CPQCC
Care and Management of the Late Preterm Infant Toolkit:
Section I: Concept, Care Planning, Gestational Age Assessment, Physiologic Monitoring, Education and Evaluation

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Preamble:

Late preterm infants (LPI) (those born 34 to366/7 weeks gestation) comprise a unique population requiring enhanced awareness and sensitivity to issues of delivery, transition, infection, nutrition, discharge readiness, and parent education that need to begin shortly after birth.

Provisional Best Practice Statement:

Every perinatal unit, regardless of level of care, should implement an organized plan to address the unique physiologic needs and challenges of the late preterm infant.

A growing number of infants are born between 34 and 366/7 weeks gestation, comprising 70% of the preterm population in the United States (Davidoff 2006; Raju 2006; Kamus 2008). Perinatal caregivers should become aware of this population's special needs or risk the consequence of rising morbidity and mortality (Escobar 2006a; Escobar 2006b). Because of their "near term" size and gestational dating, these infants are often managed as full term infants (FTI) with infrequent observation, routine term care, and environments risking hypothermia, hypoglycemia (Laptook 2006), hyperbilirubinemia and rehospitalization (Escobar 2005; Shabnam 2006).

The multidisciplinary healthcare providers who care for late preterm mothers and infants should have an agreed upon plan for assessing the physiologic challenges and heightened risks of such infants. This plan should address universal assessment and management of the following:

1. Assessing gestational age at birth
2. Risk for sepsis (see Section 3)
3. Physiologic Monitoring
4. Respiratory compromise (see Section 4)
5. Initial and ongoing nutritional assessments and support throughout the hospital stay, emphasizing the essential role of human milk feeding (see Section 5)
6. Severe hyperbilirubinemia prevention (see CPQCC Toolkit: Severe Hyperbilirubinemia Prevention 2005)
7. Consultation, transfer, and/or referral for higher level of care, as appropriate
8. Discharge assessment and preparation/parent education
9. Follow-up after discharge
10. Timing of Infant Delivery
11. Practice processes and outcomes evaluation

These issues have recently led to Symposia (Raju 2006) and the publication of collections of articles, such as in the first two issues of the 2006 Seminars in Perinatology and issue 4 of the 2006 Clinics in Perinatology.

1. Assessing Gestational Age:

Care of the late preterm infant requires a competent individual to screen, assess, recognize at-risk situations, implement appropriate interventions, and ensure follow-up. In order to accomplish this, a gestational age assessment should be completed on all newborns to identify late preterm infants at risk for complications. Knowledge gained from the newborn physical assessment findings leads to the identification of a population who would benefit from early intervention and more vigilant observation.

The neonate's gestational age can be estimated from the mother's menstrual history (using mother's last menstrual period or LMP) or the results of an ultrasound examination before 20 weeks of gestation, as well as from the physician's or nurse's assessment of gestational age. Competency in postnatal assessment of gestational age is critical when LMP may be unreliable, early ultrasound may not have been performed, the ultrasonographer may not be that skillfull, or the maternal record may not be available. Any marked discrepancy between the presumed duration of pregnancy by obstetric assessment and the postnatal assessment in the neonate should be documented. Determination of gestational age and its relationship to weight can be used to identify neonates at risk for postnatal complications (ACOG/AAP Guidelines for Perinatal Care, 7th edition).

Clinical gestational age assessment tools have two components: external physical characteristics and neurological or neuromuscular development evaluations (Olds 2000). The physical characteristic components include appearance of the skin, presence of lanugo, plantar surface creases, and amount of breast tissue, ear development and genitalia. Neuromuscular maturity assessment focuses on the determination of tone and angles of resistance, which includes posture, square window, arm recoil, popliteal angle, scarf sign and heel to ear. Ballard and colleagues' (Ballard 1979) estimation of gestational maturity rating is a simplified version of the well-researched Dubowitz tool (Dubowitz 1977). Each component is given a value of 1 to 5 and the total score is matched to a gestational age.

There is no "best" method, and the National Institute of Child Health and Human Development task force stated as a goal, the need to "develop gestational-age specific anthropometric indices for singleton and multiple gestations among different ethnic groups to classify infants into appropriate risk categories" (Raju 2006). Thus, the most reliable test, the goldstandard of gestational age determination, is the early prenatal ultrasound. However, the postnatal assessment is necessary, because of the

aforementioned concerns of having no early prenatal ultrasound or an error in dating. Both the Ballard and the Dubowitz scores were found to have a ± 2 week correlation with the gestational age by LMP. This is a large window, particularly in the late preterm population of 34 - 366/7 weeks gestation. It is essential to choose only one gestational age method, Dubowitz or Ballard, train the staff well and become comfortable with it. The Ballard is more commonly used because it is simpler, faster and easier to do (Sunjoh 2004).

