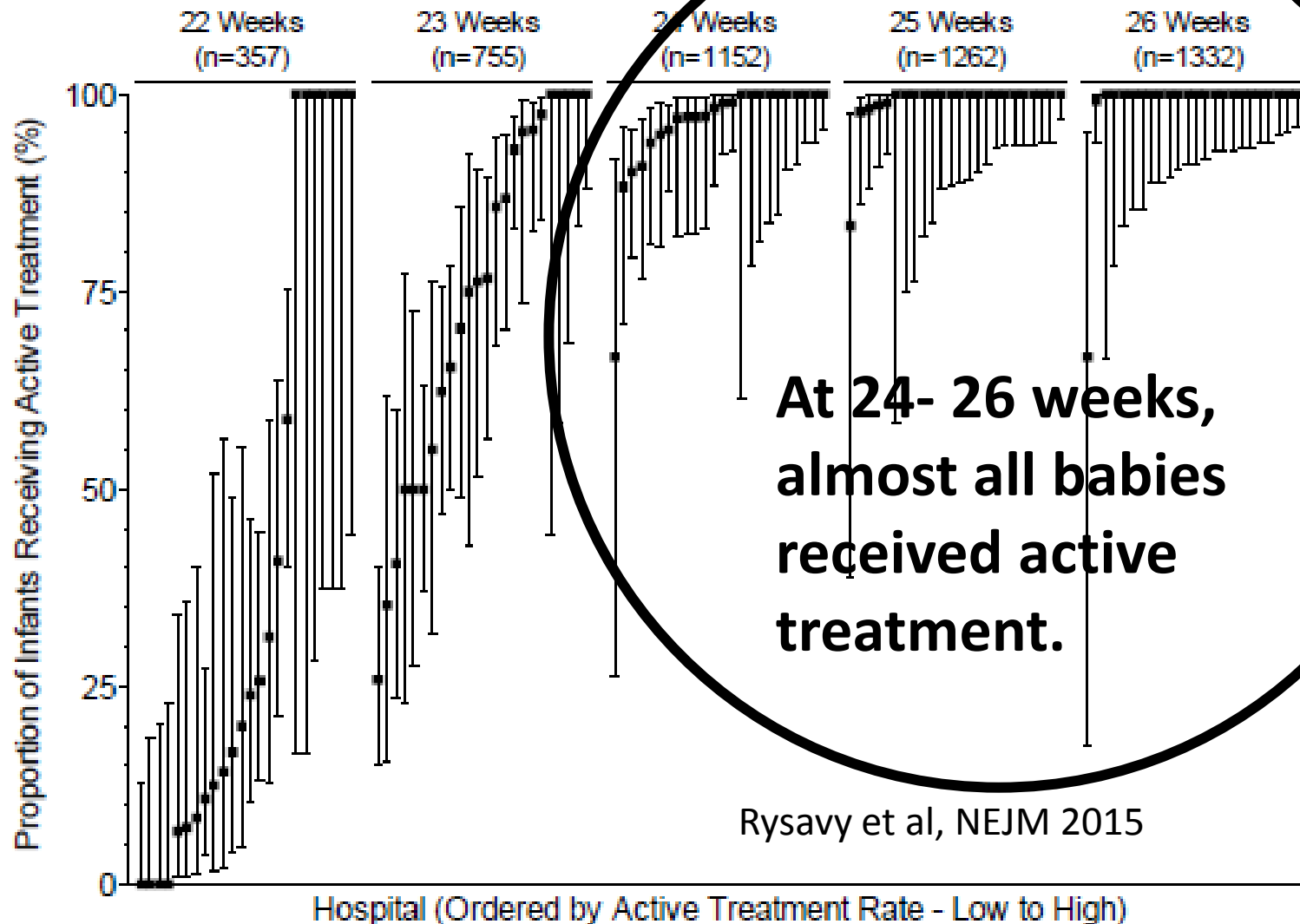
Current practice variation in the USA

Figure S1. Rates of Neonatal Active Treatment for Infants Born at 22 to 26 Weeks' Gestation in 24 Hospitals in the NICHD Neonatal Research Network



