Late Preterm and Early Term Birth—At Risk Populations and Targets for Reducing Such Early Births

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Disclosures: The authors have nothing to disclose.

Key words: late preterm, early term, late term, morbidity, mortality, outcomes

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Educational Gap(s)

- Awareness of the etiologies of late preterm and early term delivery, and strategies available to safely prevent such preterm deliveries
- 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 full term.

Learning Objectives

- Describe the causes of late preterm and early term birth and targets of prevention
- Describe the reasons for delivery prior to full term
- Identify the short term morbidities associated with late preterm and early term birth
- Recognize the long term neurocognitive consequences of late preterm and early term birth

This is the author's manuscript of the article published in final edited form as:

Kardatzke, M. A., Rose, R. S., & Engle, W. A. (2017). Late Preterm and Early Term Birth: At-risk Populations and Targets for Reducing Such Early Births. NeoReviews, 18(5), e265–e276. https://doi.org/10.1542/neo.18-5-e265

Abbreviations:

LPT: Late preterm

ET: Early term

Introduction and Background

Preterm birth is an important public health matter as it accounts for $26.2 billion in health care expenses each year, and is the most frequent cause of infant mortality in the US. 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 to 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 (Figure 1) with an estimated 327,133 LPT births per year in the US [2]. Late preterm births also account for 9.8% of all infant deaths. In 2008 the infant mortality rate in late preterm infants was 3.6 times that of term infants and accounted for 2753 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 late-preterm birth has led to investigations of the etiologies, long-term outcomes, and optimal management of late-preterm infants [4-6]. These reports revealed long term implications of late preterm *and early term* (37 to 38 weeks of gestation) birth including influences on respiratory, cognitive, social, and cardiovascular outcomes with some studies spanning into the 7th decade of life [7].

Increased awareness of the risks of late preterm birth led to educational and policy efforts to reduce non-medically indicated preterm birth. From 2006 to 2013 the rate of preterm birth decreased from a peak of 12.8% to 11.4%, with 82% of the reduction due to 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 prior to 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 neccessary to limit unnecessary LPT and ET births while providing optimal care to such infants when birth before full 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 late preterm and early term 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 weeks and 0/7 days through 36 weeks and 6/7 days of gestation (Figure 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 policy makers to refer to this population more consistently. However, the categorization is 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 (Figure 3) associated with birth in each week prior to 39-40 weeks of gestation, a multidisciplinary workgroup met in 2013 to further categorize the description of births after 37 weeks and 0/7 days gestation. This group defined "early term" as birth between 37 weeks and 0/7 days through 38 weeks and 6/7 days, "full term" between 39 weeks and 0/7 days through 40 weeks and 6/7 days, and "late term" between 41 weeks and 0/7 days through 41 weeks and 6/7 days [10].

