



## Should We Try to Save 22 Weekers?

Miami Neonatology 2019—43rd Annual International Conference

### Overview

Survival rates are improving for neonates born at  $\leq 22$  weeks through implementation of innovative active lifesaving treatment protocols. The most significant common denominator to improve the chance of survival is having an actual resuscitation plan in place. **John D. Lantos, MD**, discusses active treatment protocols, which require an institutional commitment with collaboration between NICUs and maternal fetal medicine specialists, steroids routine after 20 weeks of gestation, and Tiny Baby Units with expertise to provide the best possible outcomes. Dr. Lantos describes the need for continued clinical studies of supporting evidence for specific protocols that will continue to increase survival of the lowest gestational-age neonates.

### Target Audience

This activity was developed for neonatologists, pediatric physicians, nurses, nurse practitioners, dietitians, and other health care providers who have an interest in newborns, infants and toddlers.

### Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Recognize that survival rates for neonates born at 22 weeks are improving with better outcomes
- Describe the need and cost-effectiveness of active treatment protocols to improve survival rates for neonates born at  $\leq 22$ –24 weeks.

### Faculty

#### **John D. Lantos, MD**

Professor of Pediatrics  
University of Missouri – Kansas City  
Director, Children's Mercy Hospital Bioethics Center  
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This activity was released on February 7, 2020 and is eligible for credit through February 7, 2022.



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## Should We Try to Save 22 Weekers?

*Editor's Note: This is a transcript of a live presentation on November 11, 2019, at the Miami Neonatology International Conference. It has been edited and condensed for clarity.*



**John D. Lantos, MD:** Thirty years ago, 35 years ago, the President's Commission on Bioethics issued a report on life-sustaining treatment decisions for children. They had this 2-by-3 table [Slide 1],<sup>1</sup> and they talked about how doctors need to decide whether treatment [is] beneficial, futile, or somewhere in between—in the gray zone—and then about whether parents should have the last say on whether treatment should be provided. The real topic for today is whether treatment for 22 weekers belongs in this gray zone where outcomes are ambiguous or uncertain. The President's Commission and many bioethicists say in those situations, parents' preferences should determine whether treatment [is] offered, or whether it belongs in the futile category, in which case, we should not offer it.

Treatment Options for Seriously Ill Newborns — Physician's Assessment in Relation to Parent's Preference

Physician's Assessment of Treatment Options*	Parents Prefer to Accept Treatment**	Parents Prefer to Forego Treatment**
Clearly beneficial	Provide treatment	Provide treatment during review process††
Ambiguous or uncertain	Provide treatment	Forego treatment
Futile	Provide treatment unless provider declines to do so	Forego treatment

\* The assessment of the value to the infant of the treatments available will initially be by the attending physician. Both when this assessment is unclear and when the joint decision between parents and physician is to forego treatment, this assessment would be reviewed by intra-institutional mechanisms and possibly thereafter by court.

†† The choice made by the infant's parents or other duly authorized surrogate who has adequate decisionmaking capacity and has been adequately informed, based on their assessment of the infant's best interests.

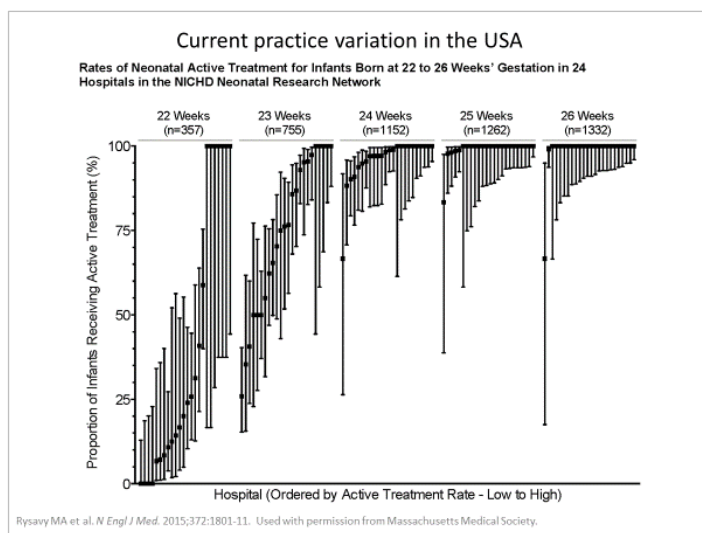
President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Deciding to Forego Life-Sustaining Treatment*. 1983.

Slide 1

### No Standard Approach to Active Treatment

You can get some evidence. This is one of the few areas where we actually have some data on what neonatologists collectively think about this treatment. This was data from the NICHD Neonatal

Research Network study [Slide 2] that was published in the *New England Journal of Medicine* a couple of years ago looking at which babies received active treatment by gestational age.<sup>2</sup> It's a sort of a complicated graph, but the Y-axis is the percent of babies who got active treatment, and then it's by gestational age: 22, 23, 24, 25, 26 [weeks]. Each dot represents one center and the bars are the standard error bars.



