Late Preterm and Early Term Birth: At-risk Populations and Targets for Reducing Such Early Births

Matthew A. Kardatzke, MD,* Rebecca S. Rose, MD, MS,* William A. Engle, MD*

*Section of Neonatal-Perinatal Medicine, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN

Education Gaps

1. Awareness of the etiologies of late preterm and early term delivery and strategies available to safely prevent such preterm deliveries are necessary.
2. Knowledge of the short- and long-term morbidities facing late preterm and early term infants is necessary for appropriately judging the balance of risk associated with delivery prior to term.

Abstract

The risks of late preterm (LPT) and early term (ET) birth have been recognized during the last decade. Increased awareness accompanied by efforts to reduce elective delivery before 39 weeks of gestation have led to a decline in LPT/ET births. Despite this success, strategies to identify and reduce preventable LPT/ET births using traditional and novel prevention methods are still needed. Because preterm birth is a common endpoint associated with many different preventable and nonpreventable causes, the efforts for reducing such early births must be multifaceted. For neonates born LPT/ET, there is an inverse relationship between gestational age and morbidity and mortality, with a nadir at 39 to 40 weeks of gestation. Recognition of the short-term complications of LPT/ET is important for timing of delivery and the initial clinical management of these patients. In addition, the recognition of the long-term respiratory and neurocognitive complications of LPT/ET birth helps inform the evaluation, treatment, and monitoring for impairments and disabilities that benefit from early detection and intervention. In this article, we review the definition of LPT/ET birth, prevention strategies, indications for LPT/ET birth, and the short- and long-term outcomes for such infants.

Objectives After completing this article, readers should be able to:

1. Describe the causes of late preterm and early term birth and targets of prevention.

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ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
CI	confidence interval
ET	early term
IVF	in vitro fertilization
LPT	late preterm
MRI	magnetic resonance imaging
NICHD	National Institute of Child Health and Human Development
OR	odds ratio
RR	relative risk
UNICEF	United Nations Children's Fund
WHO	World Health Organization

2. Describe the reasons for delivery before term.
3. Identify the short-term morbidities associated with late preterm and early term birth.
4. Recognize the long-term neurocognitive consequences of late preterm and early term birth.

INTRODUCTION AND BACKGROUND

Preterm birth is an important public health matter because it accounts for $26.2 billion in health care expenses each year and is the most frequent cause of infant mortality in the United States. In 2005, the National Institute of Child Health and Human Development (NICHD) held a workshop on "Optimizing Care and Outcome for Late-Preterm (Near-Term) Infants."(1) Workshop participants sought to form a united definition of late preterm birth (34–36 weeks of gestation) and to bring attention to this previously under-recognized and vulnerable population. Late preterm (LPT) births account for 70% of preterm births (Fig 1), with an estimated 327,133 LPT births per year in the United States. (2) LPT births also account for 9.8% of all infant deaths. In 2008, the infant mortality rate in LPT infants was 3.6 times that of term infants and accounted for 2,753 of the total 28,076 infant deaths. (3)

In the decade since the 2005 NICHD workshop on late prematurity, the increased awareness of the risks of LPT birth has led to investigations of the etiologies, long-term outcomes, and optimal management strategies for LPT infants. (4)(5)(6) These reports revealed long-term implications of LPT *and early term* (ET; 37–38 weeks of gestation) birth, including influences on respiratory, cognitive, social, and cardiovascular outcomes, with some studies spanning into the seventh decade of life. (7)

Increased awareness of the risks of LPT birth led to education and policy efforts to reduce nonmedically indicated preterm births. From 2006 to 2013, the rate of preterm birth decreased from a peak of 12.8% to 11.4%, with 82% of the reduction occurring because of a decline in LPT births. (8) Importantly, during this same period, the rate of stillbirth has remained stable, (9) indicating that the decline in preterm birth was not associated with an increase in "hidden" mortality before delivery.

Despite this increased awareness of morbidity and mortality in LPT and ET births and success in reducing LPT birth, questions remain, and continued efforts are necessary to limit LPT and ET births while providing optimal care to such infants when birth before term is inevitable. In this article, we will review definitions of gestational age categories, factors leading to birth from 34 and 38 weeks of gestation, interventions that may reduce births of such infants, and short- and long-term complications of LPT and ET birth.

GESTATIONAL AGE CATEGORY DEFINITIONS

The 2005 NICHD workshop recommended use of the phrase "late preterm" instead of "near term" to describe infants born between 34 and 0/7 weeks through 36 and 6/7 weeks of gestation (Fig 2). (1) This standardized definition emphasizes the physiologic immaturity and associated increased morbidity and mortality of these infants and provides a framework for clinicians, researchers, and policymakers to refer to this population more consistently. However, the categorization is