Etiology of Late Preterm (and Early Term) Birth—Targets for Prevention

Late preterm and early term births are not caused by a single entity, but instead are a common endpoint caused by a heterogeneous group of conditions in both mother and fetus (Figure 4). Examples of factors that contributed to an increase in late preterm infants, and likely early term 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
- Early delivery of 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 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 babies. Increased surveillance facillitates the early detection of findings that could have implications for the health of the mother or the fetus before life threatening events occur. Prior to 2005, fear of risks associated with abnormal findings on surveillance screening, combined with lack of recognition of the morbidities and mortality risks of late preterm and early term infants 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 late preterm and early term births has led to lower rates of such births. Because many deliveries of LPT/ET infants occur 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 2/3 of preterm births are "spontaneous" with the remaining 1/3 being the result of medical intervention [11]. Spontaneous LPT birth can be further categorized as spontaneous labor or premature preterm rupture of membranes (PPROM). 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 provided an overview of strategies currently available in high-resource settings aimed at preventing preterm birth (Figure 5). While not specifically directed toward LPT/ET births, the general strategies presented may be applicable to such births. In addition to limiting non-medically indicated elective LPT/ET births, the two 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 the prevention of preterm birth. While the mechanism by which it prevents preterm birth is unclear, progesterone therapy for women with a prior history of spontaneous preterm birth has been shown to reduce mortality (RR 0.5, 95% CI 0.33 to 0.75), preterm birth less than 34 weeks of gestation (RR 0.31, 95% CI 0.14 to 0.69), preterm birth less than 37 weeks of gestation (RR 0.55, 95% CI 0.42 to 0.74), and admission to NICU (RR 0.24 (0.14 to 0.40) [13]. While 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 on ultrasonogram. A metaanalysis by Romero et al showed that progesterone in women with a sonographic short cervix (<25mm) is effective at preventing preterm delivery at <35 weeks gestation (RR 0.69, 95% CI 0.55 to 0.88), although the effect was not present when considering prevention of preterm birth <37 weeks (RR 0.89, 95% CI 0.75 to 1.06) [14]. While cervical length screening has yet to be tested on a large scale and is not currently recommended by the American College of Obstetricians and Gynecologists, 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 <15mm, cervical cerclage has been shown to reduce the outcome of preterm birth <35 weeks (OR, 0.23, 95% CI 0.08 to 0.66), and for those with cerclage for women with cervical length <25mm cerclage significantly reduced the secondary outcome of preterm birth <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 first trimester ultrasonography be used for identifying gestational age as in most pregnancies this will be the most accurate measure, with the exception of pregnancies resulting from in vitro fertilization. When first trimester ultrasonography is not performed, the best clinical estimate based on the LMP and/or second or third trimester ultrasonography is recommended for gestational age dating. Changes to the estimated due date should only occur 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 there is an increased risk of monozygotic twinning with IVF. In addition, women older than 30 years of age are at higher risk of having twins or other higher multiple fetuses during a pregnancy [18]. With greater numbers of pregnancies in women beyond 30 years of age, it is understandable that more multiple births are occurring.

Since prevention of preterm birth must be multi-faceted to address the many key contributing drivers, dedicated preterm birth prevention clinics have been proposed to provide specialized and up-to-date expertise on prevention of preterm birth for women with a history of preterm delivery. The services provided by these clinics is variable, but a large scale implementation of this care showed a rate of preterm delivery of 7.4% vs 9.1% ($p < 0.05$) for women receiving care in a preterm birth prevention clinic and standard prenatal care respectively [19]. These clinics provide a setting for providing progesterone therapy, cervical cerclage, tobacco use reduction, and subsequent birth planning to optimize birth interval spacing. Since stress has been associated with preterm birth, 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 non-medically indicated induction of labor has been a focus for improvement in the decade since the NICHD workshop increased attention to the LPT population. Several reports describe quality improvement efforts aimed at reducing induction of labor prior to 39 weeks without an indication [20-23]. Successful strategies include education of physicians and nurses, with or without a "hard stop" where induction prior to 39 weeks and 0/7 days requires authorization from a chain of command, or a "soft stop" where compliance depends on individual clinicians but all elective deliveries <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 without an increase in stillbirths. A goal rate of 5% elective delivery prior to 39 weeks has been suggested as a national quality benchmark, and this has been shown to be possible in diverse hospital systems [20, 23].

Family education and involvement in delivery planning is also important for reducing non-medically 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 late preterm and early term births. This approach of parental education can help families partner with their healthcare 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 non-medically indicated preterm delivery an uncommon event.

Indicated Late-Preterm Birth

Despite the increased morbidity and mortality of LPT birth, there are indications that merit delivery prior to term in order to prevent maternal complications, stillbirth, neonatal death, and neonatal morbidity. However, Gyamfi-Bannerman et al. found that 56.7% of LPT births analyzed were "non-evidence based" [24], 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 "Timing of Indicated Late Preterm and Early Term Births" [25]. During 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 Late Preterm and Early Term Births

Late preterm and early term infants are physiologically and metabolically less mature than late term infants. Although many such infants have few or no complications of early birth, the risks of morbidities increases 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 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 lowest risk 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 late preterm and early term infants than in those born at term gestation [29]. For example, bag mask ventilation was provided in 14% of late preterm infants versus 6% of term infants (OR 2.61, 95% CI 2.14 to 3.17).