Slide 2

So, 24 to 26 weeks in these 24 hospitals, almost all babies at almost all centers received active treatment. At 23 weeks, some centers treated every single baby, but about two-thirds of centers seemed to personalize the decision, or to have variation in the decision. The range of babies who got active treatment went from 100 [percent] down to about 25%. The biggest variation was in the 22 weekers, where 5 hospitals didn't treat any babies born at 22 weeks. And remember, these are the elite hospitals in the Neonatal Research Network.<sup>3</sup> Seven hospitals treated every baby born at 22 weeks, and the rest of the hospitals were somewhere in the middle.

Collectively, it would seem doctors are uncertain about whether treatment for these babies is

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beneficial, futile, or somewhere in between. And it's pretty clear from that data that **in the United States today there is no standard approach to babies born at 22 weeks**. By that first graph from the President's Commission, one could conclude that when there is this sort of professional disagreement, parents' values should prevail. We should offer treatment, saying some people think it's a good idea, but we should be willing to forego treatment because many people think it's a bad idea.

What is the data that the people who think treatment ought to be provided used to say that such treatment is not futile? Well, in this same study from the Neonatal Research Network, overall survival for babies born at 22 weeks was just 5%, and some people say that's pretty good evidence of medical futility. However, if you looked at the **babies who got active treatment, the overall survival rate was 23%**. That looks a little bit better and gets you away from the idea that this treatment is absolutely futile.

Variation in Treatment and Outcomes in Preterm Infants

Table 2. Crude Outcomes by Gestational Age at Birth.<sup>o</sup>

Outcome	All Infants		Infants Who Received Active Treatment	
	Overall Rate <sup>‡</sup>	Hospital Rate <sup>‡</sup>	Overall Rate <sup>‡</sup>	Hospital Rate <sup>‡</sup>
22 Wk of gestation				
Survival	5.1 (3.2–7.9)	3.4 (0.0–10.6)	<b>23.1 (14.9–34.0)</b>	21.1 (0.0–50.0) <sup>§</sup>
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) <sup>§</sup>
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) <sup>§</sup>

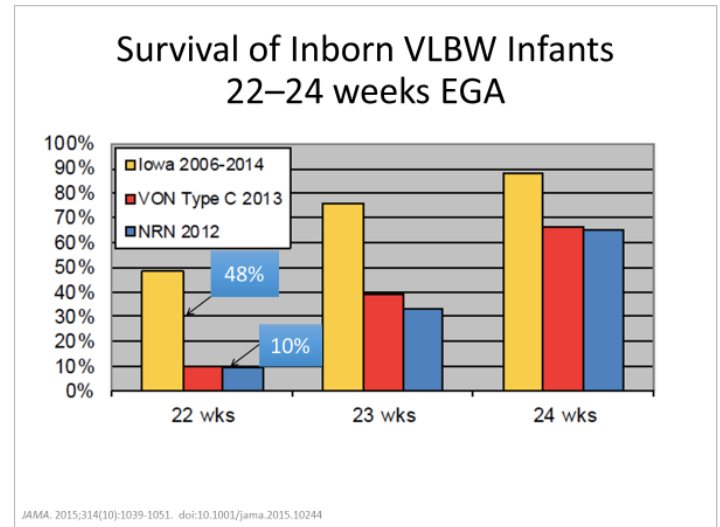
**Among infants who were treated, it was 23%, with one hospital reporting 34%**

Rysavy MA et al. *N Engl J Med*. 2015;372:1801-11.

### Slide 3

At one center, we just heard about a current outcomes [paper]—which I'll show you in a minute—from Iowa, but at the time that this study came out, Iowa was reporting 48% survival, [which is] vastly different from the rest of either the

Neonatal Research Network or the centers that report to Vermont Oxford Network, which are shown in those other 2 bars down here [Slide 4].<sup>4</sup>



### Slide 4

In a paper just published last month from the **Iowa group**,<sup>5</sup> they're now **reporting 70% survival for babies at 22 weeks, 82% at 23**, and most of the babies, as you can see in the column over there on the right [Slide 5], do not have severe neurodevelopmental impairment—but I'll get back to that in a minute.

Current survival rates in Iowa

EGA	Survival rates	% no/mild NDI
22 weeks –	12/20; 70%	55%
23 weeks –	41/50; 82%	68%
24 weeks –	70/79; 87%	79%
25 weeks –	89/99; 90%	73%

Watkins PL, et al. *J Pediatr*. 2020;217:52-58e1. doi:10.1016/j.jpeds.2019.08.028

### Slide 5

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### Proactive Protocols

How do they do it in Iowa? Again, I'm not a neonatologist, but it seems like there are some features of the Iowa program that have not been studied, but that the people there seem to believe are important. The first is collaboration with their maternal fetal medicine specialists so that all women within labor and impending delivery start getting antenatal steroids starting around 20 or 21 weeks. There's discussion about C-section, if indicated, even at these low gestational ages. There's parental informed consent for NICU treatment. They have what they call a Golden Hour Protocol, which I'll show you in a minute, and then there's a Tiny Baby Unit within the NICU, where all the health professionals spend their entire professional lives caring for these very tiny babies.