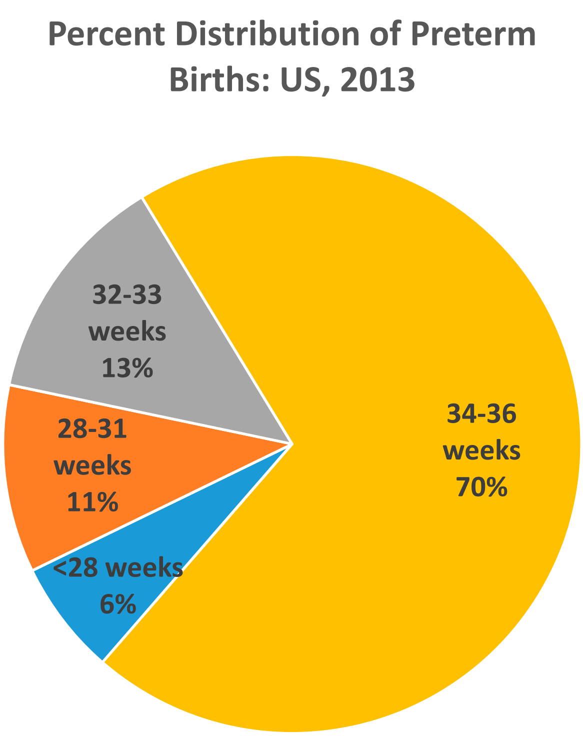

Figure 1. Distribution of preterm births in the United States, 2013. (Reprinted with permission from Martin JA, Hamilton BE, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2013. *Natl Vital Stat Rep.* 2015;64(1):1-65.)

relatively arbitrary and blurs the fact that a continuum exists, with risk of morbidity and mortality increasing at lower gestational ages. (5)

Recognizing the continuum of morbidity and mortality (Fig 3) associated with birth in each week before 39 to 40 weeks of gestation, a multidisciplinary workgroup met in 2013 to further categorize the description of births after 37 and 0/7 weeks of gestation. This group defined "early term" as birth between 37 and 0/7 weeks through 38 and 6/7 weeks, "full term" between 39 and 0/7 weeks through 40 and 6/7 weeks, and "late term" between 41 and 0/7 weeks through 41 and 6/7 weeks. (10)

ETIOLOGY OF LPT (AND ET) BIRTH: TARGETS FOR PREVENTION

LPT and ET births are not caused by a single entity, but instead are a common endpoint caused by a heterogeneous group of conditions in both the mother and fetus (Fig 4). Examples of factors that contributed to an increase in LPT birth, and likely ET births, between 1990 and 2006 include:

- Increased surveillance during pregnancy, especially with ultrasonography and fetal stress testing
- Increased rate of spontaneous preterm labor and preterm premature rupture of membranes
- Inaccurate gestational age assessment
- Increased multifetal pregnancies (related to assisted reproductive techniques)
- Early delivery in stable high-risk mothers and infants at risk for fetal death
- Elective induction of labor or cesarean delivery

Understanding the various etiologies of preterm birth enhances the implementation of targeted prevention strategies.

Advances in the medical care of pregnant women and their fetuses and fears of stillbirth have led to increased surveillance. Frequent prenatal visits, fetal ultrasonography, fetal stress testing, aneuploidy screening, and other testing or monitoring have improved outcomes for mothers and infants. Increased surveillance facilitates the early detection of findings that could have implications for the health of the mother or the fetus before life-threatening events occur. Before 2005, fear of risks associated with abnormal findings on surveillance screening, combined with lack of recognition of the morbidities and mortality risks of LPT and ET births encouraged decisions to deliver at 34 weeks of gestation or beyond to avoid stillbirth or other complications. Since 2005, knowledge of the risks associated with LPT and ET births has led to lower rates of such births. Because many LPT/ET infants are delivered to prevent intrauterine fetal demise, the decline in LPT/ET births could unintentionally increase the rate of stillbirth. However, despite the decline in LPT/ET births, the stillbirth rate has remained stable since 2005, indicating an overall improvement in perinatal outcomes.

It is estimated that two-thirds of preterm births are "spontaneous," with the remaining one-third being the result of medical intervention. (11) Spontaneous LPT birth can be further categorized as spontaneous labor or preterm premature rupture of membranes. The underlying pathogenesis of spontaneous premature birth remains poorly understood. Nevertheless, the large number of births in this category make it an important target for preventive strategies. Contrary to the common attitude of resignation that preterm birth is simply inevitable, Newnham et al (12) provided an overview of strategies currently available in high-resource settings aimed at preventing preterm birth (Fig 5). Although not specifically directed toward LPT/ET births, the general strategies presented may be applicable to such births. In addition to limiting nonmedically indicated elective LPT/ET births, the 2 efforts with the largest potential impact on preterm delivery are progesterone supplementation and judicious use of fertility treatment. (12)

For several decades there has been interest in the use of progesterone in preventing preterm birth. Although the mechanism by which it prevents preterm birth is unclear,

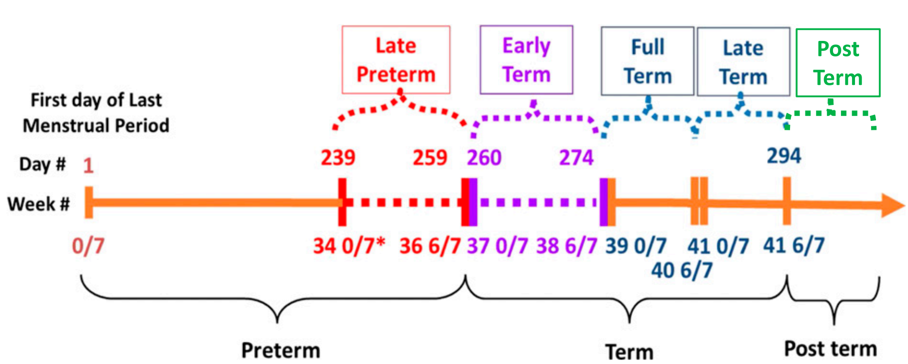

Figure 2. Definitions of gestational age periods from late preterm to post term. (Adapted with permission from Engle WA, Kominiarek M. Late preterm infants, early term infants, and timing of elective deliveries. *Clin Perinatol.* 2008;35:325–341.)

