The Late Preterm Infant

Marvin L. Wang, MD

MassGeneral Hospital for Children


CelebrityPicturesArchive.com

Background

- Definition - 34-36 6/7 weeks
- Now called “Late-preterm infant”
- Premature infants=12.3% of US births (<37 wks)
- 74% of all preterm births were late-preterm (342,234 of 394,996 singleton births)

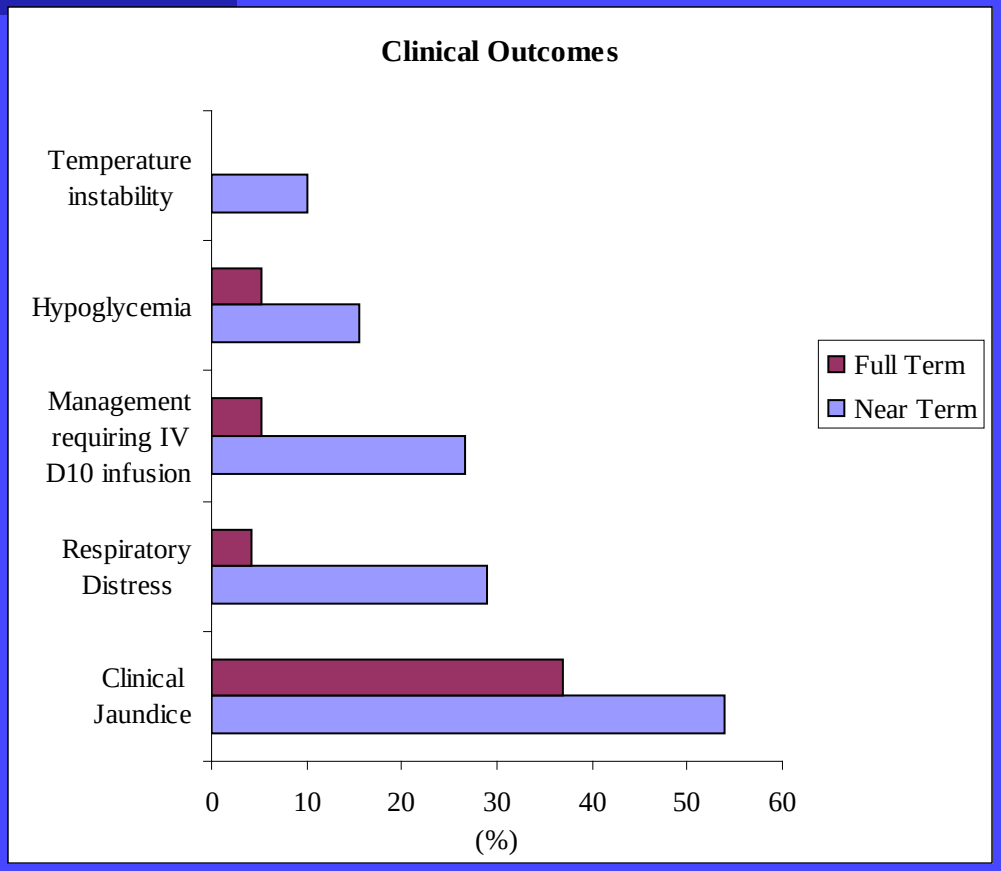
The study itself

- This study- uses 35-36 6/7 weeks gestational age
- Obstetrical Electronic Medical Record
  - 3 years worth of babies-7474 babies
  - Randomly take about 120 from near term and 125 from full term infants
  - Exclude major anomalies, triplets (or higher), maternal substance abuse, and INCOMPLETE RECORDS

Results

Characteristics	Near Term	Full Term	Comment
N	90	95	Total = 185
Median birthweight (g)	2598	3180	
Mean birthweight (g)	2638	3295	
Vaginal deliveries	66	62	Total = 128
Cesearean deliveries	24	33	Total = 57
Table 1. Characteristics of study infants			

Results


Clinical Outcomes
Temperature instability
Hypoglycemia
Management requiring IV D10 infusion
Respiratory Distress
Clinical Jaundice
Full Term
Near Term
0
10
20
30
40
50
60
(%)

Near Term Morbitidies

- Late preterm infants shown to be at higher risk of hypoglycemia and hypothermia in 1st 12 hrs of life
- LP infants also shown to have slower lung fluid clearance, less surfactant compared to FT infants
- There is 2x relative risk of Sudden Infant Death Syndrome for LP infants (1.4/1000 compared to 0.7/1000 for FT infants
- LP infants have slower peristalsis, immature sphincter controls leading to poorly developed coordinating suck/swallow
- LP infants shown to have more prolonged physiologic jaundice

Near Term Morbidities (cont.)