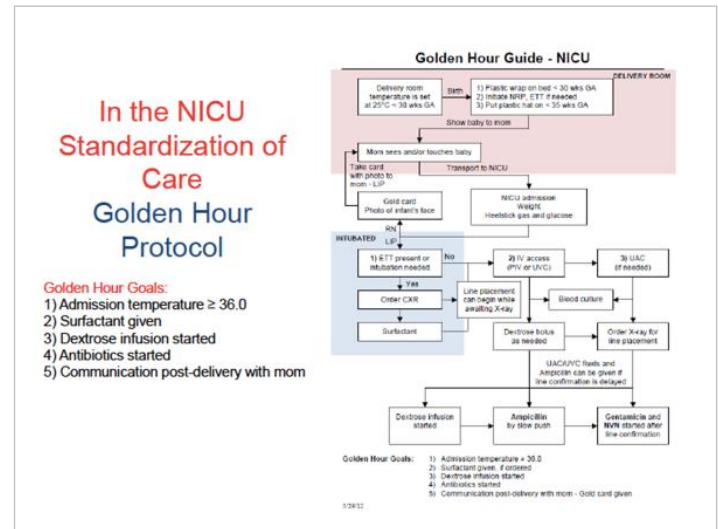
#### A number of innovations

- Collaboration with MFM
  - All women get antenatal steroids, starting at 21-22 weeks.
    - Reduces mortality, IVH, and severe NDI.
  - 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 pCO<sub>2</sub>.

#### Slide 6

Again, complicated slides [Slides 7 and 8]. The details for my purposes are less important than the fact that there is a protocol. There is proactive and anticipatory planning for the treatment of these babies. There is attentiveness to psychosocial features. They take pictures of the baby. The mom gets to see and touch the baby. They start lines. They give antibiotics. They do exquisite temperature control. They have guidelines for CO<sub>2</sub>

management, and again, I'm not focusing on the details of the medical management, because my point here is that we don't know which aspects of this treatment work, but **what seems to work is having a plan**, giving some thought to what to do, and [to] not be in the situation that many doctors and many hospitals are in when a baby is born at 22 weeks, where people go, "Oh, dear, what are we going to do? We don't have a plan. Should we resuscitate? Should we not? Should we talk to the parents? How do we deal with it?" Having a plan seems to help.



#### Slide 7

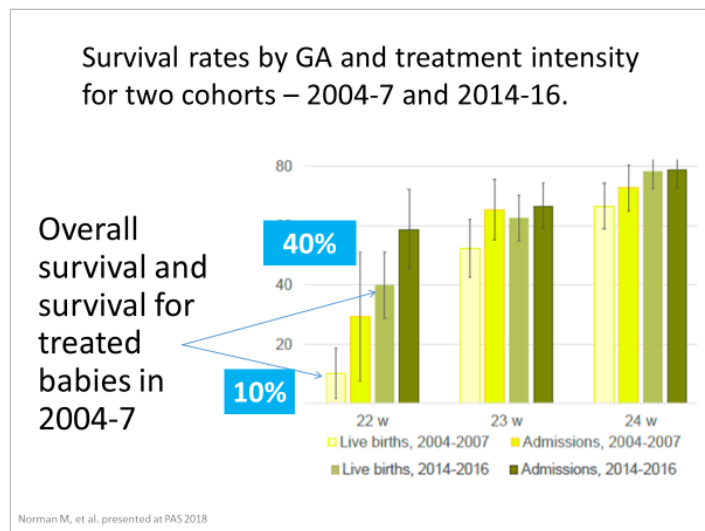
### Standardized Ventilator Goals

- 1) 1<sup>st</sup> 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 pCO<sub>2</sub> 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

#### Slide 8

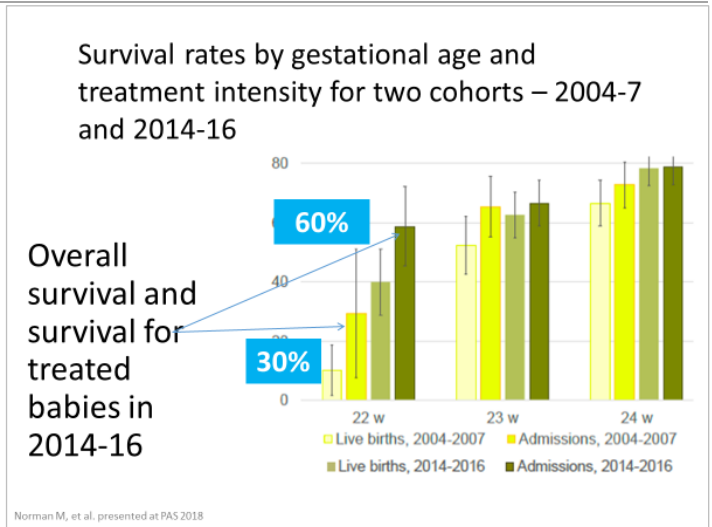
## Should We Try to Save 22 Weekers?

The whole country of Sweden reports similar results. Here is a complicated graph [Slide 9], but for my purposes, just look at these 4 bars, which are babies born at 22 weeks. The first 2 are in the period 2004–2007, the third and fourth are in a later period. From 2004–2007, overall survival was 10%, but among the babies who were admitted to the NICU, just like in the NICHD study, many more survived.