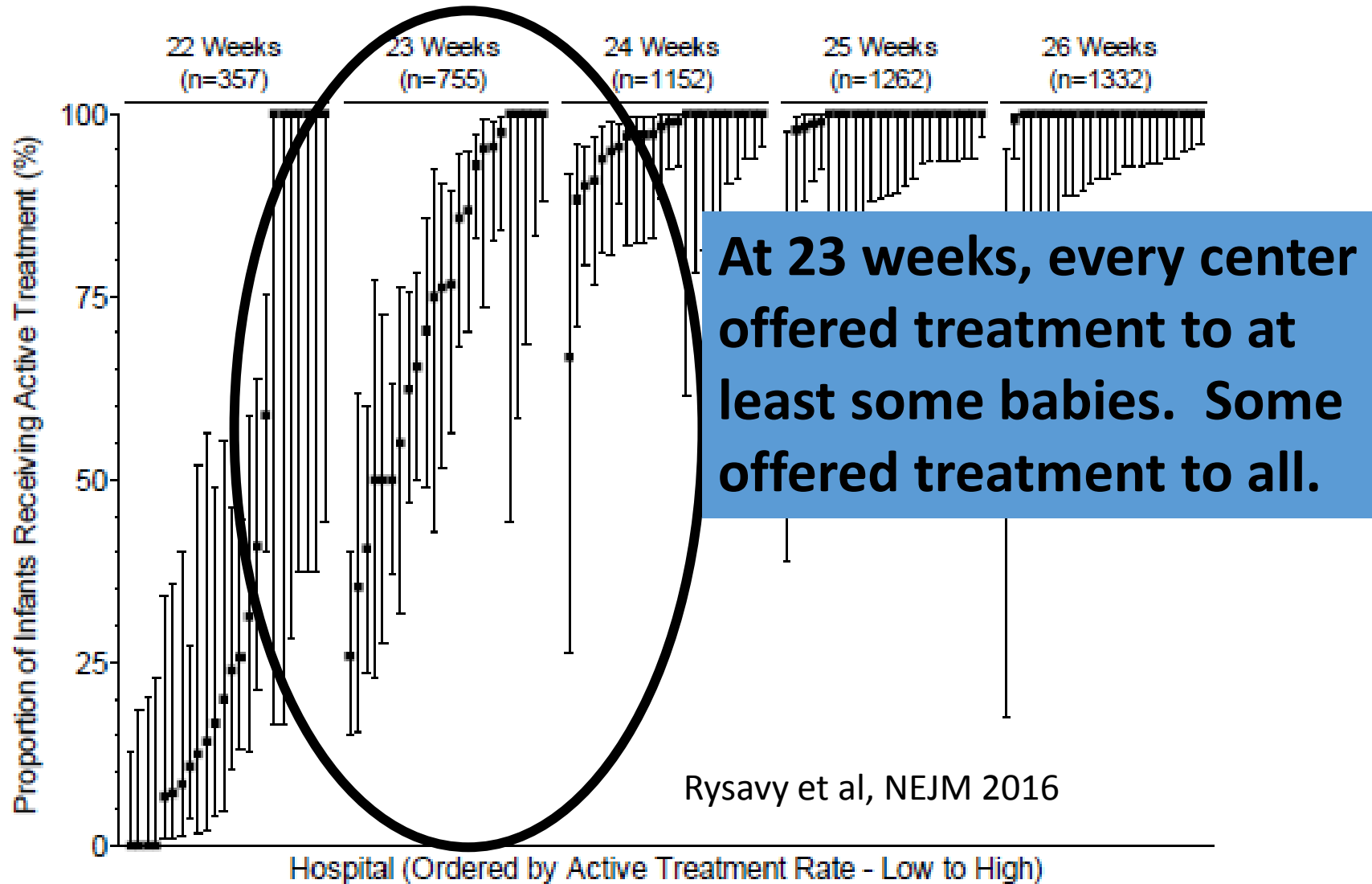
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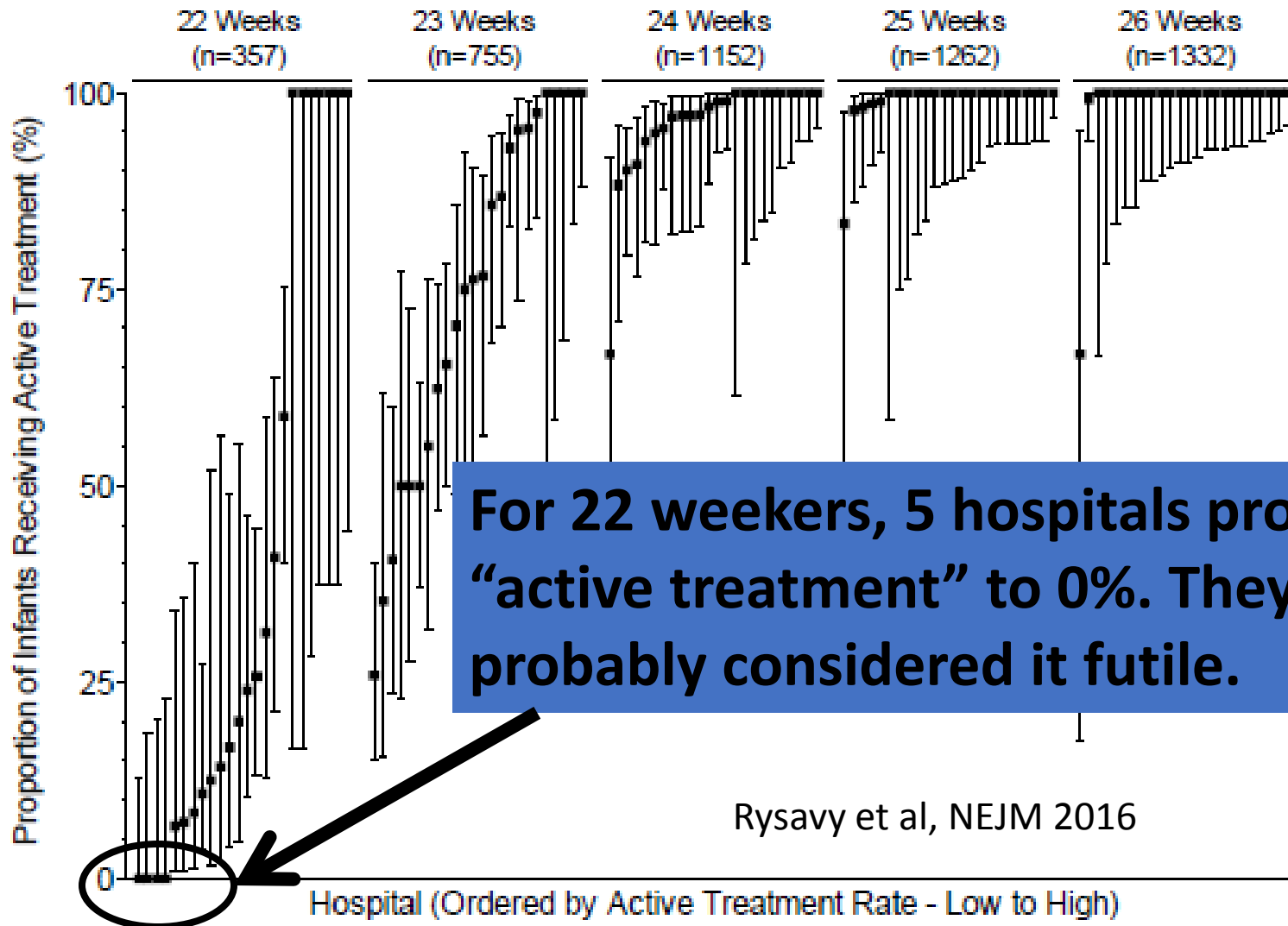
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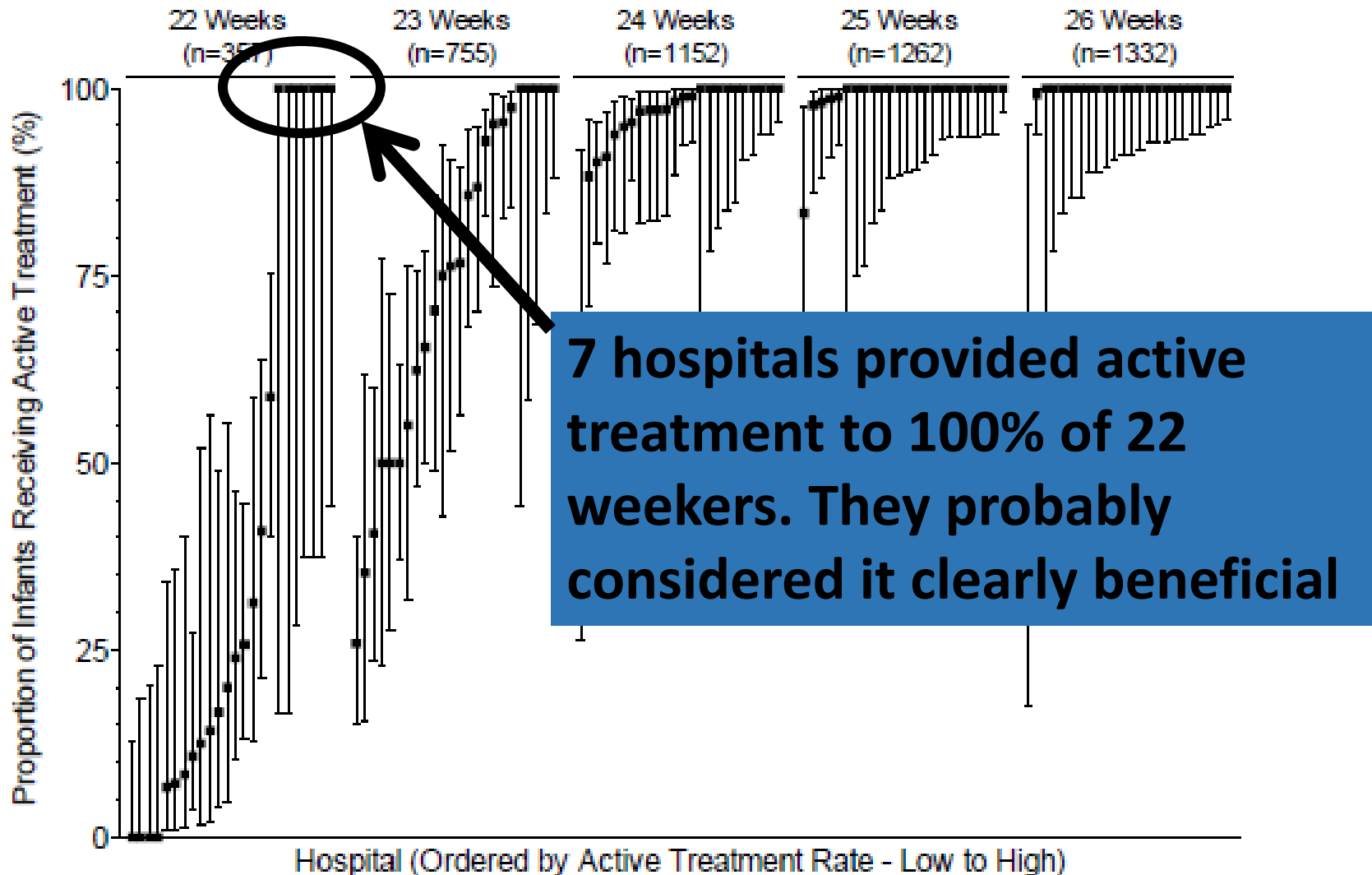
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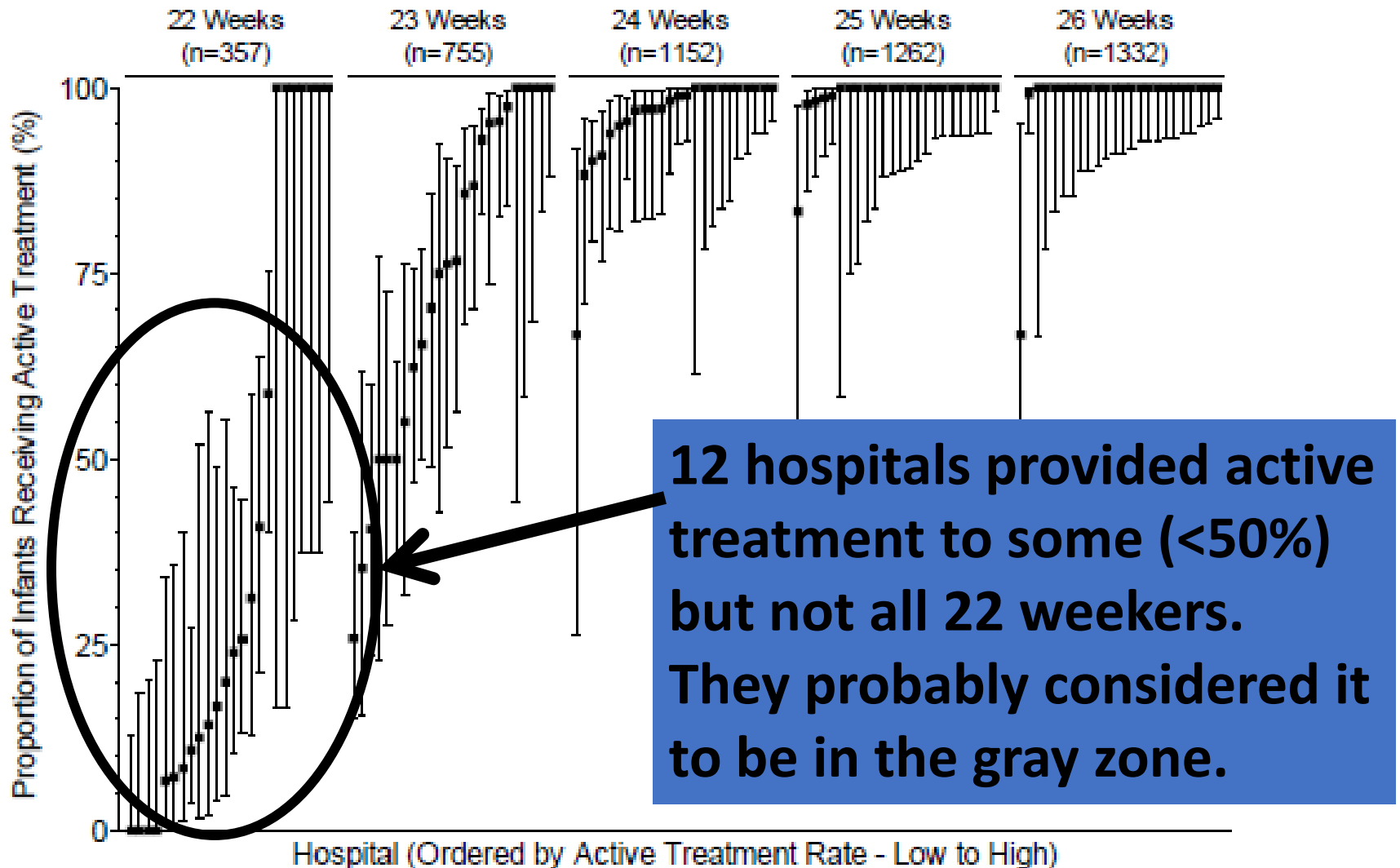
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VARIATION IN TREATMENT AND OUTCOMES IN PRETERM INFANTS

Table 2. Crude Outcomes by Gestational Age at Birth.*

Outcome	All Infants <i>mean (95% CI)</i>	Infants Who Received Active Treatment		
		Hospital Rate‡ <i>median (interquartile range)</i>	Overall Rate† <i>mean (95% CI)</i>	Hospital Rate‡ <i>median (interquartile range)</i>
22 Wk of gestation				
Survival	5.1 (3.2–7.9)	3.4 (0.0–10.6)	23.1 (14.9–34.0)	21.1 (0.0–50.0)§
Survival without severe impairment	3.4 (1.9–5.9)	0.0 (0.0–6.9)	15.4 (8.8–25.4)	5.0 (0.0–33.3)§
Survival without moderate or severe impairment	2.0 (0.9–4.1)	0.0 (0.0–0.7)	9.0 (4.3–17.9)	0.0 (0.0–14.6)§

Overall survival at 22 weeks was just 5%

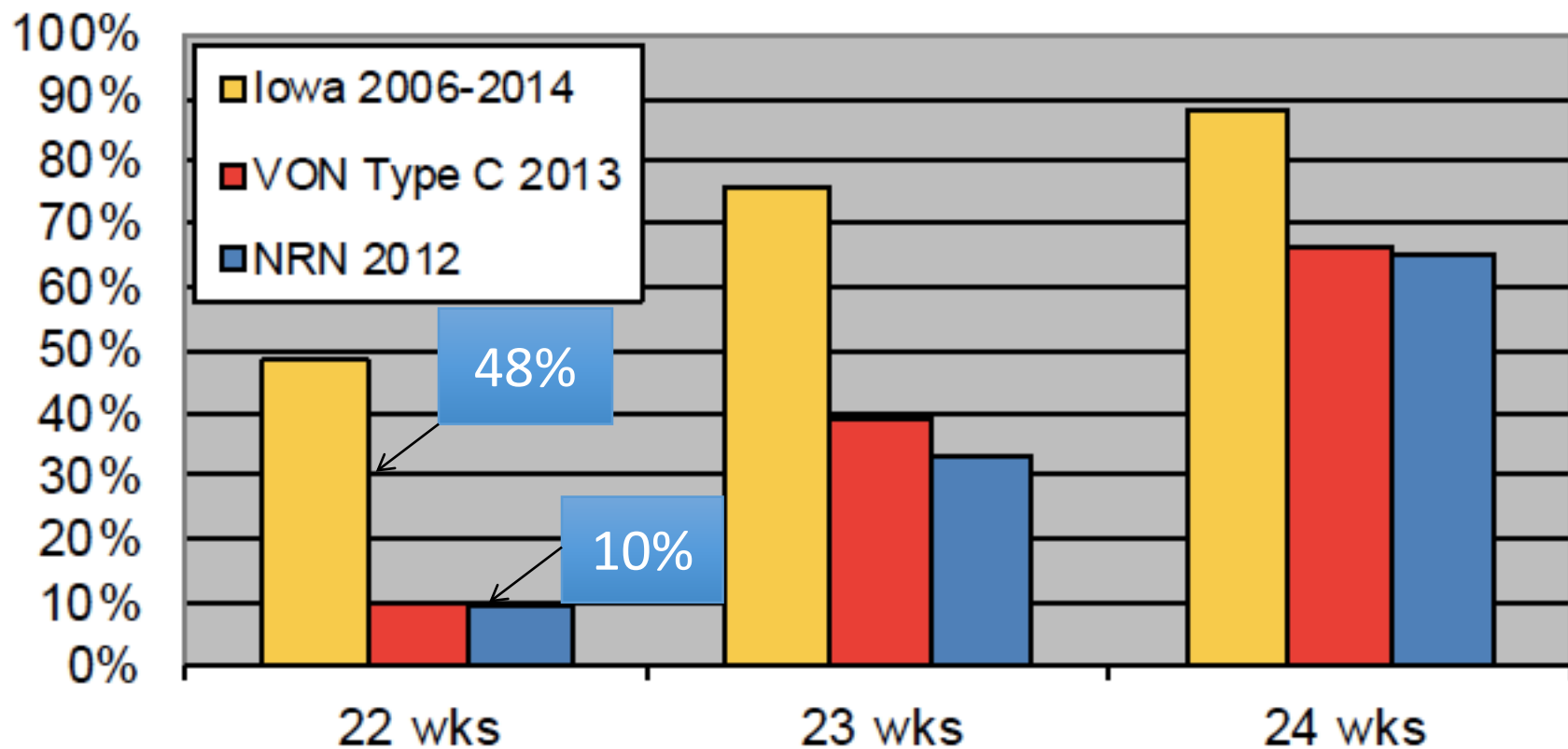
VARIATION IN TREATMENT AND OUTCOMES IN PRETERM INFANTS

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Among infants who were treated, it was 23%, with one hospital reporting 34%

Survival of Inborn VLBW Infants 22 - 24 weeks EGA



NRN data: JAMA September 8, 2015; Volume 314, Number 10

How do they do it?