- At 35 wks, brain shows fewer sulci, & weight is ~60% that of term infants
- Kidneys and liver immature in Late preterm infants. Unknown differences in drug clearance or metabolism compared to term infants
- Unknown differences in immune response compared to term infants

Results

Morbidities	Near Term	Full Term	Fisher Exact Test
Incidence of jaundice	49 (54%)	36 (37.9%)	p=0.27, 95%CI=1.05, 3.67, OR=1.95
Incidence of temperature instability	9 (10%)	0 (0%)	p=infinte 95% CI – 2.22, Infinite
Incidence of hypoglygemia	14 (15.6%)	5 (5.3%)	p=0.028, 95%CI=1.06, 12.2, OR=3.30
Incidence of respiratory distress	26 (28.9%)	4 (4.2%)	p<0.00001, 95%CI=2.97, 37.8, OR=9.14
Incidence of apnea	4 (4.4%)	0 (0%)	p=0.054
Incidence of bradycardia	4 (4.4%)	0 (0%)	p=0.054
Management requiring IV D10 infusion	24 (26.6%)	5 (5.2%)	P=7.33e-05, 95% CI=0.0436, OR=6.49
Management requiring sepsis observation	33 (36.7%)	12 (12.6%)	P=0.00015, 95% CI=1.82, 9.21, OR=9.14

Results

Sepsis evaluation	Near Term (n=33)	Full Term (n=12)
CBC, Blood culture only	42.4%	58.3%
CBC, Blood Culture, & 48 hours antibiotics	27.3%	25.0%
CBC, Blood Culture, and >48 hrs. antibiotics	30.3%	16.7%

Table 2. Comparison of management approaches for possible neonatal sepsis.

Discharge Delay

Discharge Delay	Near Term	Full Term	Fisher Exact Test
Jaundice	8/49 (16.3%)	1/36 (.03%)	p=0.0721, 95% Cl=0.0032, OR=6.71
Respiratory Distress	8/26 (30.8%)	2/4 (50%)	p=0.584, 95% Cl=0.1359, OR=0.46
Poor feeding	22/29 (75.9%)	2/7 (28.6%)	p=0.0289, 95% Cl=0.0107, OR=7.69

Table 3. Comparison of reasons for discharge delay in near term and full term infants.

Cost analysis

Cost Analysis	Near Term	Full Term	Silcoxon rank sum test.
Total Charges (mean, median)	$9278, $2679	$2333, $1384	W=2926.5, p=0.0002
Direct Cost (mean, median)	$2443, $901	$864, $680	W=2964.5, p=0.0003
Total Cost (mean, median)	$3989, $1534	$1359, $1105	W=2985, p=0.0003

Table 4. Cost and charge comparison of newborn hospital admission.