Slide 9

Take home lesson: if you have a tiny baby and don't admit them to the NICU, they're going to die. If you do, their outcomes are much better, and **as of 2016, survival rates in the whole country of Sweden for babies who were born at 22 weeks and admitted to neonatal intensive care units is now 60%.**<sup>6</sup>



Slide 10

### Survival Rates Increase

The common element, as I say, is not any particular type of treatment. Other centers (eg, Cologne, Germany; the whole country of Japan) report increasing survival rates at this low gestational age. Everybody does things differently. In Iowa, they use jet ventilation from the first breath. In Cologne, they give less invasive surfactant and put babies on CPAP. We don't know what works, but it does seem that **having a protocol is better than not having one.**

Here's what makes this really interesting for me as a bioethicist rather than as a neonatologist, and I would view these as very promising preliminary results. Here's a disease, being born at 22 weeks, which previously had been thought of as almost universally fatal. And now some centers are starting to report that they're getting very promising early preliminary results. And in most situations in medicine, when that happens, people say, "Wow, let's find out what they're doing. Let's go study it. Let's try it. Saving people's lives is better than letting them die. Here's some promising results. Let's do it." But what seems to be happening with babies at 22 weeks, instead, is most other centers don't want to try it. The NICHD doesn't seem to want to study

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it, and professional societies even misrepresent the data in developing guidelines for such treatment.

### Not Treating Is A Great Mystery

Here's a statement that came from the American College of Obstetrics and Gynecology [ACOG] Society of Maternal Fetal Medicine<sup>7</sup> after the Rysavy study, the *New England Journal of Medicine* study, which I just showed you, citing that study in making the claim that delivery before 23 weeks results in neonatal death, irrespective of newborn resuscitation, even though 5% survived when there was no resuscitation, 25% when there was, and significant morbidity among survivors is universal. The study showed that 60% of survivors didn't have severe impairment. So, how you can write a statement citing a study that has data that contradicts exactly what you're saying is mind boggling to me. It's a mystery. Is there any other situation in medicine where patients have a disease that's almost uniformly fatal? Some centers report 40%, 50%, or now 70% survival. Other centers don't offer treatment. Some say it's unethical to offer treatment, and many bioethicists support them. It's hard to think of one. That's really weird.

#### 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;
- Other centers do not offer treatment;
- Some even say that it is unethical to offer treatment;
- And many bioethicists support them!?

Slide 11

But I know what you're thinking. All the survivors must be severely disabled, right? Survival rates are only one aspect of this, and that's just wrong. Here were the outcomes for babies in the 24 centers of the Neonatal Research Network. Among the babies who were treated, as I said, at 22 weeks, 23% survived. About one-third of the survivors had severe impairment. That means **two-thirds of the survivors didn't have severe impairment**. The data are a little complicated, though, because people report results using different denominators.

Again, the question is, do you report outcomes for all live births, or do you report outcomes for live births where people actually admitted them and treated them in neonatal intensive care units? And then if you report the results, what outcome do you use?

#### NDI at 2 years for babies born at 22-24 weeks, who received treatment, NICHD (2006-11)

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

#### Slide 12

Often in neonatal studies, and for example, as I'll show you in a minute, in the Neonatal Research Network outcomes calculator, people use a combined variable of death or severe neurodevelopmental impairment [NDI] as sort of a total lump sum of bad; but, you can also report overall survival without severe NDI or rates of neurodevelopmental impairment among survivors, and those yield very different results.

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### Data are complicated because....

- People report results using different denominators
  - Outcomes for all live births
  - Outcomes for babies who received active treatment
- What are the important outcomes?
  - Combined variable of “Death or NDI”
  - Overall survival without severe NDI
  - Rates of NDI among survivors

How data get reported: NICHD “Neonatal Calculator”  
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

These numbers combine “death” and “severe disability.”  
So to count as surviving unimpaired you had to  
a) survive; and b) be unimpaired.

[http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/Pages/epbo\\_case.aspx](http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/Pages/epbo_case.aspx)

### Slide 13

Here's an example [Slide 14]. If you go to the website for the Neonatal Research Network outcome calculator,<sup>8</sup> and you put in 500 g, 23 week singleton (they don't go down to 22 weeks), and you put in boys and girls, and steroids or not steroids, you get this result for 23 week singletons who survive unimpaired: 5% for boys whose moms didn't get steroids, going up to 18% for girls whose moms did get steroids.

A couple of things to notice about this. **Girls whose moms get steroids do 4 times better than boys whose moms didn't**, so to say, "What's the survival rate at 23 weeks?" is not an adequate question. That was really the point of the study that published these data.

### Slide 14

But look what happens, if instead of asking how many 500 g and 23 week singletons survive unimpaired, you ask a slightly different question? How many 500 g, 23 week singletons who survive are unimpaired? This is using the same dataset [Slide 15], although this data is not available on the Neonatal Research Network neonatal calculator as a number. You have to calculate it yourself by subtracting out all the babies who died, and then looking at the rates of neurodevelopmental impairment among survivors. If you think of this as a problem for informed consent, and you want to give parents accurate statistics on outcomes, which statistic should you give them?