A team approach

- **Close collaboration with MFM**

- Antenatal steroids starting at 21-22 weeks.
- Discussion about C-section if indicated.
- Parental informed consent for NICU treatment.

- **Golden Hour Protocols for first hour of life**

- Attention to physiological and psychological needs

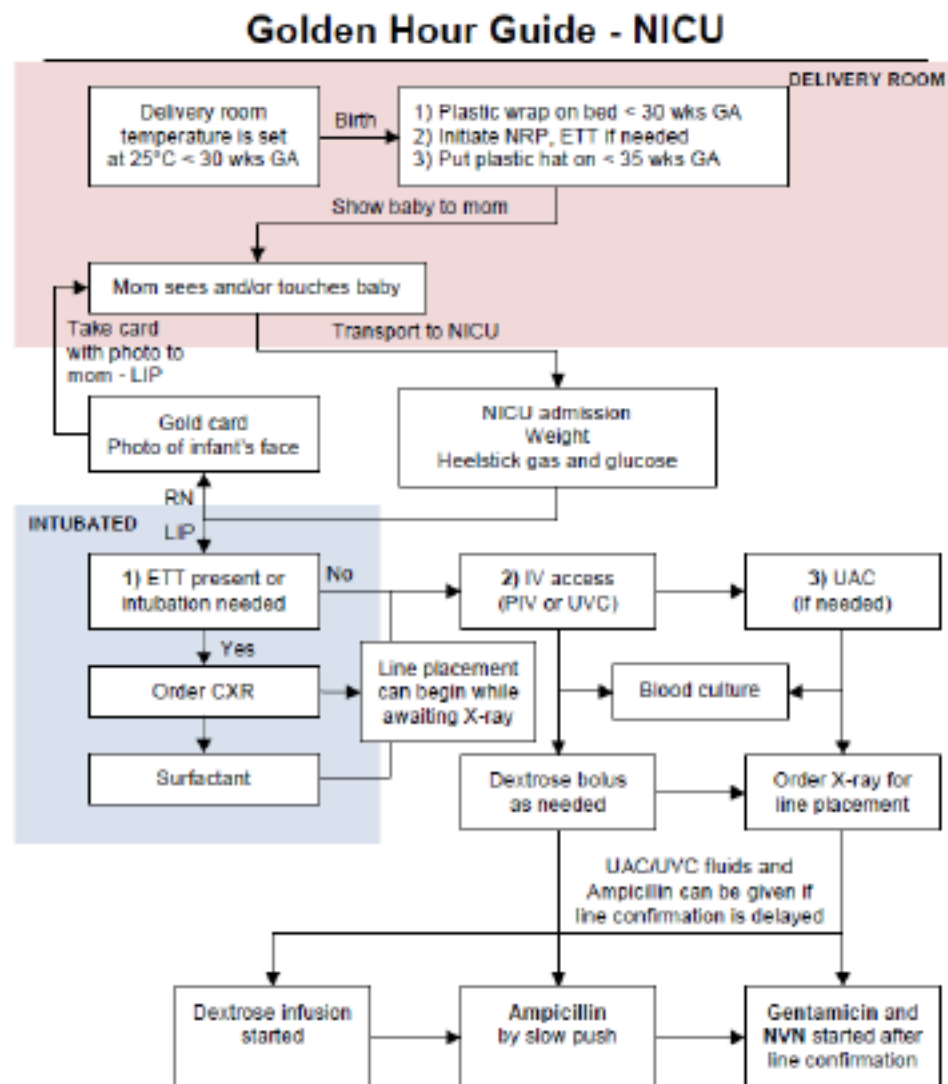
- **Tiny Baby Unit within the NICU**

- RNs and RTs both highly trained in care of tiny babies
- Meticulous attention to pCO₂.

In the NICU Standardization of Care Golden Hour Protocol

Golden Hour Goals:

- 1) Admission temperature ≥ 36.0
- 2) Surfactant given
- 3) Dextrose infusion started
- 4) Antibiotics started
- 5) Communication post-delivery with mom



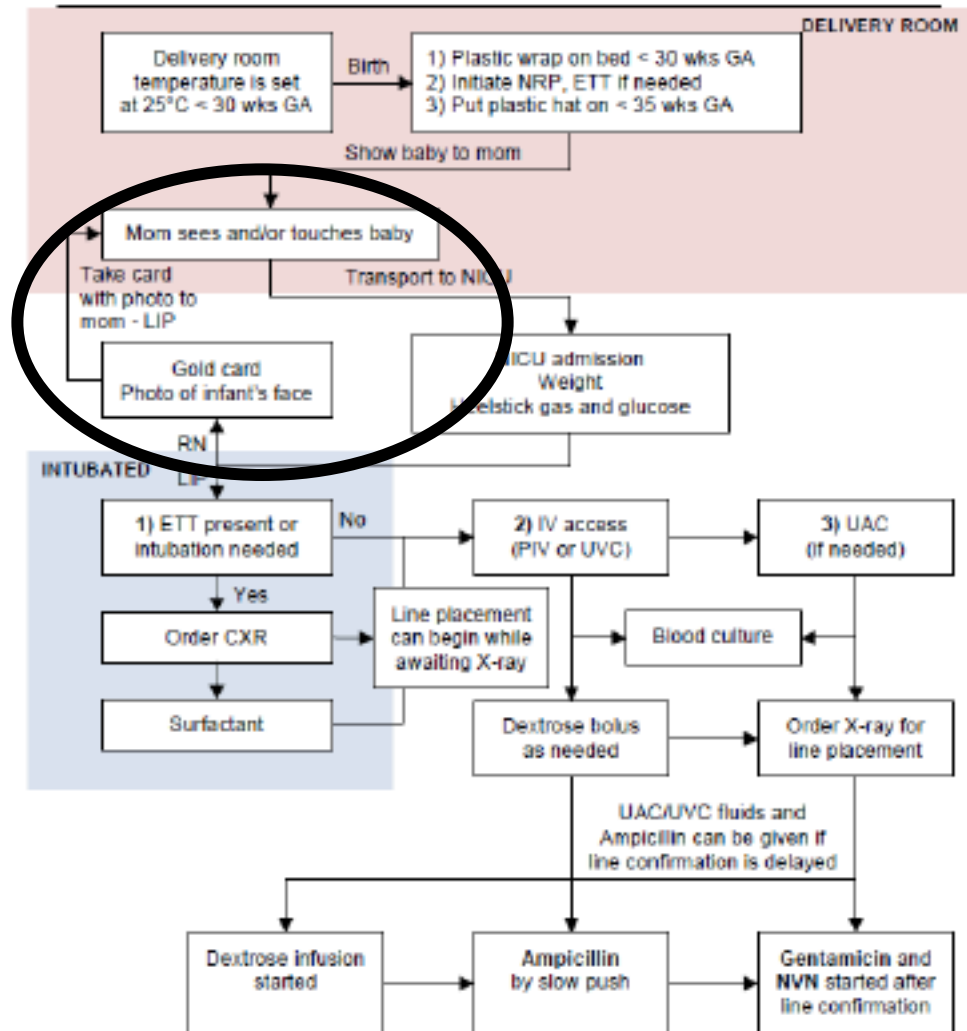
- Golden Hour Goals:
- 1) Admission temperature ≥ 36.0
 - 2) Surfactant given, if ordered
 - 3) Dextrose infusion started
 - 4) Antibiotics started
 - 5) Communication post-delivery with mom - Gold card given

In the NICU

Golden Hour Guide - NICU

Mom sees, touches baby
Photo of baby given to parents

- 2) Surfactant given
- 3) Dextrose infusion started
- 4) Antibiotics started
- 5) Communication post-delivery with mom



- Golden Hour Goals:
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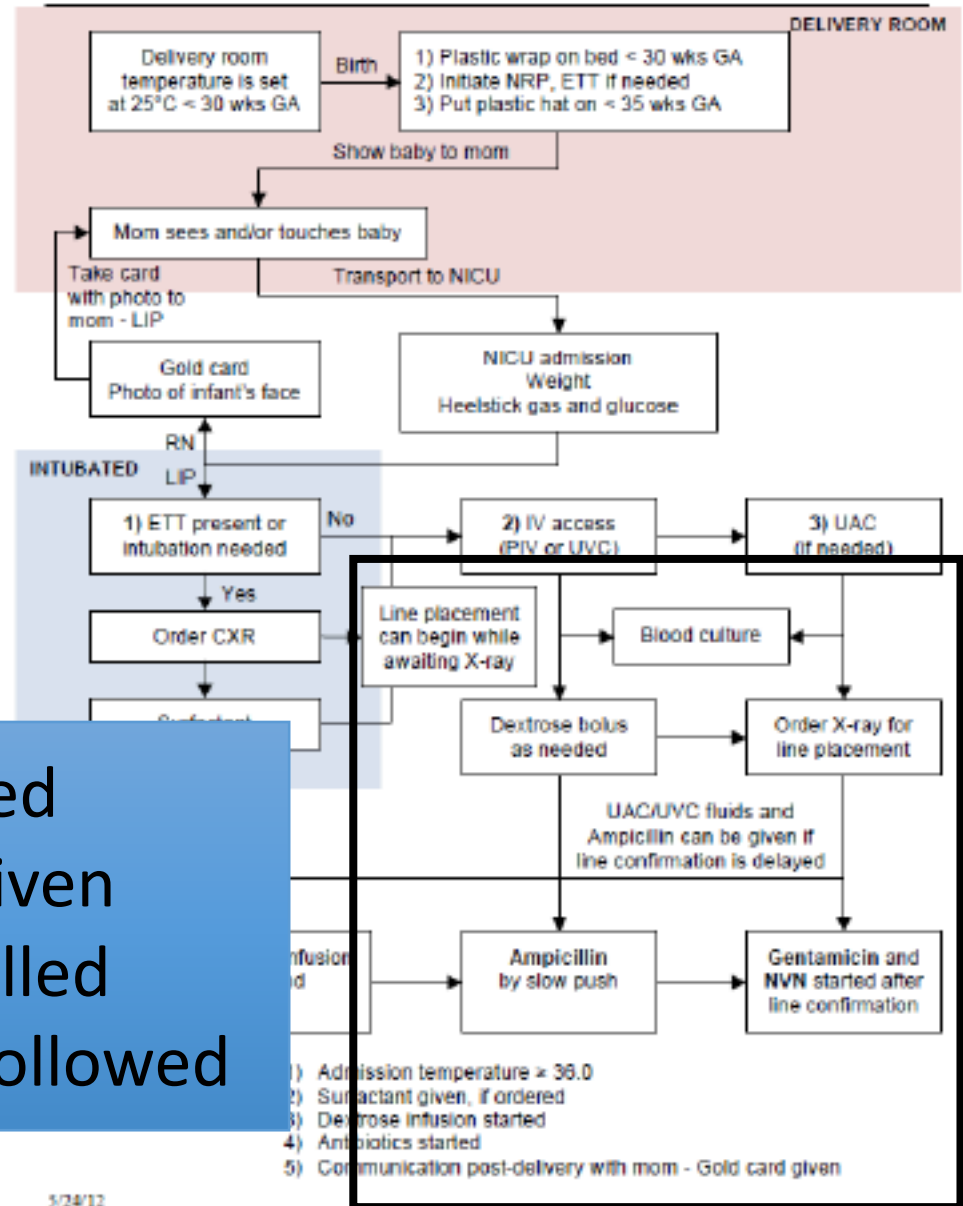
In the NICU Standardization of Care Golden Hour Protocol