Cost analysis

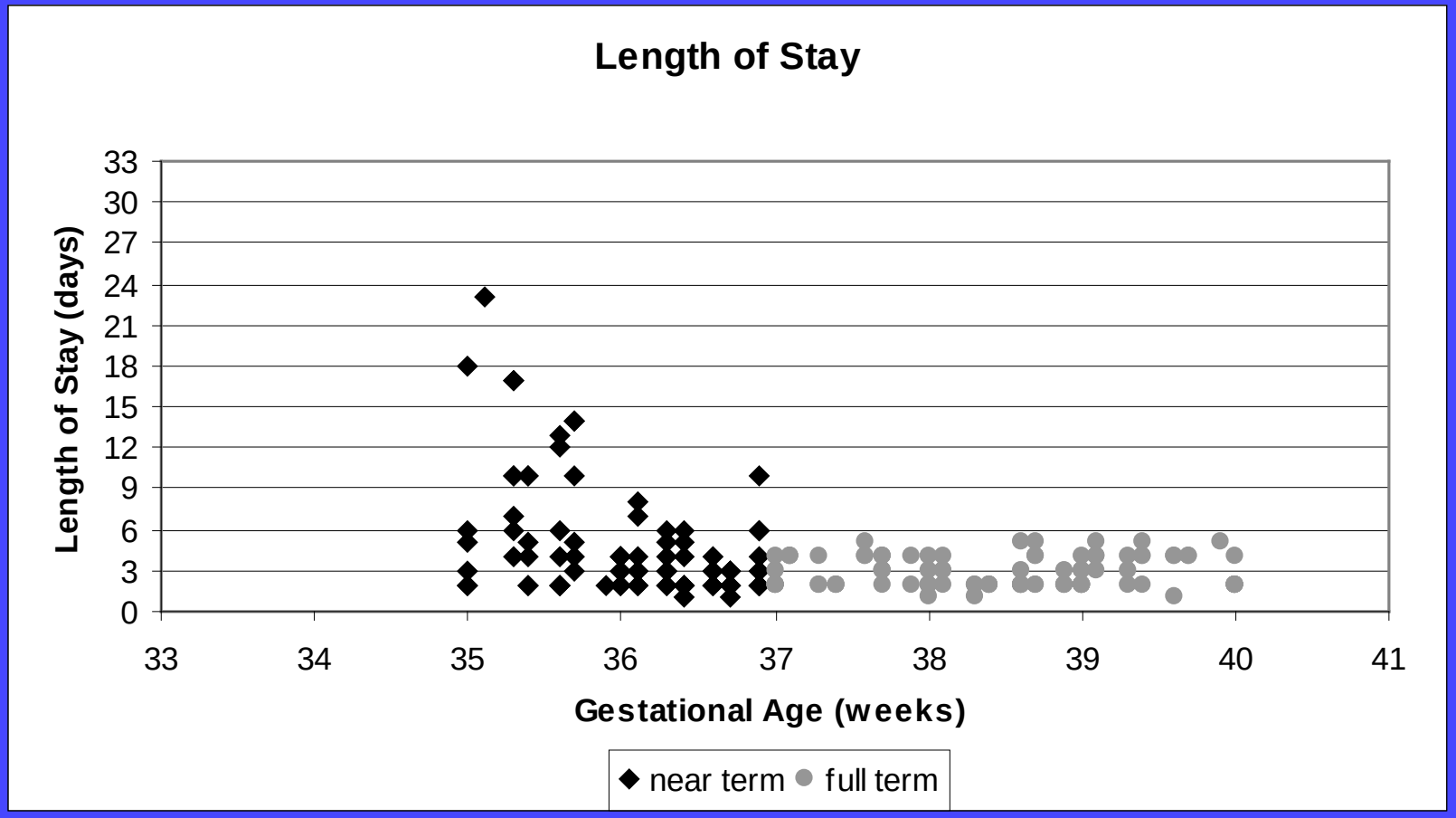
- **Gilbert, et al- ObGyn 2003; 102:488-492**
- Neonatal hospital costs averaged $2600 for a 36-week newborn and $1100 for a 38-week newborn
- Significant "excess" costs were found for births between 34 and 37 weeks' gestational age when compared with births at 38 weeks.