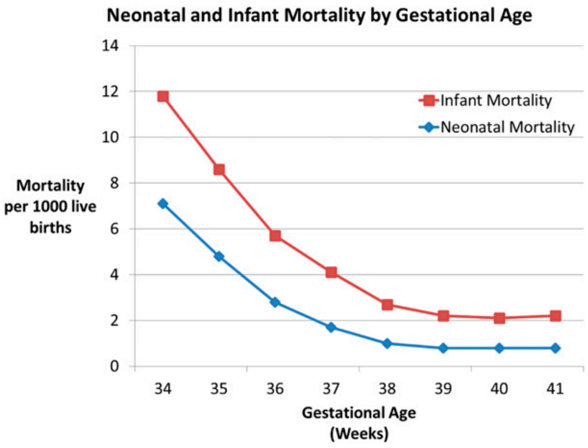

Figure 3. Neonatal and infant mortality by gestational age. (Reprinted with permission from Reddy UM, Ko CW, Raju TN, Willinger M. Delivery indications at late-preterm gestations and infant mortality rates in the United States. *Pediatrics.* 2009;124:234–240.)

progesterone therapy for women with a prior history of spontaneous preterm birth has been shown to reduce mortality (relative risk [RR], 0.5; 95% confidence interval [CI], 0.33–0.75), preterm birth before 34 weeks of gestation (RR, 0.31; 95% CI, 0.14–0.69), preterm birth before 37 weeks of gestation (RR, 0.55; 95% CI, 0.42–0.74), and admission to NICU (RR, 0.24; 95% CI, 0.14–0.40). (13) Although promising, these improvements are limited to singleton pregnancies, and similar benefits have not been shown for multiple pregnancies.

Progesterone is also effective in reducing premature births in women with short cervix noted on ultrasonography.

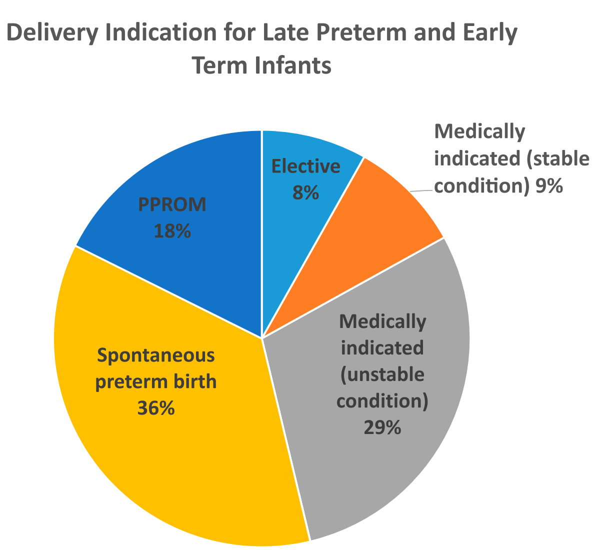

Figure 4. Indications for delivery of late preterm and early term infants. PPROM=preterm premature rupture of membranes. (Reprinted with permission from Holland MG, Refuerzo JS, Ramin SM, Saade GR, Blackwell SC. Late preterm birth: how often is it avoidable? *Am J Obstet Gynecol.* 2009;201(4):404.e1-4.)

A meta-analysis by Romero et al (14) showed that progesterone in women with an ultrasonographically evident short cervix (<25 mm) is effective in preventing preterm delivery before 35 weeks' gestation (RR, 0.69; 95% CI, 0.55–0.88), though the effect was not present when considering prevention of preterm birth at less than 37 weeks (RR, 0.89; 95% CI, 0.75–1.06). Although cervical length screening has yet to be performed on a large scale and is not currently recommended by the American College of Obstetricians and Gynecologists (ACOG), it has been estimated that for every 100,000 women screened, progesterone treatment could lead to savings of $12 million and an increase of 424 quality-adjusted life-years. (12) Cervical length screening may also identify women who would benefit from cervical cerclage. In women with ultrasound evidence of shortened cervix less than 15 mm, cervical cerclage has been shown to reduce the outcome of preterm birth less than 35 weeks (odds ratio [OR], 0.23; 95% CI, 0.08–0.66), and for women with cervical length less than 25 mm, cerclage significantly reduced the secondary outcome of preterm birth before 37 weeks. (15)

When considering prevention of preterm birth, it is essential to recognize the importance of accurate gestational age assessment. An accurate estimation of gestational age allows for accurate assessment of fetal growth and appropriate timing of antepartum care and testing. Inaccurate dating of a pregnancy may lead to unintended premature delivery if there is an overestimate of gestational age. In its 2014 statement, ACOG recommends that first-trimester ultrasonography be used for identifying gestational age, because in most pregnancies, this will be the most accurate measure, with the exception of pregnancies resulting from in vitro fertilization.