Early Respiratory Morbidity

Infants born LPT or ET are at increased risk for multiple early morbidities following delivery. While it is apparent that overall morbidity, as measured by NICU admission, is higher among babies born at earlier gestations, it is important to recognize that the inverse relationship between gestational age and NICU admission remains until 39 to 40 weeks gestation. Of babies born at 34, 35, and 36 weeks gestation 67.4%, 42.4%, and 22.1% are admitted to the NICU respectively. Importantly, infants born early term continue to have an increased rate of NICU admission at 11.8% and 7.2% at 37 and 38 weeks respectively compared to those born at full term (39-40 weeks) of 6.1-6.6% [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 (Figure 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%), reflective of the lower pulmonary reserve in the late preterm neonatal population [31]. Apnea of prematurity is also more frequently found in late preterm neonates (4 to 7%) compared to term neonates (1 %) [32, 33].

Cheng et al analyzed the gestation-specific risk of respiratory distress syndrome and mechanical ventilation in early term versus late term neonates in a cohort of over 2 million pregnancies with live, singleton fetuses in cephalic position [34]. Although the absolute risk of respiratory distress syndrome and treatment with mechanical ventilation were low (0.57% at 37 weeks of gestation versus 0.32% at 38 weeks versus 0.28% at 39 weeks), the risks are significantly different at both 37 weeks (Adjusted Odds Ratio 2.20, 95% confidence interval 1.88 to 2.18) and 38 weeks (Adjusted Odds Ratio 1.15, 95% confidence interval 1.08 to 1.23) compared to 39 weeks of gestation. Despite the low absolute risk, the large volume of deliveries at these gestations nationwide translates into 2 to 3 thousand cases of respiratory distress syndrome and need for mechanical ventilation each year. These cases are particularly significant because this data applies to low risk neonates without other complications.

In a recent multicenter, randomized trial, Gyamfi-Bannerman et al 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% versus 14.4%; relative risk 0.80; 95% confidence interval 0.66 to 0.97], and reductions in severe respiratory complications, transient tachypnea of the newborn, surfactant use, and bronchopulmonary dysplasia. While there was more neonatal hypoglycemia in the betamethasone treated group compared with placebo, there was no difference in chorioamnionitis or neonatal sepsis [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 late preterm infants requiring treatment during the initial birth hospitalization include temperature instability, low blood glucose, requirement of intravenous infusion, jaundice, and feeding problems (Figure 7). These morbidities are all significantly more common in late preterm infants than in full term infants [32].

The duration of the birth hospitalization, like morbidities and mortality, correlates with gestational age [36, 37]. Mean length of stay in a single center report on 235 late preterm 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' gestation versus the usual length of stay for term infants following vaginal delivery of 2 days and following cesarean delivery of 3 days. In this same group of late preterm 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 late preterm infants (4.3%) than term infants (2.7%) [38]. Readmissions are 3-fold higher in late preterm infants who were never in neonatal intensive care than term infants never in neonatal intensive care corroborating the physiologic and metabolic immaturities of late preterm, and by extension early term, neonates [39]. Such readmissions most often are related to jaundice, feeding problems, proven or suspected infection, and breathing problems. Risk factors for late preterm readmission, in addition to care in a normal nursery with short duration of initial hospitalization, include primigravida mothers, first born, 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 late preterm neonate readmissions.

Breastfeeding Morbidity and the Late Preterm Infant

The benefits of exclusive breastfeeding is well recognized and both the World Health Organization (WHO) and American Academy of Pediatrics (AAP) recommend exclusive breastfeeding through 6 months of age. Despite this, LPT infants are less likely to have breastfeeding initiated compared to term infants (70.4% vs 76.5%), and much less likely to continue breastfeeding compared to term (54.6% vs 64.1%) [40]. The reasons for this discrepancy are multifactorial including early separation of mother and baby, maternal illness limiting breastfeeding ability, and physiologic immaturity (Table 2). This physiologic immaturity as compared to term infants is manifested as lower muscle tone, less frequent awakening, fewer feeding cues, and an increased likelihood of falling asleep with feedings. Additionally, LPT infants can have difficulty with latch due to 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].