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How many 500g, 23 week singletons who survive are unimpaired?

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

Very different if the statistic is “disability among survivors,” rather than “overall survival without disability.”

Simple way to think about this

- Imagine 100 babies
  - 90 die
  - Among survivors, 3 have severe NDI
- Two claims are true
  - 93% of babies (93/100) either died or had severe NDI
  - 70% of survivors (7/10) did not have severe NDI

Slide 15

### Presenting the Data

Here’s a way to think about this just as a simple thought experiment [Slide 16]. Imagine 100 babies, 90 of them die, so 90% mortality, and among the survivors, 3 have severe neurodevelopmental impairment. You can say 2 totally true, totally factual things about this. One is that 93% of babies born like this either die or have severe neurodevelopmental impairment, or you can say 70% of survivors have no neurodevelopmental impairment. Both are true. It might lead to a very different decision by both doctors and parents.

Another quirk. Studies usually don’t account for nontreatment, substandard treatment, or decisions to withdraw life support. Here’s an example from the EPICure study [Slide 17], the big study in the UK of outcomes.<sup>9</sup> Among 22 weekers,

Slide 16

they had 152 live births. Six percent of the moms got steroids. Fewer than half were delivered in a tertiary care center. Only about a quarter got active treatment, and of those, only about half made it to the NICU. Overall survival, they reported, was 3 out of 152 babies or 1.5%. That sucks, and anybody who reads that would say there’s no point in offering this treatment, even if one-third survived without major morbidity.

But this would be a little like reporting outcomes for leukemia, where you said these babies were treated by general practitioners in their offices with vitamin C, and they didn’t do very well, **if you don’t give a baby state-of-the-art treatment when they have a severe life-threatening disease, that’s not a good measure of whether the treatment is effective.** It’s a measure of whether you’re providing the treatment. Bottom line is in all of these studies, most of the babies who survive do pretty well, but you may not know it from the way the data are usually reported.

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EPIcure: Among 22 weekers (n=152)

- 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%
- 1/3 survived without major morbidity.

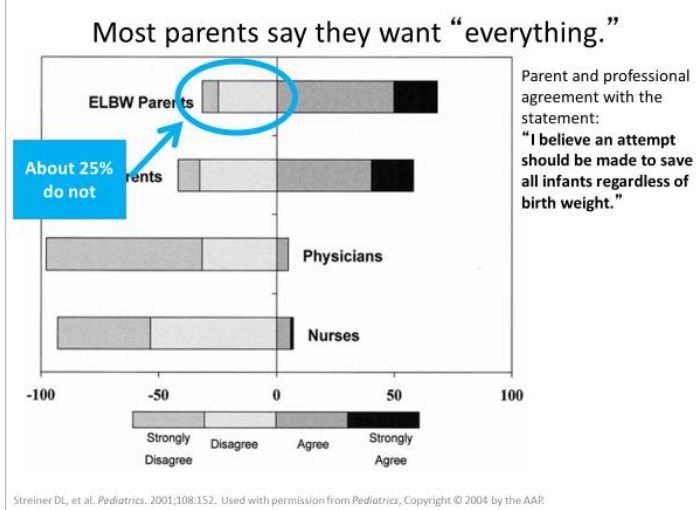
Costloe KL, et al. *BMJ*. 2012;345:e7976.

Slide 17

### Clinicians' and Parent's Preference

What do parents want—that is if we think this belongs in the zone of shared decision making where parental preferences should determine the outcome—what do you think parents would say if you gave them accurate outcome statistics? Well, we know from some studies, and actually there are a number of studies comparing the attitudes of health professionals with the attitudes of parents, and most look something like this [Slide 18].

This was a study where parents of extremely low-birth-weight babies, control parents, doctors, and nurses who worked in the NICU were asked, "Do you agree or disagree with the statement: 'I believe an attempt should be made to save all infants regardless of birth weight?'" Most doctors and nurses strongly disagreed with that statement. Most parents agreed or strongly agreed with that statement. Although parents are much more variable than doctors and nurses— about 25% did not agree with that statement. So, the only way to know what a particular parent would think would be to sit down, talk about the outcomes, and ask them. Most parents say we should try to save babies at all costs and are less troubled by disabilities than health professionals.



Slide 18

This was a study that asked both health professionals and parents to rank these 3 states.<sup>10</sup> "Which do you think is worse: for a baby to be dead, [or] for a baby to survive with severe global impairment," which in the study they defined as you can see, "or to survive with moderate global impairment?" So, think in your mind how you would rank those now. Which is worse: death or severe global impairment? Most doctors and nurses say severe global impairment is worse than death. Many fewer parents say that.

More likely to rank "death" lower than "severe global impairment"

Death.

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

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

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

Slide 19

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### Is severe disability worse than death?