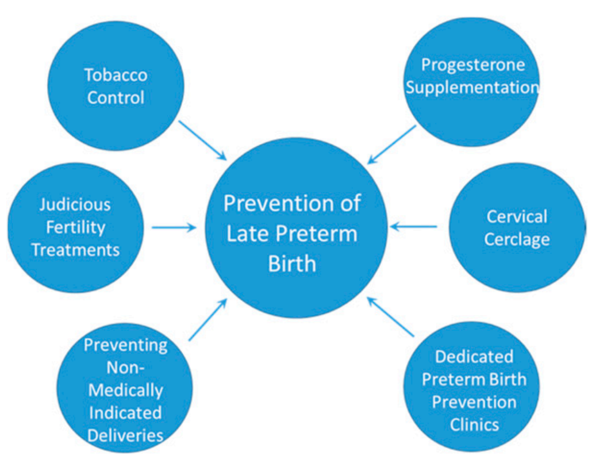

Figure 5. Select initiatives to prevent late preterm birth. (Adapted with permission from Newnham JP, Dickinson JE, Hart RJ, Pennell CE, Arrese CA, Keelan JA. Strategies to prevent preterm birth. *Front Immunol.* 2014;5:584.)

When first-trimester ultrasonography is not performed, the best clinical estimate based on the last menstrual period and/or second- or third-trimester ultrasonography is recommended for gestational age dating. The estimated due date should only be changed in rare circumstances. (16)

Multifetal gestation has increased as a result of medically assisted reproductive technologies, and these pregnancies are at increased risk for preterm delivery. (17) Efforts to reduce this burden include using single embryo transfer when using in vitro fertilization (IVF). Single embryo transfer techniques may reduce some but not all pregnancies with multiple fetuses because of the increased risk of monozygotic twinning with IVF. In addition, women older than 30 years are at higher risk of having twins or greater multiple fetuses during a pregnancy. (18) With greater numbers of pregnancies in women older than 30 years, it is understandable that more multiple births are occurring.

Prevention of preterm birth must be multifaceted to address the many key contributing drivers. Therefore, dedicated preterm birth prevention clinics have been proposed to provide specialized and up-to-date expertise on preventing preterm births among women with a history of preterm delivery. The services provided by these clinics are variable, but a large-scale implementation of this care showed a rate of preterm delivery of 7.4% compared with 9.1% ($P<.05$) for women receiving care in a preterm birth prevention clinic and standard prenatal care, respectively. (19) These clinics provide a setting for progesterone therapy, cervical cerclage, tobacco use reduction, and subsequent birth planning to optimize birth interval spacing. Because stress has been associated with preterm births, these clinics may also provide benefit by reducing maternal anxiety. Further efforts to standardize care and make it more widely available may also reduce preterm delivery.

Elective or nonmedically indicated induction of labor has been a focus for improvement in the decade since the NICHD workshop increased attention to the LPT birth population. Several reports describe quality improvement efforts aimed at reducing induction of labor before 39 weeks without an indication. (20)(21)(22)(23) Successful strategies include education of physicians and nurses, with or without a "hard stop," in which induction before 39 and 0/7 weeks requires authorization from a chain of command, or a "soft stop," in which compliance depends on individual clinicians but all elective deliveries before 39 weeks are referred for peer review. A comparative effectiveness study of these methods by Clark et al (20) showed that hospitals with a hard stop policy were the most effective, with a decrease in NICU admissions and no increase in stillbirths. A goal rate of 5% elective delivery before 39 weeks has been suggested as a national quality benchmark, which has been shown to be possible in diverse hospital systems. (20)(23)

Family education and involvement in delivery planning is also important for reducing nonmedically indicated LPT or ET births. The March of Dimes campaign "Healthy Babies Are Worth the Wait," available at https://www.prematurityprevention.org/, is an example of a prenatal education toolkit for parents to help reduce LPT and ET births. This approach of parental education can help families partner with their health care provider in deciding optimal timing of delivery. Also available from the March of Dimes is a provider toolkit entitled "Elimination of Non-medically Indicated (Elective) Deliveries Before 39 Weeks Gestational Age."

Further work combining hospital system policies with family education efforts will be important to further reduce LPT and ET births and make the nonmedically indicated preterm delivery an uncommon event.

INDICATED LPT BIRTH

Despite the increased morbidity and mortality of LPT birth, there are indications that warrant preterm delivery to prevent maternal complications, stillbirth, neonatal death, and neonatal morbidity. However, Gyamfi-Bannerman et al (24) found that 56.7% of LPT births analyzed were "non−evidence based," suggesting a need for evidence-based guidelines for LPT delivery. In 2011, the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Society for Maternal-Fetal Medicine held a workshop entitled "Timing of Indicated Late Preterm and Early Term Births."(25) In this workshop, experts analyzed the condition-specific indications for LPT delivery, emphasizing the most common causes: placental/uterine, fetal, and maternal conditions (Table 1). The workshop recommendations are based on available data and expert opinion, thus it is important to note that the suggested gestational age at delivery in this article cannot account for individual variability, and a patient-specific risk analysis is required when considering delivery timing. Further research clarifying the optimal timing of delivery by indication is essential and is an ongoing area for potential reduction of LPT and ET births.