Golden Hour Goals:

- 1) Admission temperature ≥ 36.0
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- 3) Dextrose infusion started
- 4) Antibiotics started
- 5) Communication post-delivery with mom - Gold card given

Lines started
Antibiotics given
Temp controlled
CO2 guidelines followed

Golden Hour Guide - NICU

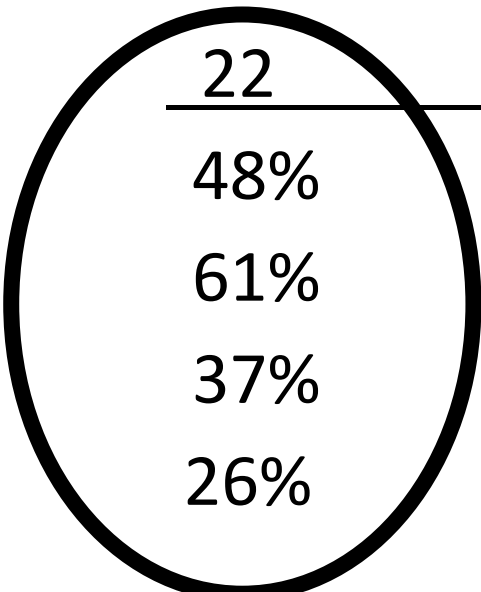


Standardized Ventilator Goals

- 1) 1st Intention HFV Center at Iowa
 - ✓ High Frequency Jet Ventilation for all infants < 25 weeks at birth
- 2) Critically important to avoid volutrauma (shear force injury) to the lung especially at 22 to 23 weeks gestation
 - ✓ Follow pCO₂ levels closely with **rigid adherence** to goals to avoid fluctuations in Cerebral Blood Flow
 - 1) Target 45 - 55 first 3 days
 - 2) Target 45 - 60 next 4 days
 - 3) Gases Q2-3 hours or more frequently in the beginning
 - 4) After ventilator change, repeat in 20 minutes

Others also report high survival rates

	Week of gestation		
	22	23	24
Iowa	48%	76%	88%
Cologne (Mehler)	61%	71%	
Japan (Ishi)	37%	65%	78%
Express*	26%	65%	73%

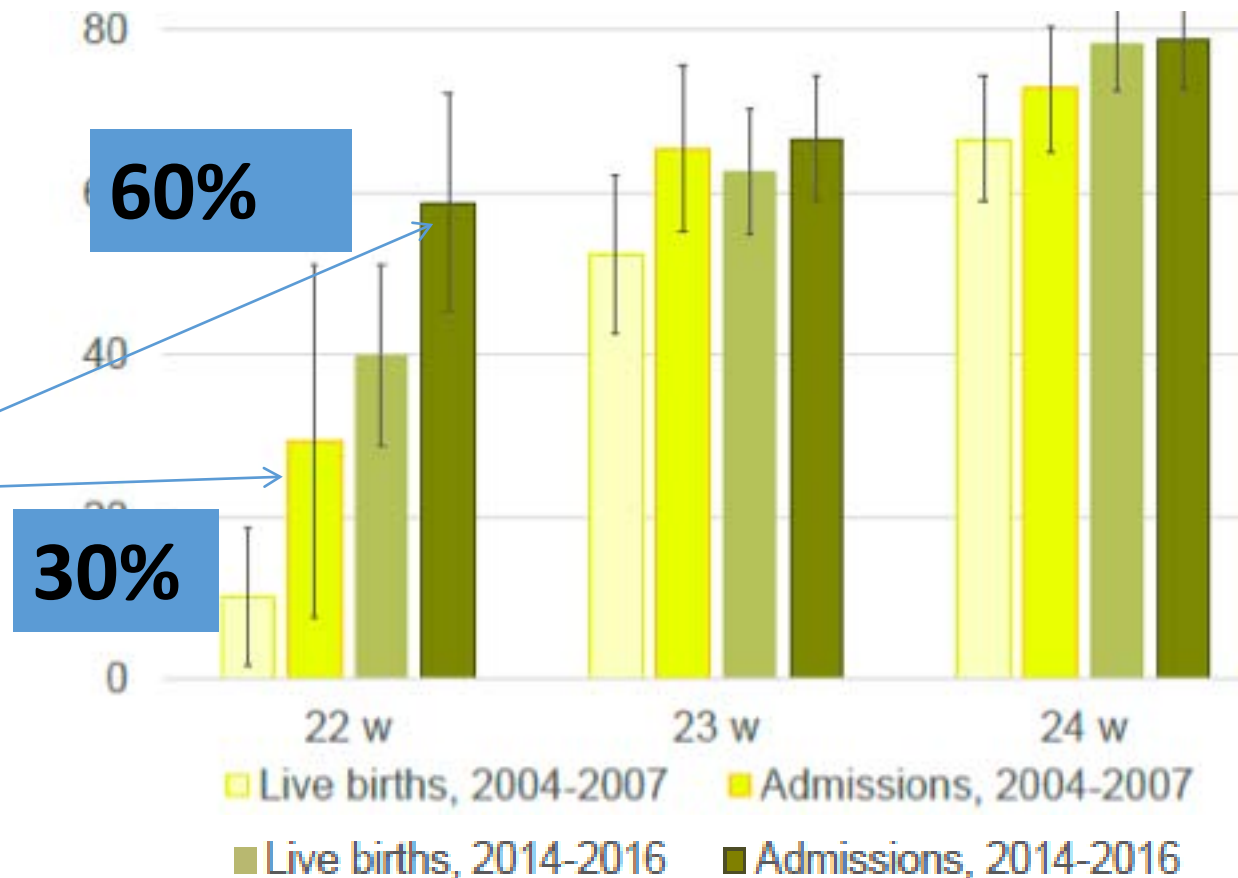


- The Express Group, Acta Paediatrica 2010

*derived from tables 2 and 3

Survival rates by gestational age and treatment intensity for two cohorts – 2004-7 and 2014-16

Survival 2-3x
as high
among
babies
admitted to
NICU



Common elements of proactive treatment

- They anticipate medical and psychosocial needs...
- They have a well-developed protocol
- They implement it smoothly and consistently

- And it seems to work – though we don't know what, exactly is working.

Very promising preliminary results

- Other centers don't want to emulate it.
- NICHD doesn't want to study it.
- Professional societies misrepresent the data.

ACOG/SMFM statement (2016)

- “Delivery before 23 weeks typically results in neonatal death irrespective of newborn resuscitation (5-6% survival) and, among rare survivors, significant morbidity is universal. (98-100%).”
 - <http://www.acog.org/Resources-And-Publications/Obstetric-Care-Consensus-Series/Perivable-Birth>

A great mystery

- Is there any other situation in medicine in which...
 - A patient has a disease that is uniformly fatal;

A great mystery

- Is there any other situation in medicine in which...
 - A patient has a disease that is uniformly fatal;
 - Some centers report 40-50% survival rates;

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 - Most centers do not offer treatment;
 - Many say that it is unethical to offer treatment;

A great mystery

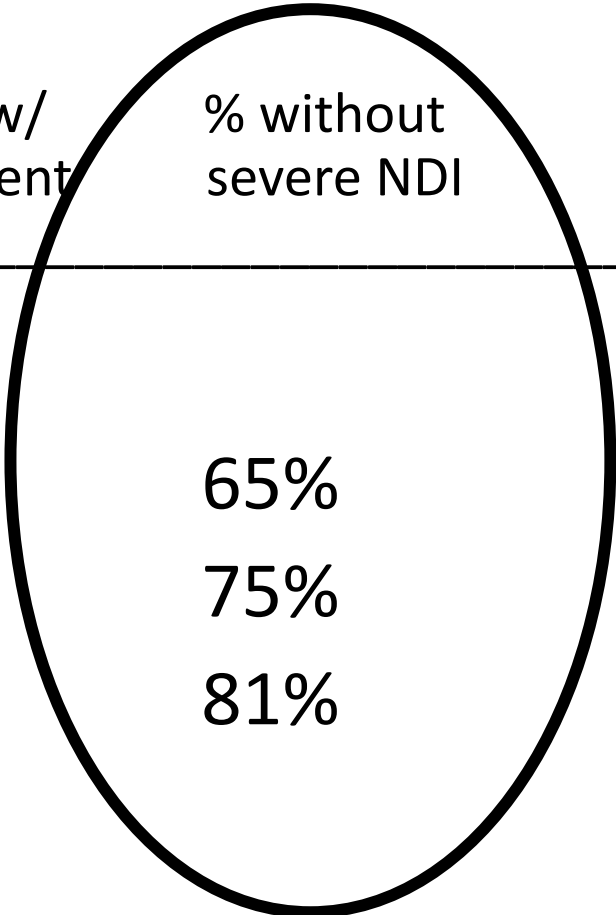
- Is there any other situation in medicine in which...
 - A patient has a disease that is uniformly fatal;
 - Some centers report 40-50% survival rates;
 - Professional societies misrepresent the data;
 - Most centers do not offer treatment;
 - Many say that it is unethical to offer treatment;
 - And most bioethicists support them!?

Possible explanations

**Belief that the survivors
must all be severely disabled.**

Most survivors do not have severe NDI

EGA (wks)	survival	% of survivors w/ severe impairment	% without severe NDI
—			
22	23%	35%	65%
23	33%	25%	75%
24	57%	19%	81%



Data from Rysavy et al NEJM 2015

Survival of 22 weekers in Japan

- 48 tertiary care centers
- All infants (1057) born at 22-25 wks gestation
- At 22 weeks
 - 23/75 babies
 - 37% survival
 - 24% had grade 3-4 IVH, 3% had cystic PVL
 - 20% had ROP requiring treatment
- Unimpaired or minimally impaired 9/75 (12%)
- Unimpaired among survivors 9/23 (39%)

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Denominator problems

- Studies don't often account for either
 - Non-treatment
 - Substandard treatment
 - Decisions to withdraw life support.