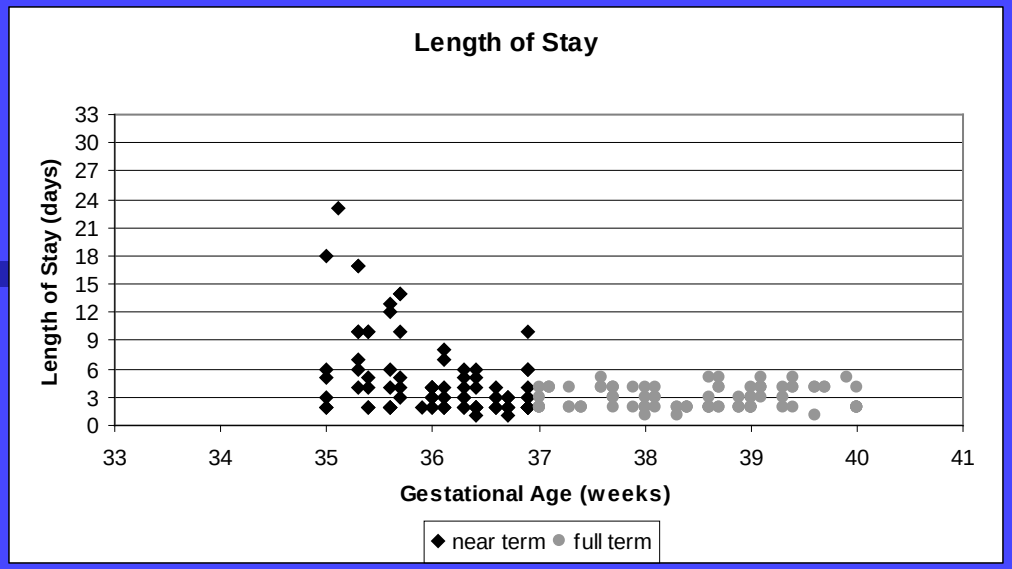
Cost savings for each week

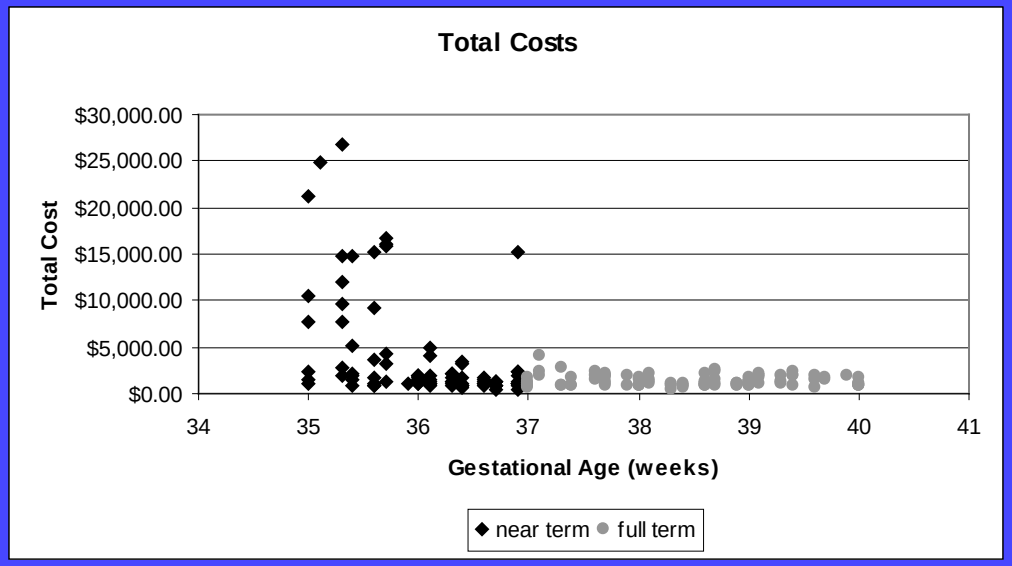
	34 wks	35 wks	36 wks	37 wks
Difference in mean cost vs. term ($1000)	6.01	3.01	1.44	0.55
Total excess cost ($1000)	34,784	29,797	23,880	18,858
After removing cesarean or induced deliv.				
Difference in mean cost vs. term ($1000)	4.26	2.15	0.83	0.39
Total excess cost ($1000)	16,570	14,403	9,534	9,399

Gest age	N	Mean	Median	$1000/case	RDS (%)
34	5788	5.9	2	7.2	7.4
35	9898	3.9	2	4.2	4.5
36	16609	2.8	1	2.6	2.3

Length of Stay




Length of Stay
Length of Stay (days)
33
30
27
24
21
18
15
12
9
6
3
0
33
34
35
36
37
38
39
40
41
Gestational Age (weeks)
near term
full term


Total Costs
Total Cost
$30,000.00
$25,000.00
$20,000.00
$15,000.00
$10,000.00
$5,000.00
$0.00
34
35
36
37
38
39
40
41
Gestational Age (weeks)
near term
full term

New Questions...

- Are these “well” premies or “sick” full termers?
  - e.g. Respiratory distress- RDS or TTN/Pneumonia – how will you treat them?
  - e.g. Temperature instability- sepsis or typical premie behavior?