MORBIDITIES AND MORTALITY IN LPT AND ET BIRTHS

LPT and ET infants are physiologically and metabolically less mature than full-term infants. Although many such infants have few or no complications of early birth, morbidity risks increase significantly as gestational age decreases. In a large population-based study, severe respiratory failure increased from 0.3% of live births at 39 to 41 weeks of gestation

TABLE 1. **Select Perinatal Conditions and Recommended Gestational Age at Delivery**

SELECT CONDITIONS	GESTATIONAL AGE AT DELIVERY
Placenta previa	36–37 weeks
Prior classic cesarean	36–37 weeks
IUGR singleton—uncomplicated	38–39 weeks
IUGR twins	36–37 weeks
Fetal anomalies	34–39 weeks
Dichorionic-diamniotic twins	38 weeks
Chronic maternal hypertension – no medications	38–39 weeks
Preeclampsia—mild	37 weeks
Prior stillbirth—unexplained	LPT/ET delivery not recommended—Consider amniocentesis for fetal pulmonary maturity if delivery planned at <39 weeks
Diabetes—pregestational or gestational, poorly controlled	34–39 weeks
Diabetes—gestational well controlled on diet or medication	LPT birth/ET birth not recommended

ET=early term; IUGR=intrauterine growth restriction; LPT=late preterm.
Modified with permission from Spong CY, Mercer BM, D'Alton M, et al. Timing of indicated late-preterm and early-term birth. Obstet Gynecol. *2011;118(2 pt1):323-333.*

to 20% at 34 weeks of gestation. (26) In this same population, the risk of death and/or severe neurologic disorder also increased from 0.15% to 0.16% at 38 to 41 weeks of gestation to 1.7% at 34 weeks of gestation. Morbidity encompassing many causative factors, defined by a hospital stay longer than 5 nights and a life-threatening condition, a hospital stay less than 5 nights, and transfer to a higher level of care or death before discharge from the initial hospitalization, is significantly correlated with gestational age, with the lowest risk seen at 39 to 40 weeks of gestation. (27)(28) The morbidity rate increased from 2.5% at 40 weeks of gestation to 52% at 34 weeks of gestation, with the rates doubling for each additional gestational week before 38 weeks. Furthermore, the need for resuscitation procedures, especially bag-mask ventilation, is significantly more common in LPT and ET infants than in those born at term. (29) For example, bag-mask ventilation was provided in 14% of LPT infants versus 6% of term infants (OR, 2.61; 95% CI, 2.14–3.17).

EARLY RESPIRATORY MORBIDITY

Infants born LPT or ET are at increased risk for multiple early morbidities after delivery. The rate of NICU admission is inversely related to gestational age, and this persists in a statistically significant manner until 39 to 40 weeks of gestation. (30) Similarly, ventilator use is inversely proportional to gestational age, with infants born at 38 weeks' gestation requiring ventilator support nearly twice as often as those at 39 weeks (Fig 6). Furthermore, the duration of time with oxygen saturation measurements less than 90% during the first 48 hours after birth is greater at 35 weeks of gestation (7.5%) than at 38 to 40 weeks of gestation (4.5%); this is reflective of the lower pulmonary reserve in the LPT neonatal population. (31) Apnea is also more frequently found in LPT neonates (4% to 7%) than in term neonates (1%). (32)(33)

Cheng et al (34) analyzed the gestation-specific risk of respiratory distress syndrome and mechanical ventilation in ET versus late-term neonates in a cohort of more than 2 million pregnancies with live, singleton fetuses in cephalic position. Although the absolute risks of respiratory distress syndrome and treatment with mechanical ventilation were low (0.57% at 37 weeks of gestation vs 0.32% at 38 weeks vs 0.28% at 39 weeks), the risks are significantly different at both 37 weeks (adjusted OR, 2.20; 95% CI, 1.88–2.18) and 38 weeks (adjusted OR, 1.15, 95% CI, 1.08–1.23) compared with 39 weeks of gestation. Despite the low absolute risk, the large volume of deliveries at these gestations nationwide translates into 2,000 to 3,000 cases of respiratory distress syndrome and need for mechanical ventilation each year. These cases are particularly significant because these data apply to low-risk neonates without other complications.

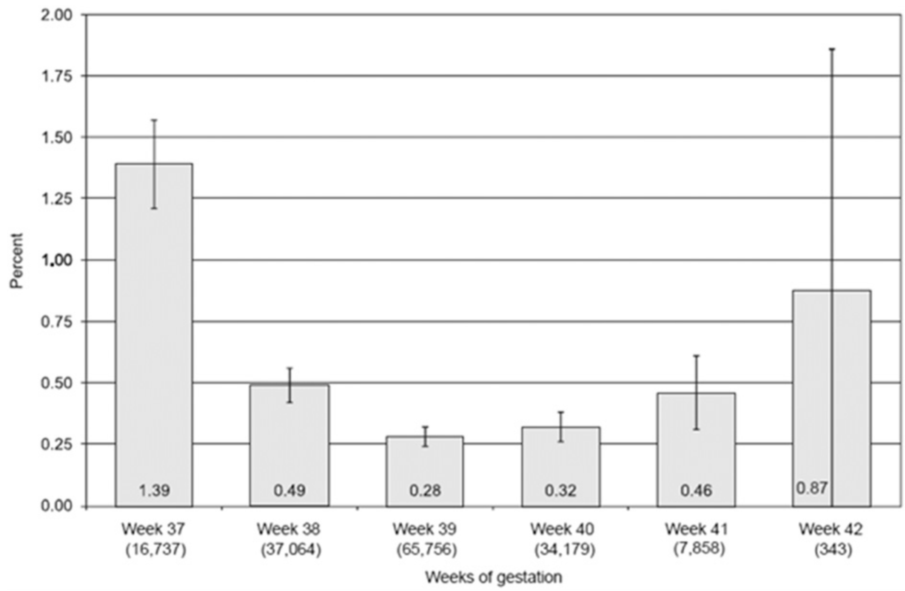

Figure 6. Rate of ventilator use for deliveries without complications by gestational age. Two standard deviations shown by *vertical lines*. Data from Intermountain Healthcare. (Reprinted with permission from Oshiro BT, Henry E, Wilson J, Branch DW, Varner MW; Women and Newborn Clinical Integration Program. Decreasing elective deliveries before 39 weeks of gestation in an integrated health care system. *Obstet Gynecol.* 2009;113(4):804–811.)