22 weekers in Epicure (UK)

Total study: 3133 births, 22-26 weeks, in UK, 2006

- Among babies born at 22 weeks
 - 272 fetuses alive at the onset of labor
 - 120 Intrapartum stillbirths
 - 152 live births

Among the 152 live births

- 8 (6%) moms received antenatal steroids
 - 69 (45%) born in tertiary care center
 - 111 (73%) treatment withheld
 - 19 (13%) admitted for intensive care
-
- Survival to discharge – $3/152 = 1.5\%$
 - $3/8$ (37%) of babies who got steroids
 - $3/19$ (16%) of babies admitted to NICU
-
- Costloe K. BMJ, 2012

Framing issues

- Which is the most important number:
 - % who survive with no disability?
 - % of survivors who have no disability ?

How many 500g, 23 week* singletons survive unimpaired?

- Boys, no steroids 5%
- Boys, steroids 11%
- Girls, no steroids 9%
- Girls steroids 18%

Three things to note:

1. Fourfold difference in survival at same BW and GA.
2. Survival rates double if given steroids
3. Doesn't distinguish death from disability in survivors

*Calculator doesn't go down to 22 weeks

How many 500g, 23 wk survivors are unimpaired?

• Boys, no steroids	5%	50%
• Boys, steroids	11%	55%
• Girls, no steroids	9%	67%
• Girls steroids	18%	67%

Key Framing Question

Is it worse to have tried and failed than not to have tried at all?

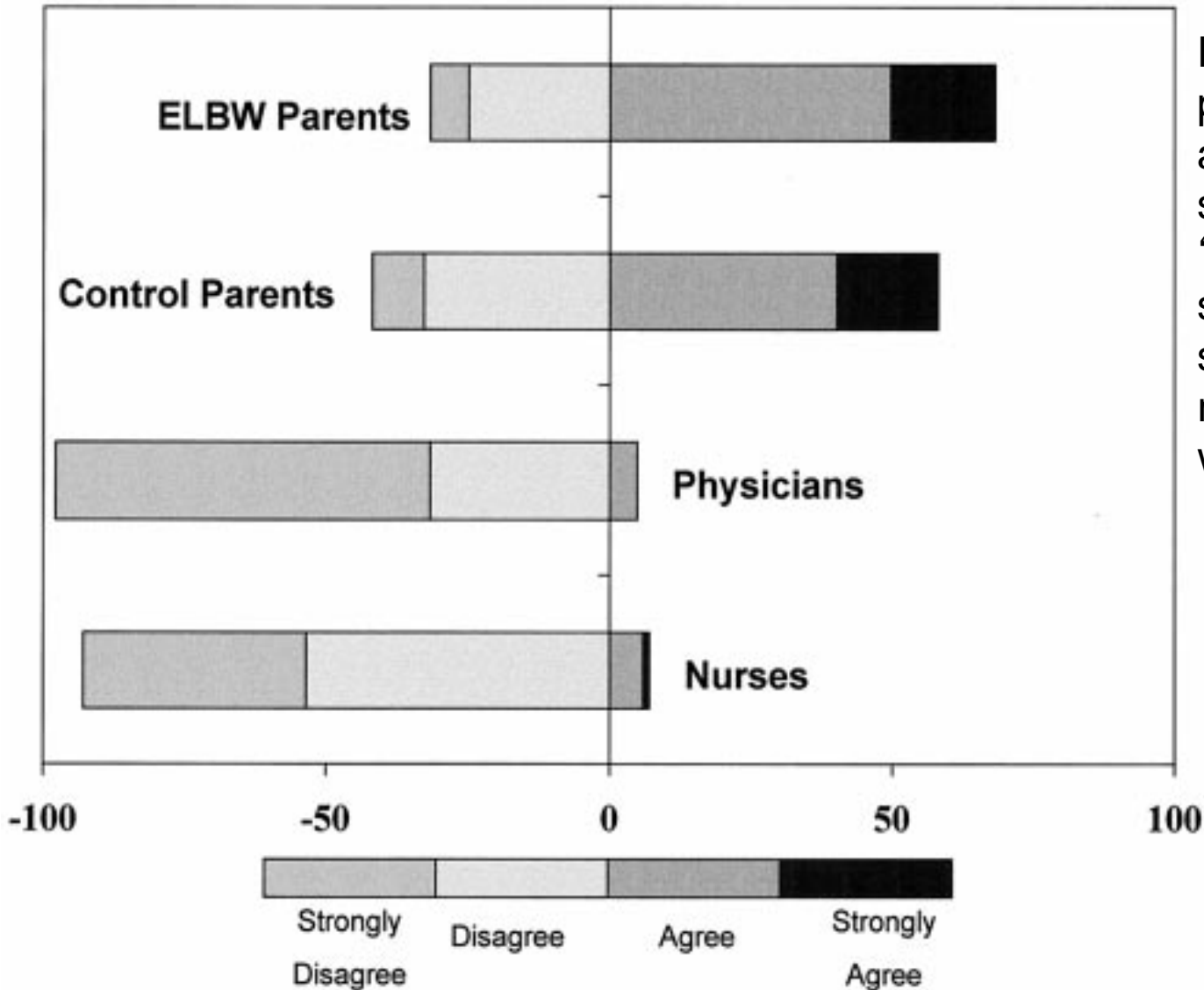
OR, to put it another way

Is it better not to offer treatment and let a preemie die, or to offer a trial of therapy and withdraw treatment if things look bad?

Belief that parents don't want such treatment, or shouldn't want it.

Parents generally want more treatment than doctors and nurses think is appropriate.

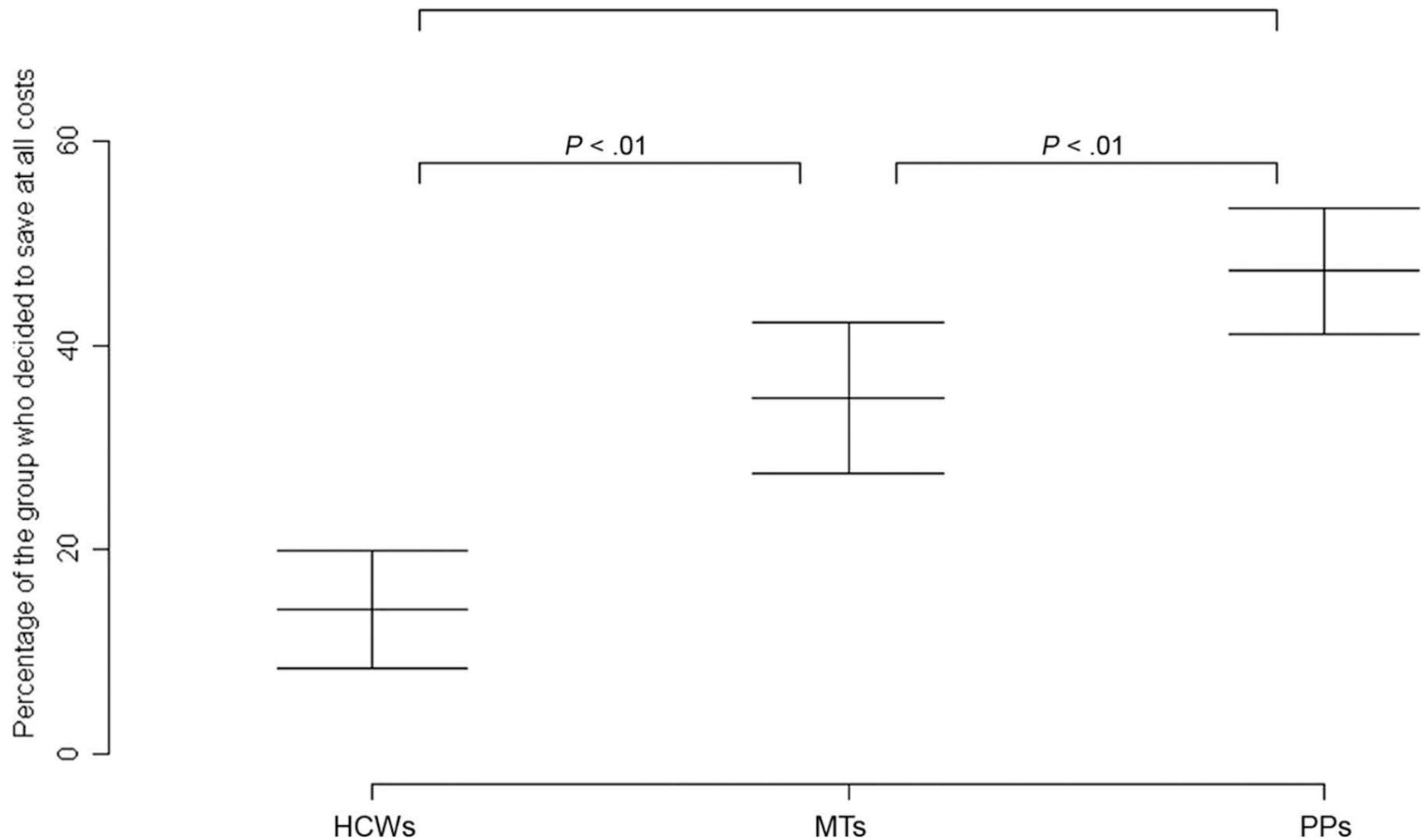
Most say they want “everything.”



Parent and professional agreement with the statement:
“I believe an attempt should be made to save all infants regardless of birth weight.”

Streiner et al
Peds, 2001

More likely than HCWs to say we should try to save babies “at all costs.”



Lam, H. S. et al. *Pediatrics* 2009;123:1501-1508

Copyright ©2009 American Academy of Pediatrics

PEDIATRICS[®]

More likely to rank “death” lower than “severe global impairment”

1. Death.

2. Severe global impairment – wheelchair, intelligence of 1y.o., unable to speak, read or write, incontinent, no independent ADLs.

5. Moderate global impairment – crutches, attends special school, cannot read or write, unable to live independently, continent.

Lam, H. S. et al. Pediatrics 2009;123:1501-1508



Children's Mercy Hospitals and Clinics

Children's Mercy Bioethics Center

 **Children's Mercy**
HOSPITALS & CLINICS
www.childrensmc.org

Is severe disability is worse than death?