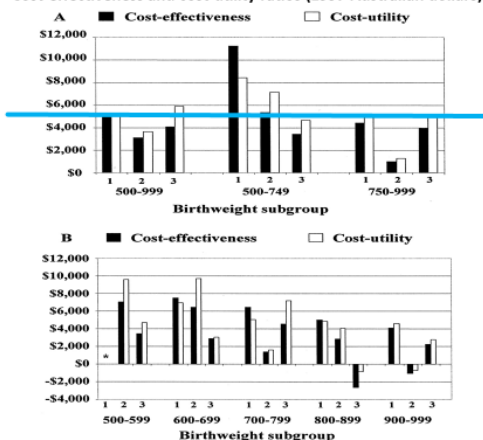
- Doctors and nurses – 55%
- Mothers of term babies – 40%
- Parents of preemies – 25%

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

#### Slide 20

We can say, maybe they just don't understand. That may be true, although these studies have now been done prior to birth, after birth, a year after birth, 10 years after birth, and Saroj Saigal, [MD,] now has a book out 30 years after birth, and it seems that at the very least these preferences are durable. Whether they're durable and just simply wrong is the sort of question that only a philosopher could answer, but it seems that if we believe parental preferences should guide treatment, we should recognize our own biases about the value of life with severe disability, or our own beliefs may not be the same as parents.

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



Doyle LW, et al. *Pediatrics*. 2004;113:510-514. Used with permission from *Pediatrics*, Copyright © 2004 by the AAP.

#### Slide 21

### Cost Effectiveness for Policy Makers

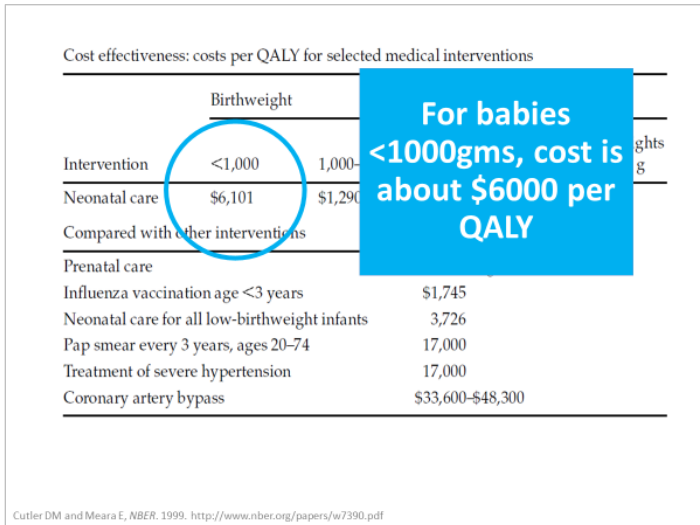
One last concern people have about this care is that it may cost too much. Again, this is simply a worry that the data don't confirm, at least not by standard measures of medical cost-effectiveness. Here's the data that's been gathered, and this hasn't specifically been done for 22 weekers. The epidemiology and the reason why costs are as they are, I think, would apply even more to 22 weekers than to bigger or older babies.

This was a study of cost-effectiveness from Lex Doyle's [MD, MS, MSc, FRACP] group in Australia [Slide 22].<sup>11</sup> The key finding, the details on this when they broke it down by different birth weight increments, gestational age increments, different measures of cost-effectiveness, however you did it... treatment of tiny babies comes out somewhere between \$5,000 and \$10,000 per quality-adjusted life-year dollars per QALY.

A study from economists at Harvard, who weren't even involved in neonatal care, got about the same number, \$6,000 per quality-adjusted life-year. Compare that to what the Harvard economists calculated was the value of things like pap smears, at \$17,000 per QALY, or treatment of hypertension

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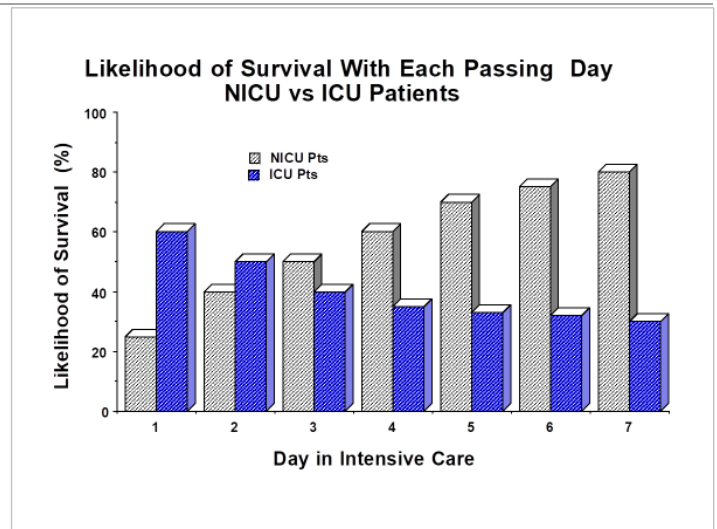
at \$17,000, or bypass surgery, which is \$40,000 per QALY.