In a recent multicenter, randomized trial, Gyamfi-Bannerman et al (35) evaluated the use of antenatal betamethasone for women with singleton pregnancies at high risk for LPT delivery. The trial found a reduction in the primary outcome of respiratory support in the first 72 hours after birth (11.6% vs 14.4%; RR, 0.80; 95% CI, 0.66–0.97) and reductions in severe respiratory complications, transient tachypnea of the newborn, surfactant use, and bronchopulmonary dysplasia. Although the betamethasone-treated group had more cases of neonatal hypoglycemia compared with the placebo-treated group, rates of chorioamnionitis or neonatal sepsis were not different. (35) Further studies evaluating the long-term respiratory outcomes for antenatal corticosteroid use in LPT will be important to further elucidate the effects of this therapy.

OTHER EARLY MORBIDITIES

Additional morbidities of LPT infants requiring treatment during the initial birth hospitalization include temperature instability, low blood glucose, requirement of intravenous infusion, jaundice, and feeding problems (Fig 7). These morbidities are all significantly more common in LPT infants than in term infants. (32)

The duration of the birth hospitalization, like morbidity and mortality rates, correlates with gestational age. (36)(37) A single center report on 235 LPT infants found the mean length of stay during the birth hospitalization to be 12.6 ± 10.6 days at 34 weeks, 6.1 ± 5.8 days at 35 weeks, and 3.8 ± 3.6 days at 36 weeks of gestation compared with the usual length of stay for term infants of 2 days after a vaginal delivery and 3 days after a cesarean delivery. In this same group of LPT infants, the percentage of infants who remained hospitalized after their mothers' discharge was also higher at lower gestational ages: 75%, 50%, and 25% at 34, 35, and 36 weeks' gestation, respectively.

Hospital readmission rates after the initial birth hospitalization are higher for LPT infants (4.3%) than term infants (2.7%). (38) Among infants who were never in the NICU, readmissions are 3-fold higher in LPT infants than in term infants, thus corroborating the physiologic and metabolic immaturity of LPT, and by extension ET, neonates. (39) Such readmissions most often are related to jaundice, feeding problems, proven or suspected infection, and breathing problems. Risk factors for LPT readmission, in addition to care in a normal nursery with short duration of initial hospitalization, include primigravida status of the mother, first born infant, labor or delivery complications, and Asian/Pacific Islander ethnicity. Targeting patients with these risk factors for education and particularly close follow-up, especially if discharged after 2 to 3 days of age, may prevent some of the LPT neonate readmissions.

BREASTFEEDING MORBIDITY AND THE LPT INFANT

The benefits of exclusive breastfeeding are well recognized and both the World Health Organization (WHO) and American Academy of Pediatrics recommend exclusive breastfeeding

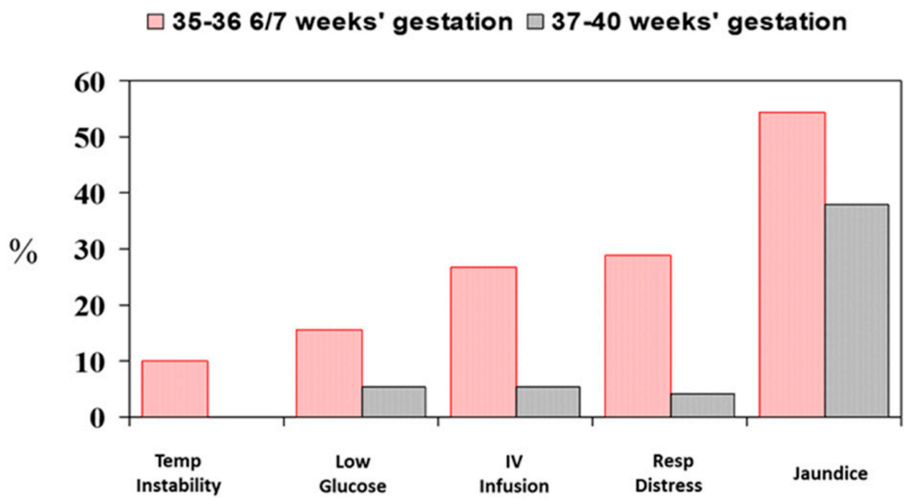

Figure 7. Acute complications of late preterm birth. (Reprinted with permission from Wang ML, Dorer DJ, Fleming M, et al. Clinical outcomes of near-term infants. *Pediatrics.* 2004;114:372–376.)