- Doctors and nurses - 55%
- Mothers of term babies – 40%
- Parents of preemies – 25%

Lam, H. S. et al. Pediatrics 2009;123:1501-1508

Problem with Zone of Parental Discretion

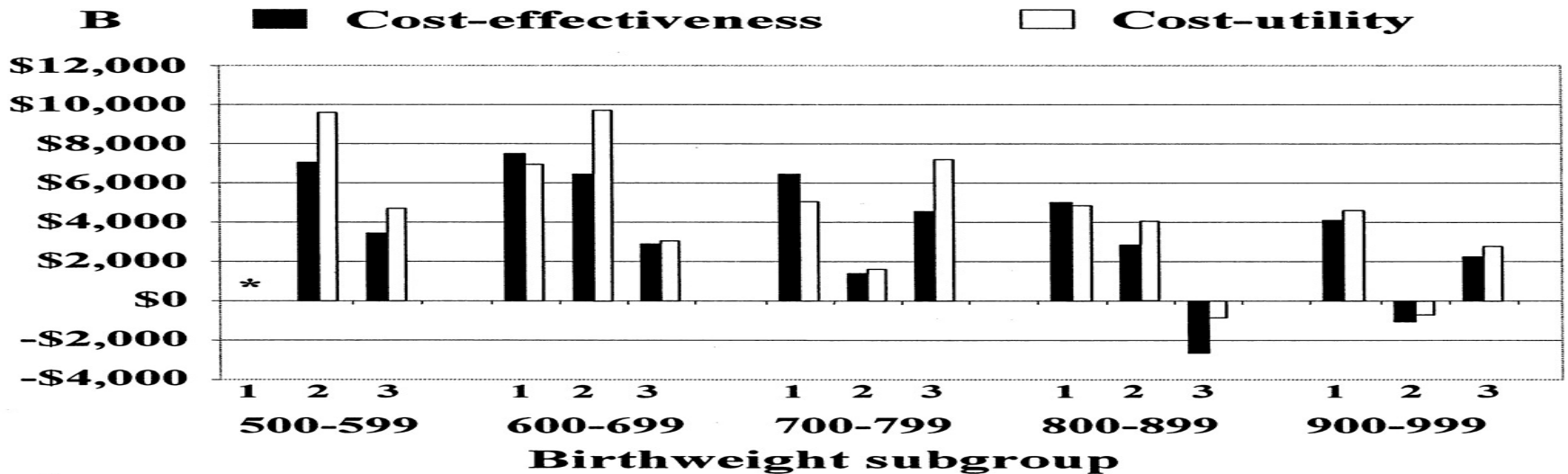
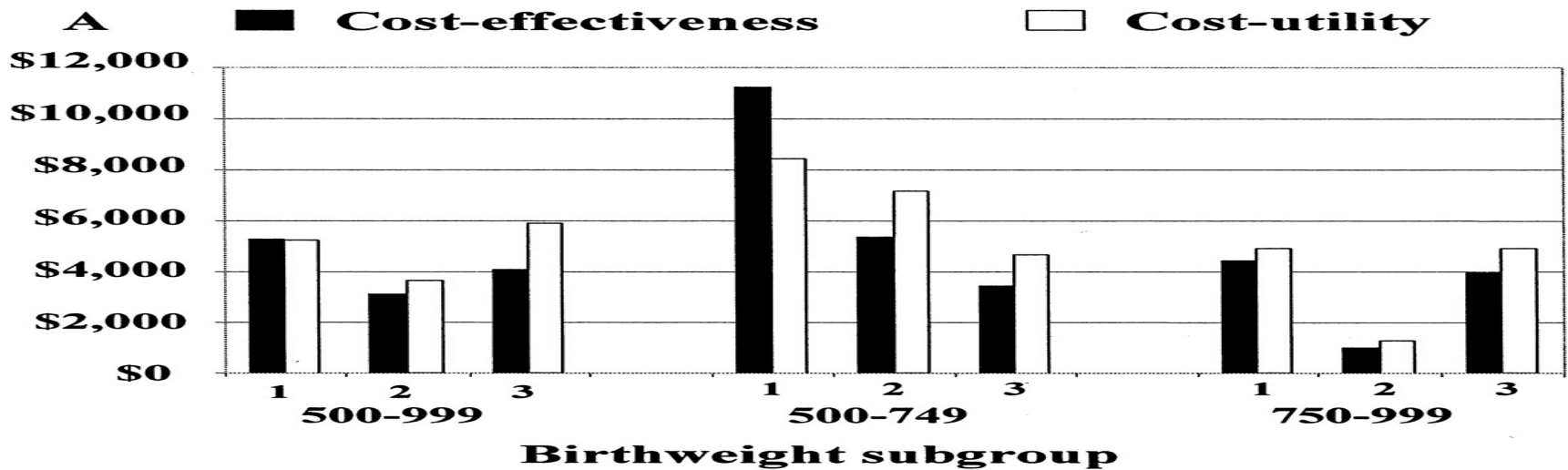
- If we ask parents whether they want us to try to save the lives of their 22 weekers, many would likely say yes.
- If we ask, we have to respect the answer.

Worry that it costs too
much.

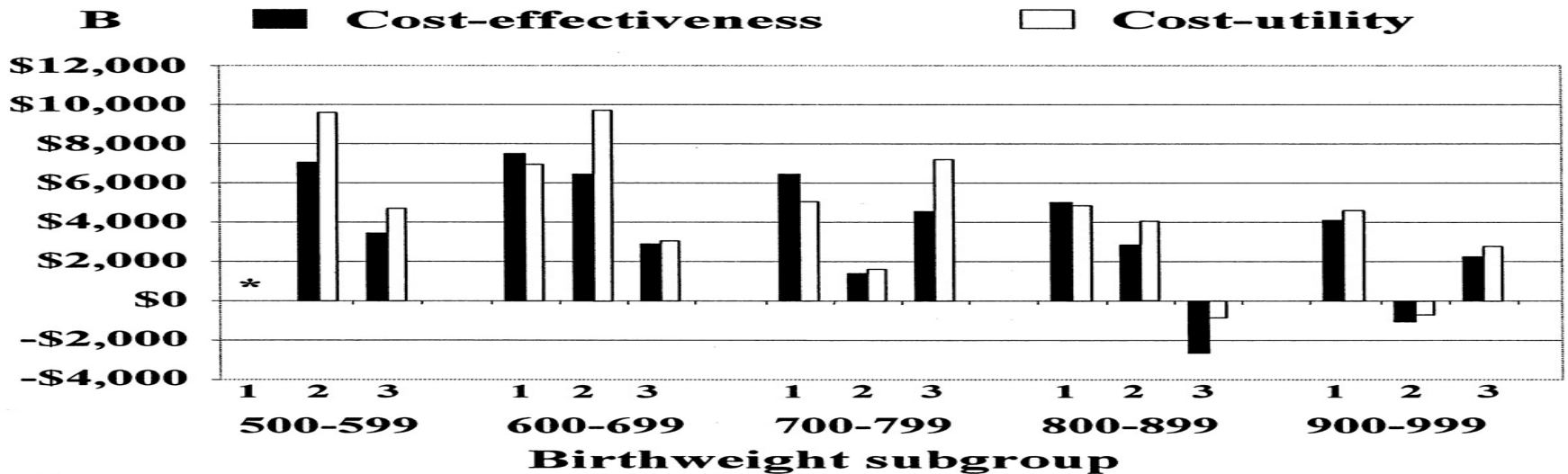
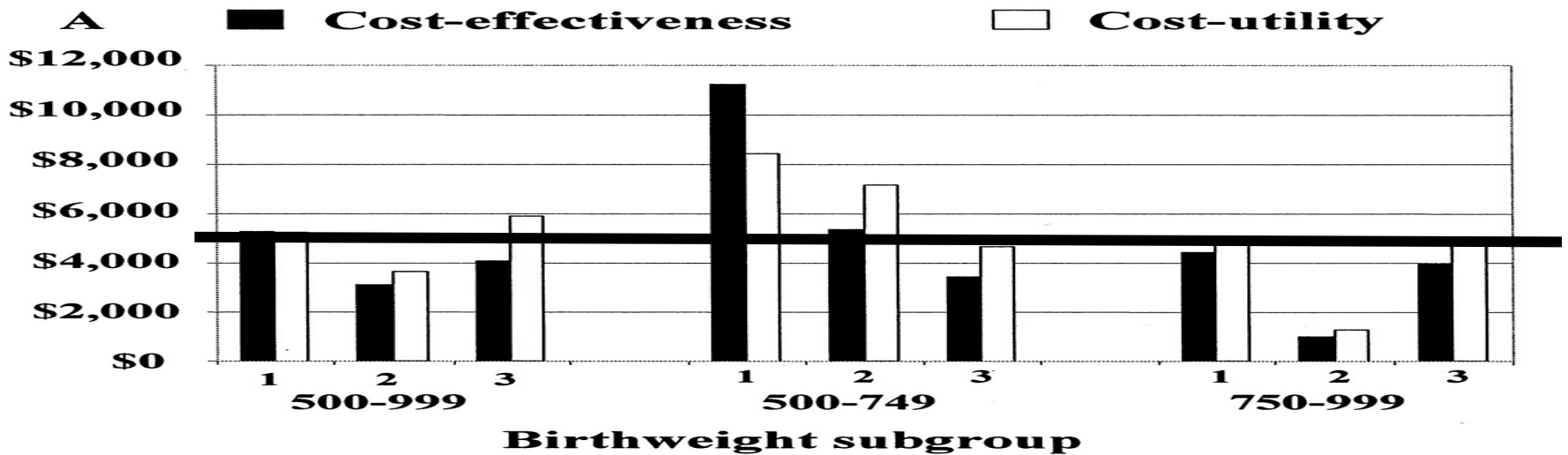
Another counter-intuitive fact

- NICU care is remarkably cost-effective

Cost-effectiveness and cost-utility ratios (1997 Australian dollars)



Cost-effectiveness and cost-utility ratios (1997 Australian dollars)



Cost effectiveness: costs per QALY for selected medical interventions

Intervention	Birthweight	
	<1,000	1,000–
Neonatal care	\$6,101	\$1,290
Compared with other interventions		
Prenatal care		
Influenza vaccination age <3 years		\$1,745
Neonatal care for all low-birthweight infants		3,726
Pap smear every 3 years, ages 20–74		17,000
Treatment of severe hypertension		17,000
Coronary artery bypass		\$33,600–\$48,300

For babies <1000gms, cost is about \$6000 per QALY

Cuttler and Meara, NBER, 1999

<http://www.nber.org/papers/w7390.pdf>

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Pap smears to prevent cervical cancer - \$17,000 per QALY

Cutler and Meara, NBER, 1999

<http://www.nber.org/papers/w7390.pdf>

Cost effectiveness: costs per QALY for selected medical interventions

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Cost effectiveness: costs per QALY for selected medical interventions

Intervention	Birthweight				All weights <2,500 g
	<1,000	1,000–1,500	1,500–2,500	>2,500	
Neonatal care	\$6,101	\$			
Compared with other interventions					
Prenatal care					
Influenza vaccination age <3 years					
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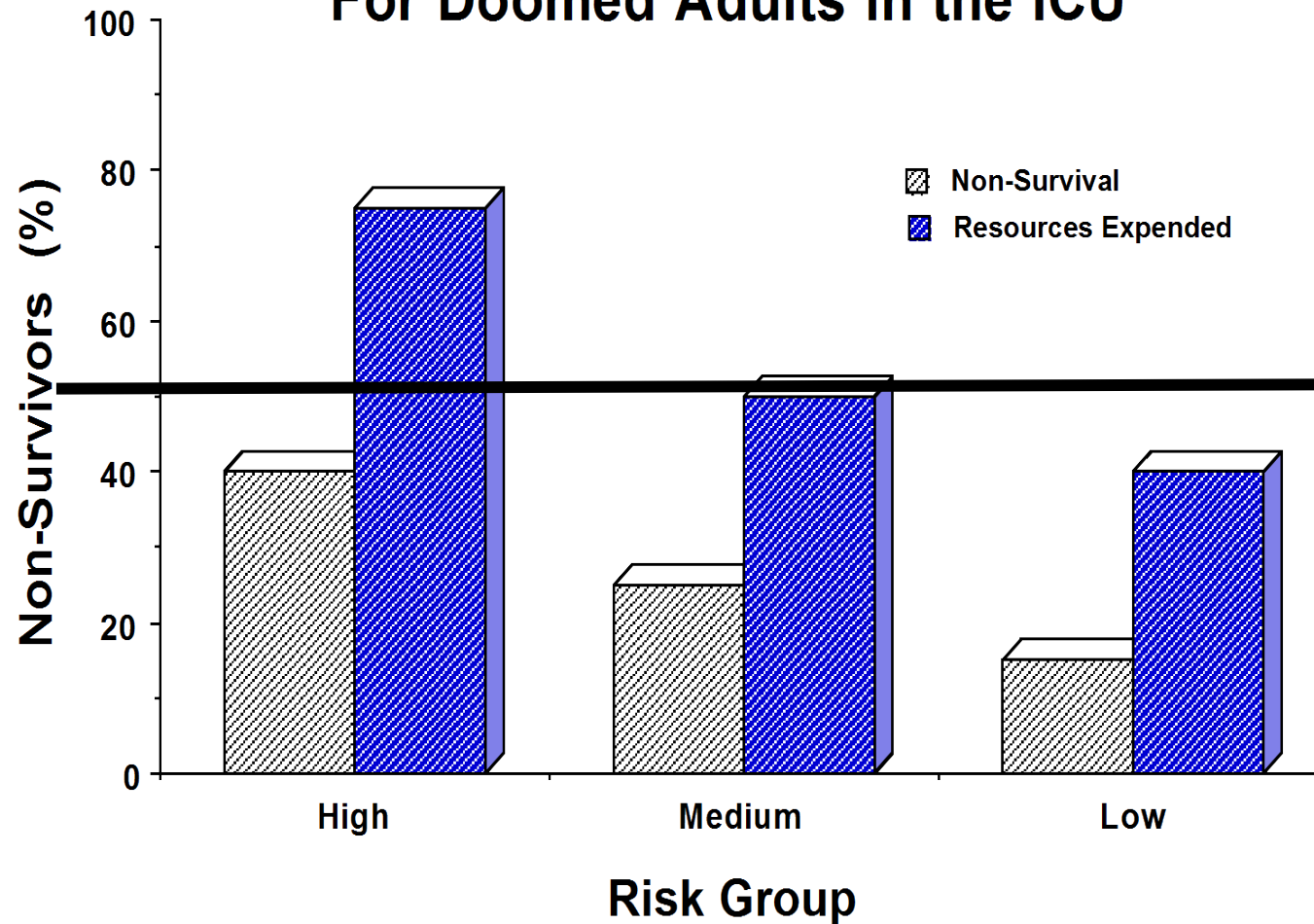
Coronary bypass surgery -- \$40K/QALY