More on Respiratory Distress

- Clark RH., J Perinatol. 2005 Aug;25(8):501-2.
- 1011 neonates , ≥34 weeks (mean 37 +/-2 wks) who were intubated within 72 hours of birth and expected to require ventilation for more than 6 hours
- Respiratory distress syndrome (n=437) was the most common pulmonary illness. Chronic lung disease was diagnosed in 109 (11%); neurological complications were reported in 86 (9%); and 51 (5%) patients died.
- CONCLUSIONS: Neonates > or =34 weeks who require mechanical ventilation represent a high-risk population who have significant morbidity and mortality.

Respiratory distress in near term babies after Cesararean section

- **Roth-Kleiner M,** Swiss Med Wkly. 2003 May 17;133(19-20):283-8.
- Infants admitted to NICU for RDS, all <2500 grams. Comparison of 2 groups
  - Elective cesarean section, no labor (n=34, mean gest. Age=37 2/7 wks)
  - Emergent cesarean section (n=22, mean gest. Age=36 2/7 wks)

	Mech. Vent	Hi Frequency Osc.	Pulmonary air leak	Catecholamine aid	death
Elective	4.4 days	13 (38%)	8 (24%)	14 (41%)	1
Emergent	3.9 days	7 (32%)	4 (18%)	5 (22%)	

More interesting questions

- Is this gestatational age, or LBW, or BOTH?
- Why no change in LOS?
- More sepsis evals in near termers-more on antibiotics for 48 hr. r/o,- NONE had +Bcx.
- IV D10 infusions- yes, more hypoglycemia, but also because more feeding problems

The biggest issue

- Feeding difficulty!
  - Limited evaluation, since we breastfeeding “success” wasn’t defined.
  - Low threshold needed to supplement
    - Neosure/Neocare 22 cal formulas
      - For as long as they are going to be on infant formula. Why?
        - They won’t catch up with length without it

Bottom line

- Near term babies vs. Full term babies- who will do better?
- Cost more
- Length of stay the same
- Feeding problems are the biggest nemesis
- You must consider the diagnoses from both sides of the continuum (full term and premie)

Long Term Outcomes

- American Academy of Pediatrics guidelines recommend discharge of singleton infants be no less than 48 hours after delivery...but that's for infants 38-42 weeks...
- Issues of early discharge
- Even longer term...

  Gray, et al

  20% of infants born in 34-37 wks had clinically significant behavior problems at 8 years of age (higher than for term infants)

Increased Mortality?

- PEDIATRICS Vol. 119 No. 3 March 2007, pp. E659-E665
- Increased mortality rate in Utah for Near term infants
- But...birth defects largest cause
- When BD’s factored out, still significant difference in mortality rates

TABLE 5 Causes of Death According to Gestational Age and Mortality Period

	Early Neonatal		Neonatal Infant				
Gestational Age, wk	Birth Defects a	All Other S	Birth Defects a	All Other S	Birth Defects a	All Other S	Total Deaths
34	18 (75)	6	19 (76)	6	28 (70)	12	40
35	19 (95)	1	22 (79)	6	31 (63)	18	49
36	27 (79)	8	35 (74)	12	46 (60)	31	77
37	19 (90)	2	34 (81)	8	50 (57)	38	88

Early Neonatal (Days 1–7) Mortality Rates and Risk Ratios for Death According to Gestational Age (Excluding Birth Defects)

Gestational Age, wk	Mortality Rates[a]	Risk Ratios	95% CI
34	1.27	3.25[b]	1.4-7.7
35	1.06	3.21[b]	1.5-6.1
36	0.66	2.69[b]	1.5-4.7
37	0.08	1.91[b]	1.2-3.1

Infant (Days 1–365) Mortality Rates and Risk Ratios for Death According to Gestational Age (Excluding Birth Defects)

Gestational Age, wk	Mortality Rates[a]	Risk Ratios	95% CI
34	3.79	4.62[b]	2.5-8.4
35	3.16	3.91[b]	2.3-6.5
36	2.55	3.14[b]	2.0-4.9
37	1.45	1.81[b]	1.2-2.8