In order to promote breastfeeding initiation and continuation, an approach focused on the specific needs of the LPT infant is required. To this point, Nyqvist et al provided an expansion of the WHO and UNICEF's Baby-Friendly Initiative aimed at the particular needs of the LPT infant, as the original Baby-Friendly Initiative focuses primarily on the well, term mother-infant dyad. 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 prior to initiation of feeding 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. This is in contrast to recommendations for term infants where pacifiers are recommended by some experts to be deferred until breastfeeding is firmly established at 3 to 4 weeks of age. Nyqvist also emphasizes adequate parental support including access to lactation services and peer support and close post-discharge 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 (NG) feedings and on average take 2 to 3 weeks to attain full oral feedings. At 35 to 36 weeks of gestation 78% receive NG feedings and take approximately 1 week to achieve full oral feeding [43]. For moderately preterm infants with the majority of their feedings (>/= 80%) being human milk, it has been shown that supplementation with a powdered human milk fortifier provides improved linear and head growth. Although it is unclear what impact non-supplemented feeding of human milk has on LPT infants, there should be close attention to the growth of LPT infants before and after discharge to ensure adequate nutritional intake [44], as the LPT infant 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 LPTI, accounting for 41% of such admissions [45].

Late morbidity and mortality associated with late prematurity

LPT infants have increased morbidities compared to term infants, and these may persist following the neonatal period and well into adulthood. A common theme reoccurs in outcomes of late preterm infants who have relatively low absolute percentages of affected individuals but significant relative risks; 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 for hospitalization for RSV (2.5% vs 1.3%) and once admitted have a longer LOS (3 vs 2 days) than term infants [46]. Respiratory morbidity has been tracked into childhood with LPT infants being at increased risk for requiring asthma medication at 5 years of age (OR 2.2, 95% CI 1.6 to 3.1), asthma at any time (OR 1.7, 95% CI 1.4 to 2.0), wheeze or asthma at 5 years (OR 1.5, 95% CI 1.2 to 1.8), bronchitis/bronchiolitis in the first 3 years after birth (OR 1.64, 95% CI 1.13 to 2), and respiratory symptoms in the first year (22% vs 13%). Compared to 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 late preterm individuals during adulthood for diabetes with any diabetic medication (LPT 1.5% versus Term 1.2%, RR 1.18, 1.04 to 1.33) and insulin (LPT 1.0% versus 0.8%, RR 1.22, 1.08 to 1.39) [48]. Additionally, 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 1924-1944 showed no differences with the general population [50].

A Swedish cohort was analyzed by Crump et al and interestingly showed increased mortality rate for individuals born LPT reoccurs in those who are 18-36 years of age; the hazard ratio for mortality was 1.31 (1.13-1.5) compared to 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 35 weeks of gestation weighing only 60% to 80% of that of the full term brain, and there is significant growth at the macroscopic and cellular level in the last 4 weeks of gestation [52]. Additionally, 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 (DTI) [54]. There may also be long-term structural changes as MRI studies of pre-adolescents and adolescents born late preterm show increased connectivity in the prefrontal and posteromedial cortex compared to term controls. It is unclear whether differences identified in this cohort represent pathology or evidence of compensatory changes as neurocognitive testing showed no differences [55]. However, other studies show an increased risk of developmental delay in those born LPT compared to term (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 [57-59]. Findings of lower educational achievement and neurocognitive scores also have been found in adults born late preterm compared to term indicating the long term impact of late preterm 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 late preterm birth and critical illness, as these factors may lead to worsened outcomes. In order to identify the long term risk of "healthy" LPT infants Morse et al compared LPT infants discharged home prior to 72 hours of age to term controls and found developmental delay or disability was 36% more likely in the LPT infant. Additionally, the 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 late preterm and early term infants as they age into adulthood (Table 3). Young adults born late preterm and early term also demonstrate increased risks for social challenges [61]. Late preterm and early term 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

Late preterm and early term 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 late preterm and early term birth versus more preterm births is defining and targeting non-indicated births. In recent years, efforts to minimize such non-indicated late preterm and early term births have been very successful.

Complications arising from late preterm and early term births impact both acute and long term outcomes. Acute medical complications, especially those in the respiratory, thermoregulatory, metabolic and breast feeding realms, are frequent causes for admission to neonatal intensive care with increasing frequency at the lower gestational ages of 34 and 35 weeks. Long term outcomes, even in healthy late preterm and early term infants, are also impacted 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 late preterm, and likely early term, births compared to term births although most individuals born late preterm and early term are competitive with their term counterparts. These outcome differences are important because of the sheer number of late preterm and early term births that contribute large numbers of individuals with subnormal outcomes that impact the medical, emotional and financial health of the individual, their family and their local and national community. Therefore, continued efforts to reduce the costs associated with individuals born late preterm and early term with subnormal outcomes by preventing their early births, when feasible, remain an important priority.

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