Cutler and Meara, NBER, 1999

<http://www.nber.org/papers/w7390.pdf>

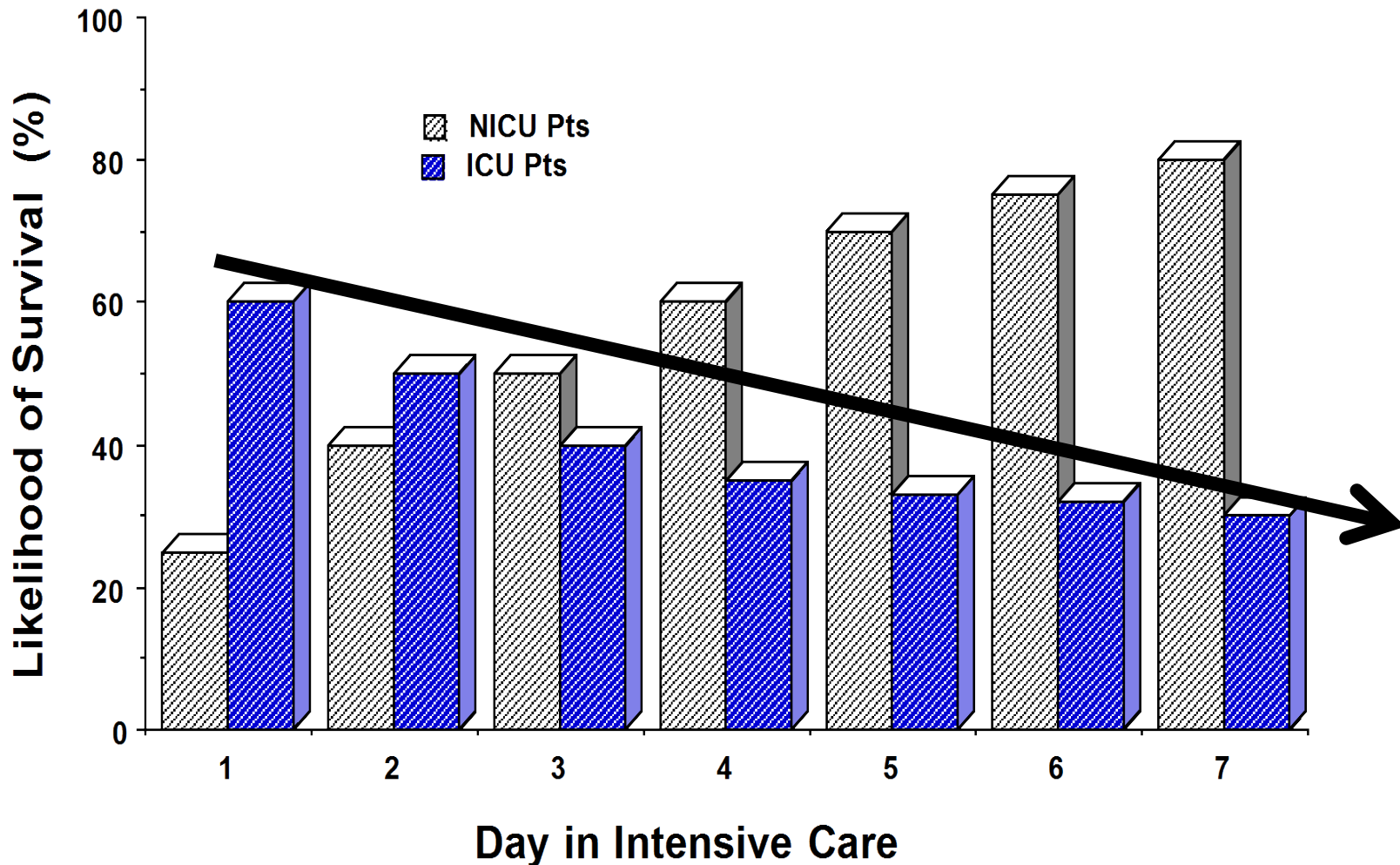
In adults, 50% of dollars are spent on patient who go on to die.

Non-Survival and Resources Expended For Doomed Adults in the ICU



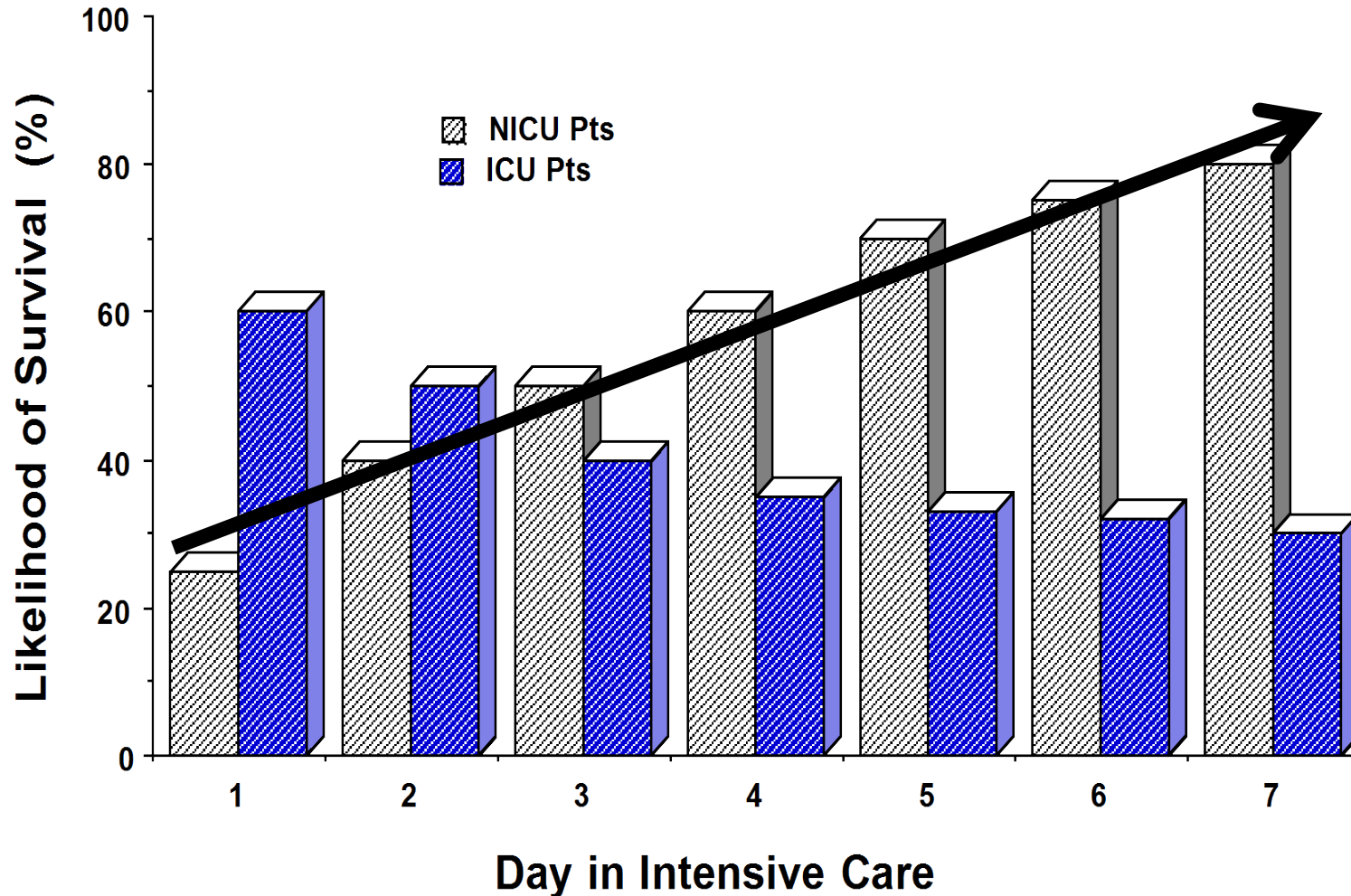
With each passing day in the MICU, the chances of survival go down

Likelihood of Survival With Each Passing Day NICU vs ICU Patients



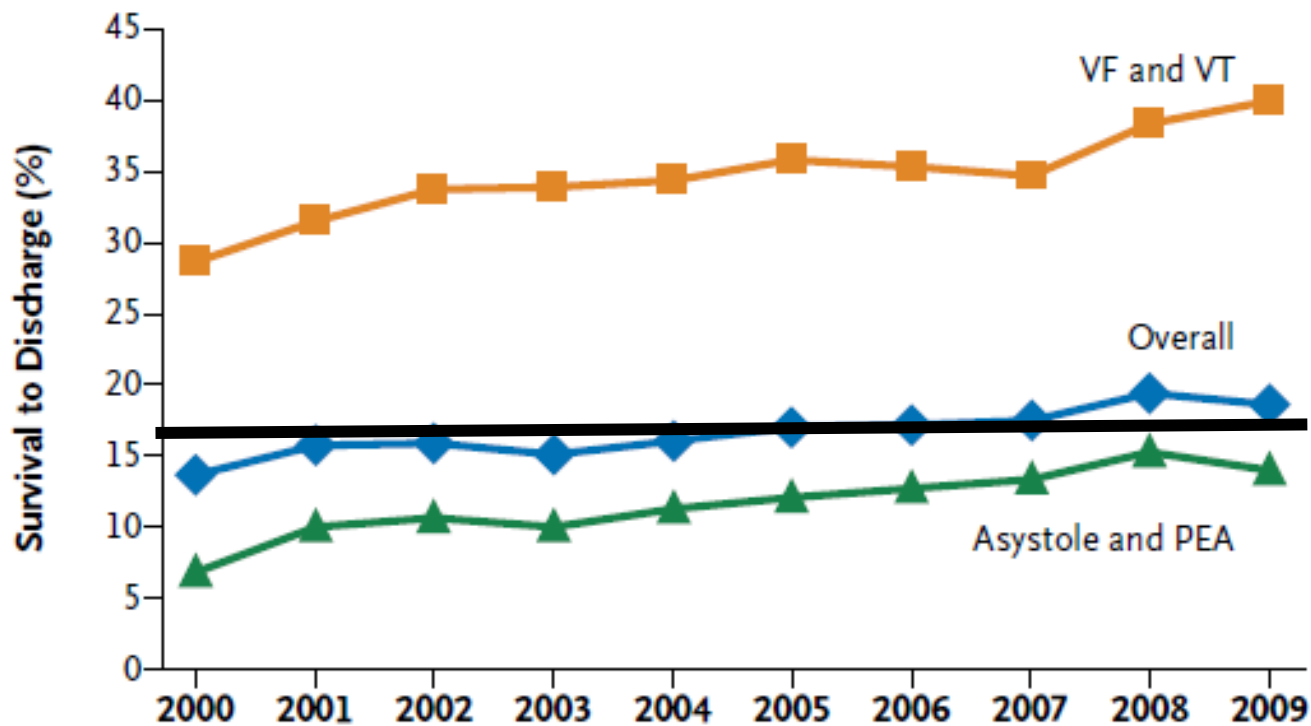
With each passing day in the NICU, the chances of survival go up

Likelihood of Survival With Each Passing Day NICU vs ICU Patients



Which is more cost-effective?