through 6 months of age. Despite this, compared with term infants, breastfeeding is less likely to be initiated in LPT infants (70.4% vs 76.5%), and much less likely to be continued (54.6% vs 64.1%). (40) The reasons for this discrepancy are multifactorial, including early separation of mother and infant, maternal illness that limits breastfeeding ability, and physiologic immaturity (Table 2). This physiologic immaturity compared with term infants is manifested as lower muscle tone, less frequent awakening, fewer feeding cues, and an increased likelihood of falling asleep with feedings. In addition, LPT infants can have difficulty with latching on because of inadequate mouth opening and abnormal tongue movements, and have an ineffective suck characterized by low suck frequency and an inability to maintain a sustained negative pressure. (41)

To promote breastfeeding initiation and continuation, an approach focused on the specific needs of the LPT infant is required. Nyqvist et al (42) expanded the Baby-Friendly Initiative of WHO and United Nations Children's Fund (UNICEF) to include the particular needs of the LPT infant; this is because the original Baby-Friendly Initiative focused primarily on the mother-infant dyad with full-term well infants. Recommended interventions include facilitation of early, continuous, and prolonged skin-to-skin contact, early initiation of breastfeeding, and mothers' access to breastfeeding support and education during the initial hospitalization. An infant-guided approach is recommended, with an assessment of infant competence and stability before feeding initiation, followed by an ongoing assessment of feeding adequacy. If the assessment shows inadequate latch, nipple shields may be considered to facilitate feeding. During the advancement of feedings, pacifiers may be used during tube-feeding, for pain relief, and for calming infants. In contrast, some experts recommend that pacifiers be deferred for term infants until breastfeeding is firmly established at 3 to 4 weeks of age. Nyqvist et al also emphasize adequate parental support,

TABLE 2. **Risk Factors and Support Interventions When Breastfeeding Late Preterm and Early Term Infants**

RISK FACTORS	SUPPORT INTERVENTIONS
Separation of mother and infant	Lactation consultant support
Maternal illness	Breast pump availability
Low muscle tone	Nipple shields /assistive devices
Decreased awakening	Close postdischarge follow-up
Immature suck and latch	Peer support group

From Briere CE, Lucas R, McGrath JM, Lussier M, Brownell E. Establishing breastfeeding with the late preterm infant in the NICU. J Obstet Gynecol Neonatal Nurs. *2015;44(1):102–113; quiz E1-2.*

including access to lactation services and peer support and close postdischarge follow-up to ensure adequate growth. (42)

While breastfeeding should be supported, it is important to recognize that at 34 weeks of gestation, approximately 98% need nasogastric feedings and on average take 2 to 3 weeks to attain full oral feedings. At 35 to 36 weeks of gestation, 78% receive nasogastric feedings and take approximately 1 week to achieve full oral feeding. (43) For moderately preterm infants, who consume mostly human milk (≥80%), it has been shown that supplementation with a powdered human milk fortifier provides improved linear and head growth. Although the impact of nonsupplemented feeding of human milk on LPT infants is unclear, close attention should be paid to the growth of LPT infants before and after discharge to ensure adequate nutritional intake (44); LPT infants may appear to do well with initial small-volume feedings, yet fail to sustain adequate intake when larger volumes are required. Early hospital discharge may not allow for an adequate assessment of the infant's ability to sustain adequate growth. Thus, feeding difficulties are the most common reason for readmission of the LPT infant, accounting for 41% of such admissions. (45)

LATE MORBIDITY AND MORTALITY ASSOCIATED WITH LATE PREMATURITY

LPT infants have higher morbidity rates compared with term infants, and these may persist after the neonatal period and well into adulthood. A common theme in the outcomes of LPT infants is that relatively low absolute percentages of individuals are affected but the relative risks are significant; these risks only become important when large populations of individuals are involved.

In the first 2 years after birth, LPT infants are at increased risk of hospitalization for respiratory syncytial virus (2.5% vs 1.3%), and once admitted, have a greater length of stay (3 vs 2 days) than term infants. (46) Respiratory morbidity has been tracked into childhood, and LPT infants have been found to be at increased risk of requiring asthma medication at 5 years of age (OR, 2.2; 95% CI, 1.6–3.1) and of developing asthma at any time (OR, 1.7; 95% CI, 1.4–2.0), wheezing or asthma at 5 years (OR, 1.5; 95% CI, 1.2–1.8), bronchitis/bronchiolitis in the first 3 years after birth (OR, 1.64; 95% CI, 1.13–2), and respiratory symptoms in the first year (22% vs 13%). Compared with term infants, respiratory physiology testing in LPT infants shows differences in compliance, forced expiratory flows, bronchial reactivity, and spirometry, with some differences persisting into the teenage years. (47)

There is an increased risk of treatment of LPT individuals during adulthood for diabetes with any diabetic medication (LPT vs term infants: 1.5% vs 1.2%; RR, 1.18; 95% CI, 1.04–1.33) and insulin (LPT vs term infants: 1.0% vs 0.8%; RR, 1.22; 95% CI, 1.08–1.39). (48) In addition, children born LPT have been shown to have higher blood pressures than those born at term. (49) Despite these findings and the link between diabetes and hypertension with cardiovascular complications, a study evaluating coronary heart disease and stroke in Finnish individuals born LPT or ET in 1924 to 1944 showed no differences with the general population. (50)

A Swedish cohort was analyzed by Crump et al (51) and interestingly showed increased mortality rate for individuals born LPT also occurs in those who are 18 to 36 years of age; the hazard ratio for mortality was 1.31 (1.13–1.5) compared with individuals born at 37 to 42 weeks of gestation. (51) This study showed a significant association with mortality and congenital anomalies, respiratory and endocrine disorders, and cardiovascular disorders in young adulthood.