Causes of Death for Each Gestational Age Cohort in the First Year

wk	Birth Defects		Immaturity		Asphyxia		Infections		Other Specific Causes		SIDS		External		Remaining		Total
	N (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	*N* (%)	OR[a]	
34	28 (70)[b]	22.2 (12.9–38.3)	2 (5.0)[b]	19.0 (2.7–135.1)	4 (10.0)[b]	12.7 (3.6–45.0)	0 (0.0)	NA	1 (2.5)	6.3 (0.66–60.1)	1 (2.5)	2 (0.3–19)	0 (0.0)	NA	4 (10.0)[b]	7.6 (2.4–24.3)	40
35	32 (64)[b]	13.7 (8.0–23.3)	7 (14.0)[b]	37.0 (7.7–178.3)	1 (2.0)	1.8 (0.21–14.6)	0 (0.0)	NA	3 (6.0)[b]	10.6 (2.1–52.4)	5 (10.0)[b]	7 (2–20)	0 (0.0)	NA	2 (10.0)	2.1 (0.45–9.7)	50
36	46 (60)[b]	9.5 (5.8–15.6)	5 (6.5)[b]	12.4 (2.4–63.8)	5 (6.5)[b]	4.1 (1.26–13.5)	1 (1.3)	0.45 (0.06–3.5)	5 (6.5)[b]	8.3 (1.97–34.5)	7 (9.1)[b]	4 (2–11)	1 (1.3)	0.62 (0.08–5.0)	7 (9.1)[b]	3.5 (1.3–9.1)	77
37	50 (57)[b]	4.8 (2.9–7.8)	3 (3.4)	3.4 (0.58–20.6)	2 (2.3)	0.77 (0.15–3.8)	4 (4.5)	0.84 (0.27–2.6)	8 (9.1)[b]	6.1 (1.6–23.1)	10 (11.4)[b]	3 (1.1–7)	5 (5.7)	1.44 (0.47–4.4)	6 (6.8)	1.4 (0.50–3.8)	88

Near Term Pathway

- The salient points (action plans)
  - Respiratory distress- baby should be on CVR monitor
  - Hypoglycemia- do the blood sugar screening
  - Temp instability- watch VERY carefully, for at least 48 hours
  - Car seat testing- <37 wks and <2500 grams
  - Feeding support- LC and Neosure/Neocare

What to tell mom/dad/OB/Pedi's

- Always consider the maternal/fetal Dx when delivery is needed (urgently or electively)
- Many near term infants will probably do just fine
- Near term infants are more likely to get poked and prodded

What to tell mom/dad/OBs/Pedi's

- Many of the diagnoses that near term babies endure are also endured by FT infants (just not as frequently).
  - When we catch these Dx's early, most everyone (FT and NT) does just fine, but…
  - Putting the NT babies on a pathway will help to reduce readmission rates (Jaundice, Poor BF/dehydration)

Directions

- Prevention of Near term infants?
  - How to best educate OB's on this topic...seemingly, more common than expected. Elective vs. urgent/emergent needs to deliver
- How to best streamline care in this population

Potential research questions

- F/u for 5 year?
- Differentiate clinical outcomes based on maternal/fetal diagnoses, stratify for urgency of delivery-compare outcomes
- Breastfeeding and near term? Worse than bottle?
  - LOS affected by BF more than near term?
- Figuring out if these kids are have more FT issues r/t NT issues- eg- RDS vs TTN/pneumonia
- Demographic differences? I.e. are OB's doing this more electively in certain populations/cultures? If there are differences, why?

Preventative care

- Options for creating universal guidelines for post-natal near term care?
  - Comparison of pre/post guideline initiation-readmission rates, LOS, number of diagnoses given

American Academy of Pediatrics Directives

- Assess extent of respiratory distress (TTN/RDS) and the cost of care
- Identify cardiopulmonary factors (including antenatal steroid treatment) that may affect TTN/RDS
- Better understand respiratory maturation to assess apnea of prematurity and feeding
- Study potential increase of SIDS
- Evaluate brain development and maturation
- Conduct more extensive studies on hyperbilirubinemia and prevention

American Academy of Pediatrics Directives

- Examine gastrointestinal issues and possible increased association of necrotizing enterocolitis, reflux, poor feeding, lifelong gut disorders, milk allergies
- Examine immune immaturity, and association with infections, allergies, asthma
- Examine differences of drug metabolism and effect

American Academy of Pediatrics Directives

- More epidemiological data on possible sub-category risks w/in LPT cohort
- By better risk assessment, how can we accelerate organ maturation when delivery is necessary
- Dvp risk/benefit analyses on LPT delivery indications
- Better precision of GA estimation