- Case #1: A baby is born at 22 weeks of gestation at 500 gms. Apgar scores of 3 and 6. He is intubated and given oxygen and his color and tone improve.
- Case #2: An 85 year old comes to the ER. He is diaphoretic, short of breath, with chest pain and ST elevation on EEG.



Overall survival after CPR in adults – 16%

Figure 2. Unadjusted Rates of Survival to Hospital Discharge by Calendar Year. Observed (crude) rates for survival to discharge are shown for the overall cohort and separately for shockable cardiac-arrest rhythms (ventricular fibrillation [VF] and pulseless ventricular tachycardia [VT]) and nonshockable cardiac-arrest rhythms (asystole and pulseless electrical activity [PEA]). $P < 0.001$ for trend for each survival curve.

Bottom Line on “the bottom line.”

- Remember “Sutton’s Law”: “Go where the money is!”



**“That’s Where
the Money is...”**

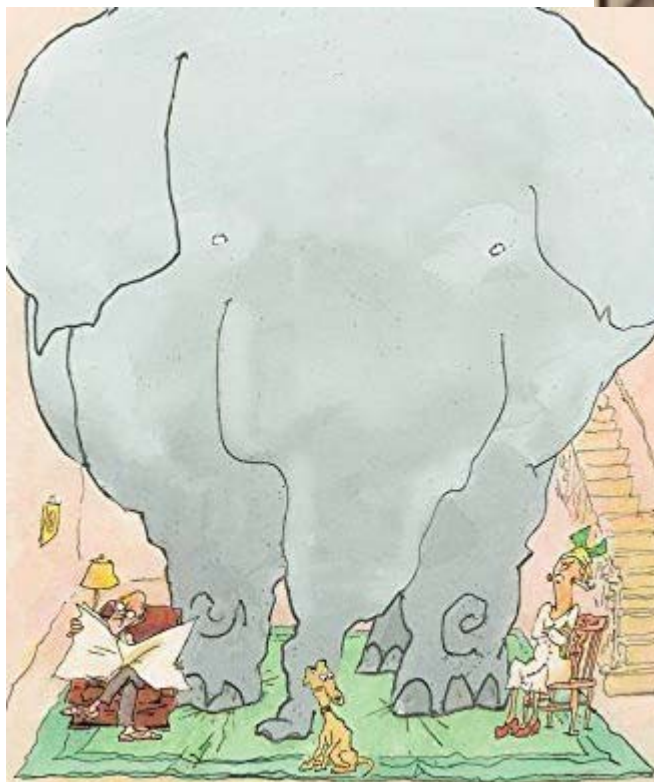
— *Willie Sutton*

Concern about maternal morbidity

Maternal morbidity

- C-sections at 22 weeks are difficult
- Higher maternal morbidity/mortality
- Can effect future reproductive possibilities
- Two responses:
 - Individualize decisions, with informed consent
 - Refuse to do C-sections, but try to save other babies.

Three elephants
in the room.



Elephants in the room

1. Institutional political culture
2. Abortion politics
3. Artificial placenta as a disruptive technology

Institutional political culture

- If we ask parents, many will want treatment
- We will need to be prepared to do it right
 - Collaboration between NICU and OB
 - Steroids routine after 20 weeks
 - Tiny baby units

Abortion politics

If 22 weekers are viable, can we permit abortion up until 24 weeks?

How many 22-23 weekers should we let die to preserve legal abortion?

If viability is morally relevant, then it should be based on facts.

*Preterm Babies
Can Be Viable
At Earlier Birth*

New York Times,
Front Page,
May 7, 2015

Amazing
Breakthrough in
Neonatal Intensive
Care!

*Preterm Babies
Can Be Viable
At Earlier Birth*

*Study Could Affect the
Debate on Abortion*

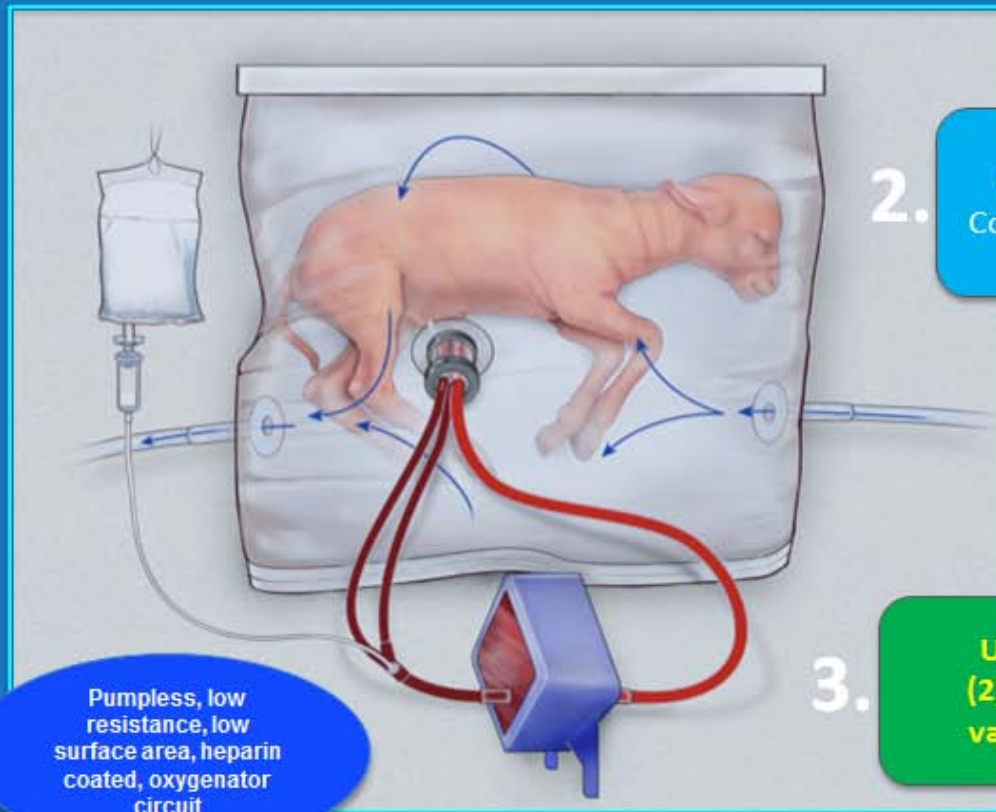
New York Times,
Front Page,
May 7, 2015

Late abortions

- Most late abortions are for fetal anomalies identified after 20 weeks.
- These circumstances are rare and quite different from those surrounding termination of pregnancy with a healthy fetus.

Babies born in Bio-bags.

Extracorporeal System for Physiologic Fetal Support – Three components



1.

Pumpless, low resistance, low surface area, heparin coated, oxygenator circuit

2.

Closed Biobag system, Continuous fluid exchange

3.

Umbilical Artery (2)/Umbilical vein vascular interface

Sheep fetal TPN, systemic antibiotics, PGE2, low heparin



(b) Representative lamb cannulated at 107 days of gestation and on day 4 of support. **(c)** The same lamb on day 28 of support illustrating somatic growth and maturation.



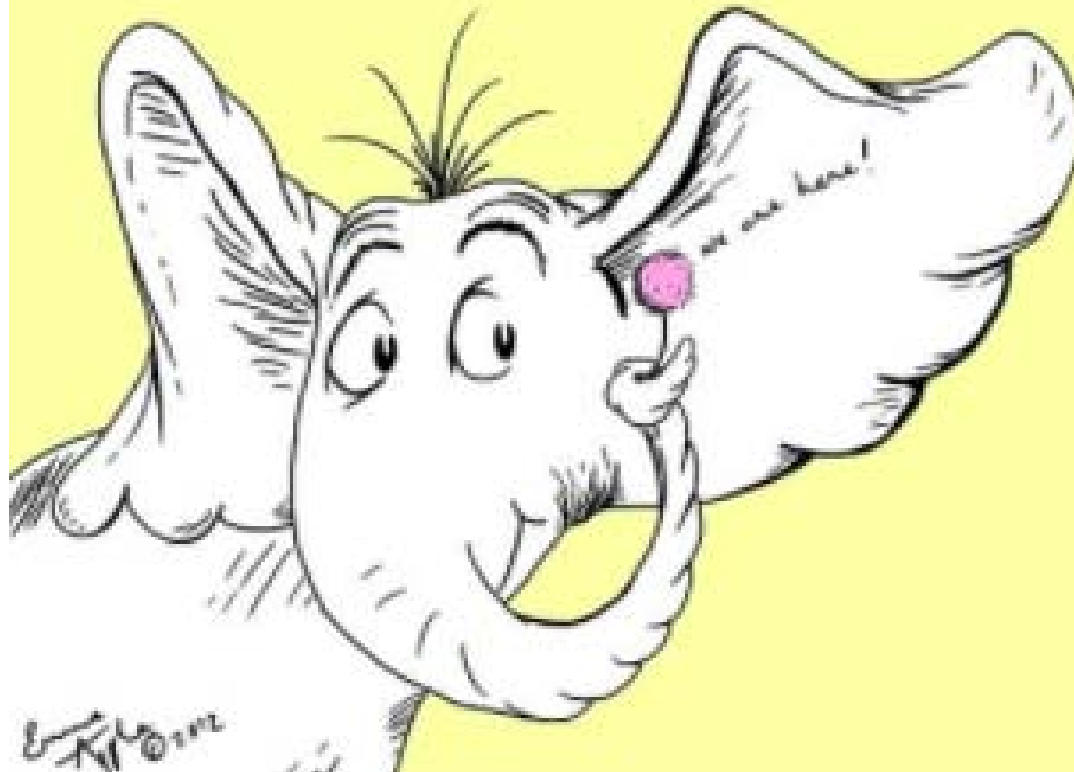
Researchers perfect an artificial womb that works as well as ewe do

Rania Sooner

Conclusion

A PERSON'S A PERSON,
NO MATTER HOW SMALL

Dr. Seuss



Conclusions

- Survival rates improving at 22 weeks.
- Non-treatment is self-fulfilling prophecy
- Many parents favor treatment
- Belongs in Zone of Parental Discretion
- Should be studied carefully
- Teamwork and institutional commitment.

Thanks!