BRAIN MATURATION, NEURODEVELOPMENT, AND COGNITIVE OUTCOMES

The final weeks of gestation represent a time of rapid growth and development of the fetal brain. Significant brain growth occurs in the final weeks of the third trimester, with the brain at 35 weeks of gestation weighing only 60% to 80% of that of the full-term infant; significant growth occurs at the macroscopic and cellular level in the last 4 weeks of gestation. (52) In addition, magnetic resonance imaging (MRI) studies of late-preterm infants at term-corrected age show smaller biparietal diameter, thinner corpus callosum, less developed gyral maturation, and decreased myelination, (53) as well as altered white matter microstructure on diffusion tensor imaging. (54) Long-term structural changes also may occur, as noted in MRI studies of preadolescents and adolescents who were born LPT, which show increased connectivity in the prefrontal and posteromedial cortex compared with term controls. It is unclear whether differences identified in this cohort represent pathology or evidence of compensatory changes, because neurocognitive testing showed no differences. (55) However, other studies show an increased risk of developmental delay in those born LPT compared with term infants (6%–11% vs 4%), (56) with the risk of developmental delays, cognitive dysfunction, and cerebral palsy increasing exponentially as gestational age decreases below 38 weeks of gestation. (57)(58)(59) Findings of lower educational achievement and neurocognitive scores also have been found in adults born LPT compared with those born at term, indicating the long-term impact of LPT birth. (7)(60) When considering the long-term cognitive outcomes of LPT infants, it can be difficult to distinguish the relative influence of prematurity separate from associated anomalies, causes for LPT birth, and critical illness, because these factors may lead to worsened outcomes. To identify the long-term risk of "healthy" LPT infants, Morse et al (52) compared LPT infants discharged from the hospital before 72 hours of age with term controls and found developmental delay or disability was 36% more likely in the LPT infant. In addition, healthy LPT infants were more likely to be suspended from school in kindergarten, require special education, and require retention in kindergarten. (52)

Several studies have further described increased risk of varied neurologic, psychiatric, and developmental conditions in LPT and ET infants as they age into adulthood (Table 3). Young adults born LPT and ET also demonstrate increased risks for social challenges. (61) LPT and ET infants have significantly lower educational achievement and employment while more often receiving social welfare, having a disability, and more frequently living with their parents.

SUMMARY

LPT and ET births account for a large number of births annually in the United States and other developed countries. The causes of such early births are similar to those of more preterm infants, so prevention strategies are generally similar: progesterone and cerclage placement in high-risk women, birth interval planning, smoking cessation, preterm birth clinic participation, and others. The major exception to prevention of LPT and ET birth versus more preterm births is defining and targeting nonindicated births. In recent years, efforts to minimize such nonindicated LPT and ET births have been very successful.

Complications arising from LPT and ET births affect both acute and long-term outcomes. Acute medical complications, especially those in the respiratory, thermoregulatory, metabolic, and breastfeeding realms, are frequent causes for NICU admission, with the frequency increasing at the lower gestational ages of 34 and 35 weeks. Long-term outcomes, even in healthy LPT and ET infants, are also affected by immaturity and the underlying pathobiology of early birth.

The risks of subnormal long-term outcomes in neurodevelopment, cognition, education, behavior, psychiatric health, and social health are higher in LPT, and likely ET, births compared with term births, though most individuals born LPT and ET are competitive with their term counterparts. These outcome differences are important because of the sheer number of LPT and ET births with subnormal outcomes that affect the medical, emotional, and financial health of the individual, the family, and the local and national community. Therefore, efforts to reduce the costs associated with individuals born LPT and ET with subnormal outcomes by preventing their early births, when feasible, remain an important priority.

TABLE 3. **Neurologic, Psychiatric and Developmental Disorders in Adult Late Preterm Infants**

NEUROLOGIC AND PSYCHIATRIC CONDITIONS	RELATIVE RISK OF LPT VS TERM
Attention-deficit/hyperactivity	1.7 (1.2–2.5)
Any psychiatric disorder	3.74 (1.59–8.78)
Any anxiety disorder	3.85 (1.52–9.52)
Cerebral palsy	2.7 (2.2–3.3)
Cognitive disability	1.6 (1.4–1.8)
Schizophrenia	1.3 (1.0–1.7)
Any disorder of psychological development, behavior, and emotion	1.4 (1.3–1.5)

Adapted with permission from Moster D, Lie RT, Markestad T. Long-term medical and social consequences of preterm birth. N Engl J Med. *2008;359(3):262–273.*

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the pathophysiology and risk factors for RDS.
- Know how body composition changes during postnatal growth and development and understand the effect of prematurity.
- Know the risks of neurodevelopmental impairments in term infants, late preterm infants, moderately preterm infants, and extremely preterm infants, with and without neurologic risk factors.

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Parent Resources from the AAP at HealthyChildren.org

- Reduce the Risk of Birth Defects: https://www.healthychildren.org/English/ages-stages/prenatal/Pages/Reduce-the-Risk-of-Birth-Defects.aspx
- Social & Economic Factors Associated with Developmental Disabilities: https://www.healthychildren.org/English/health-issues/conditions/developmental-disabilities/Pages/Social-Economic-Factors-Associated-with-Developmental-Disabilities.aspx

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