### Slide 22

By whatever measure you use, **the treatment of tiny babies looks to be remarkably cost-effective, much more cost-effective than adult intensive care.**

Old people in ICUs don't do so well. The cost-effectiveness of adult intensive care is really bad, and the reasons for that are shown in this slide [Slide 23].<sup>12</sup> This is a graph that shows ICU patients and NICU patients. This is the chance of survival with each passing day that you're in the unit. If a baby is in the unit on day one, and this baby is under 750 g, 15 years ago, chances of survival were low, but with each passing day that a baby [is] in the NICU, the chances of them surviving goes up. Most babies who die, die quickly. If you're old, and you're in the ICU, and you're on a ventilator, with each passing day, your chance of getting out of the ICU alive goes down.



### Slide 23

The net result is most dollars spent on old people in ICUs are spent on people who are going to die. **Most dollars spent on babies in the NICU are spent on people who are going to survive.** So, if you're concerned about cost-effectiveness, or if you're talking to policymakers who are, you should present them data like this [Slide 24]. If you look at a 22 weeker with Apgars of 3 and 6 compared to an 85-year-old who comes to the ER in the middle of an MI [myocardial infarction], whose survival rate at best is about 15%, and then tell them that in Iowa for the 22 weekers, you're getting 70% survival.

#### 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.

### Slide 24

## Should We Try to Save 22 Weekers?

For policymakers, the key lesson is Sutton's law. Some of you may know the famous American bank robber, Willie Sutton. When he was asked, "Why do you rob banks?" He said, "Because that's where the money is." If you're going to do cost-effectiveness, go where the money is.

A modest proposal would be to evaluate treatment for 22 weekers the way we evaluate every other treatment in medicine. That is, **if people are starting to get promising results, try to figure out what's working and emulate it.** Be prepared to treat these babies if you're going to develop a program. When deciding who to resuscitate, listen to the parents, examine the patient, and make individualized decisions based on the best data and the best clinical judgment.

### A modest proposal

- Evaluate treatment for 22 weekers and figure out what works.
- Be prepared for these babies
- In deciding who to resuscitate,
  - Listen to the parents
  - Examine the patient
  - Make individualized decisions

Slide 25

Let me just finish by saying there are a few elephants in the room in talking about this: institutional culture and abortion politics, and then the artificial placenta as a disruptive technology.

### Institutional Political Culture

If you're going to ask parents, and consider this to be a decision that's in the domain of optional treatment, then you have to have a program in place to provide the best available treatment, and if

antenatal steroids are part of that, that requires collaboration with your maternal fetal medicine colleagues, because to offer parents treatment but not give them the treatment that's going to give the best possible outcomes is, I think, unprofessional and sort of a cruel charade. If you're going to do this, it requires an institutional commitment with collaboration between NICUs and OB, steroids routine after 20 weeks of gestation, and Tiny Baby Units in the NICU that have expertise in providing such care.

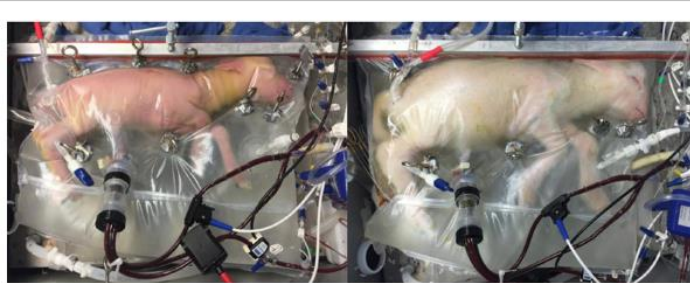
The second elephant in the room here is abortion politics. This may be more relevant in the United States than in other countries, but the Roe v Wade framework says babies are not viable until the end of the second trimester, which is 24 weeks. If babies are surviving at 22 weeks, that throws that whole framework into question, although it asks the question the wrong way. It doesn't say, "Are babies viable at earlier gestational ages?" Some people say we shouldn't save babies at earlier gestational ages because otherwise it will restrict abortion access.

As an example of this in popular culture, when the Rysavy paper was published in the *New England Journal of Medicine*, *The New York Times* wrote an article about it. Their headline was "Preterm Babies Can Be Viable At Earlier Birth,"<sup>13</sup> but their subheadline was not as I think it should have been, "This is an amazing breakthrough in neonatal intensive care." Instead, their subheadline was, "Study could affect the debate on abortion."

Final elephant in the room: babies born in biobags. Most of you have probably seen these experiments that are being done at the Children's Hospital of Philadelphia, so far just on sheep [Slide 26]. They take the sheep at the equivalent of 22 or 23 weeks gestational age, anesthetize the mom, do a C-section, immediately put in UV and UA lines and essentially put the fetal lamb in a bag of amniotic fluid, use the fetal heart as the pump, so it's like an ECMO [extracorporeal membrane oxygenation]

## Should We Try to Save 22 Weekers?

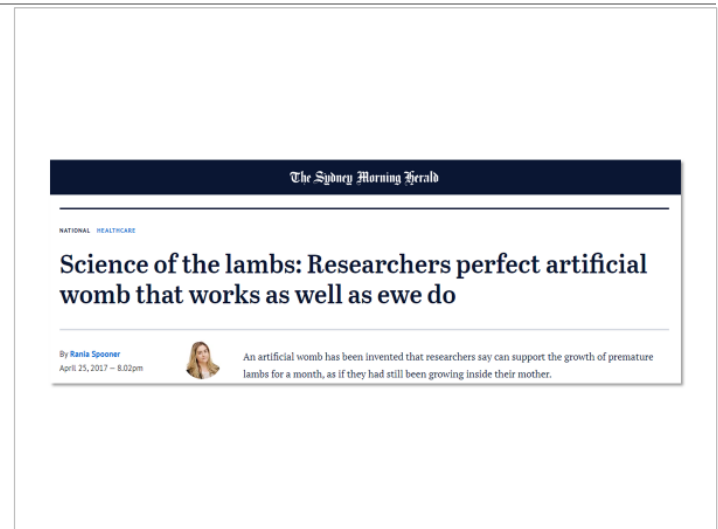
circuit without an ECMO pump. They can put nutrients in through the circuit. They grow these lambs up from the equivalent of 23 weeks to the equivalent of 32 weeks. Then for delivery, you just open the Ziploc bag and the lambs go scampering out into the field looking happy. It's generated some great headlines like this one [Slide 27].<sup>14</sup>



(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.

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Slide 26



Slide 27

**Conclusions.** Survival rates [are] improving. Nontreatment is a self-fulfilling prophecy. Most parents favor treatment. Why not study it? Find out what works. With parental permission try to save more babies.

### Abbreviations

<b>Apgar</b>	<b>A</b> ppearance, <b>P</b> ulse, <b>G</b> rimace, <b>A</b> ctivity, and <b>R</b> espiration	<b>NDI</b>	Neurodevelopment Impairment
<b>ECMO</b>	extracorporeal membrane oxygenation circuit	<b>NICHD</b>	National Institute of Child Health and Human Development
<b>MFM</b>	maternal fetal medicine	<b>QALY</b>	quality-adjusted life-year

1. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Deciding to Forego Life-Sustaining Treatment*. Library of Congress. 1983. Available at [https://repository.library.georgetown.edu/bitstream/handle/10822/559344/deciding\\_to\\_forego\\_tx.pdf](https://repository.library.georgetown.edu/bitstream/handle/10822/559344/deciding_to_forego_tx.pdf)
2. Rysavy MA, Li L, Bell EF, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. *N Engl J Med*. 2015;372(19):1801-11. doi:10.1056/NEJMoa1410689
3. <https://neonatal.rti.org>
4. Stoll BJ, Hansen NI, Bell EF, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. *JAMA*. 2015;314(10):1039-51. doi:10.1001/jama.2015.10244
5. Watkins PL, Dagle JM, Bell EF, Colaizy TT. Outcomes at 18 to 22 months of corrected age for infants born at 22 to 25 weeks of gestation in a center practicing active management. *J Pediatr*. 2019. pii: S0022-3476(19)31086-8. doi:10.1016/j.jpeds.2019.08.028

## Should We Try to Save 22 Weekers?

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6. Domellöf M, Jonsson B. The Swedish approach to management of extreme prematurity at the borderline of viability: A historical and ethical perspective. *Pediatrics*. 2018;142(Suppl 1):S533-S538. doi:10.1542/peds.2018-0478C
7. <https://www.acog.org/Clinical-Guidance-and-Publications/Obstetric-Care-Consensus-Series/Perivable-Birth?IsMobileSet=false>
8. <https://neonatal.rti.org/index.cfm?fuseaction=OTEstimator.EstimatorDE>
9. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short-term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). *BMJ*. 2012;345:e7976. doi:10.1136/bmj.e7976
10. Streiner DL, Saigal S, Burrows E, Stoskopf B, Rosenbaum P. Attitudes of parents and health care professionals toward active treatment of extremely premature infants. *Pediatrics*. 2001;108(1):152-7.
11. Doyle LW; Victorian Infant Collaborative Study Group. Evaluation of neonatal intensive care for extremely low birth weight infants in Victoria over two decades: II. Efficiency. *Pediatrics*. 2004;113(3 Pt 1):510-4.
12. Cutler D, Meara E. The technology of birth: Is it worth it? Paper presented at National Bureau of Economic Research conference on Frontiers in Health Policies Research. Cambridge, MA. October 1999. Available at <https://www.nber.org/papers/w7390.pdf>. Accessed January 6, 2020.
13. Schmeck HM Jr. Study finds premature babies are surviving at earlier ages. *The New York Times*. March 16, 1975. Available at <https://www.nytimes.com/1975/03/16/archives/study-finds-premature-babies-are-surviving-at-earlier-ages.html>.  
Follow-up article, citing NEJM Rysavy 2015:  
Belluck P. Premature babies may survive at 22 weeks if treated, study finds. *The New York Times*. May 6, 2015. Available at <https://www.nytimes.com/2015/05/07/health/premature-babies-22-weeks-viability-study.html>.
14. Spooner R. Science of the lambs: Researchers perfect artificial womb that works as well as ewe do. *The Sydney Morning Herald*. Posted April 25, 2017. Available at <https://www.smh.com.au/healthcare/science-of-the-lambs-researchers-perfect-artificial-womb-that-works-as-well-as-ewe-do-20170425-gvrw5v.html>.