3. **Physiologic Monitoring:**

Hypothermia and hypoglycemia are more prevalent in this population and may persist longer than expected for "normal newborn's transition". A large percentage of LPIs are hypothermic at NICU admission. Wang reported that 10% of LPIs had temperature instability vs. 0% for full term infants (FTI) with OR (odds ratio) approaching infinity(Wang 2004). Additionally, they reported hypoglycemia occurred in 15% LPI vs. 5.3 FTI with OR 3.3. Euglycemia is jeopardized by reduction in glucose-6-phosphatase activity and marginal nutritional intake in the first day of life(Laptook 2006). Laboratory reporting of plasma glucose levels (PGL) average 13% higher than whole blood glucose levels (WBGL). Routine bedside monitoring, using chemstrips or Point of Service devices, often references levels of $\geq$ 45mg/dl as acceptable levels without substantial foundation. While a recent meta-analysis identifies profound hypoglycemia as PGL < 25 mg/dl and associates it with a 21% incidence of neurological sequelae, standards for each delivery center need to be established for acceptable glucose levels (Alkalay 2006). Stabilization of glucose levels in the first 12 to 24 hours of life occurs in the majority of infants; however, bedside monitoring of the at-risk asymptomatic population should be routine(Garg 2006; 77-2011 New AAP guidelines for hypoglycemia).

4. **Respiratory Distress (separate presentation section):**

LPI infants have a 25% incidence of respiratory distress vs. 4.2% in FTI infants [OR 9.14, 95% CI](Wang 2004). The need for oxygen at > 24 hours of life doubles as the gestational age decreases: for the 35-36 week cohort, it is 1.5 %, and for the 34-week cohort it is 3%. (Preliminary CPQCC Data)

5. **Nutritional Support and Optimizing Breastfeeding Success (separate presentation section)**

Considering the high incidence of 75% LPIs whose discharge is delayed due to poor feeding (Wang 2004), an organized approach to mother/baby dyad nutrition is essential for timely safe discharge.

6. **Severe hyperbilirubinemia prevention (see CPQCC Toolkit: Severe Hyperbilirubinemia Prevention 2005);**

The risk of hyperbilirubinemia and/or kernicterus for LPIs is substantial and occurs most likely after discharge of a healthy patient. The odds of readmission for hyperbilirubinemia decreased with advancing gestation; infants <36 weeks (OR 13.2); 36-<37 [OR 7.7] (Maisels 1998). LPIs that were LGA had even higher incidence than the AGA cohort (Escobar 2005; Bhutani 2006). 34% of LPI with kernicterus were LGA and severe neurological sequelae were significantly higher in LPI vs. FTI (Bhutani 2006).

7. **Consultation, Transfer and/or Referral for Higher Level of care.**

The rising incidence of LPI births warrants the necessity to identify these infants (gestational age determination) and recognize as early as possible symptoms of evolving complications. Preliminary CPQCC data indicate that approximately 80-90% of infants at 34 weeks, 30-45% at 35 weeks, and 15-25% at 36 weeks will have entered the NICU for care. Establishing guidelines within each delivery center newborn nursery on the manageable level of complexity of care should be the responsibility of the Pediatric Department (see Appendix A). Additionally, having mutual understanding of these levels of care and appropriate agreements with referral centers is critical to successful provision of safe and timely care.

8. **Discharge Assessment, Preparation and Parent Education:**

Discharging LPIs not only requires that these infants meet reasonable levels of stability for high risk infants (Guidelines for Perinatal Care, 5th edition), but also that their parents have demonstrated and/or verbalized competence and readiness to assume responsibility for their care (see Appendix B1 and B2). The risk of delay of discharge for LPI vs. FTI infants was 7 times more likely in LPIs due to feeding or jaundice issues (Wang 2004).

Routine **hearing screening** for LPIs is strongly recommended and is now mandated by law for all newborn infants in California

Car Seat Discharge Test:
Centers should consider the AAP guidelines for car seat evaluation for those infants born <37 weeks (AAP 1996) but realize the limitations of a normal test which does not mimic the motion factor of the car. Consideration should be given to placing the infant in the back seat in a nearly supine position (as allowed by the car seat manufacturer) with an observant adjacent adult (Narasimhan 2005, Ojadi 2005). It is important to note that there have been no randomized studies to indicate that the car seat challenge test

accurately predicts the risk of adverse consequences while riding in a car seat (Pilley 2006). One meta-analysis that looked at adverse effect of chronic or intermittent hypoxia on childhood cognition found no adverse effect on preterm infants(Bass 2004).

LPIs are high risk infants, not normal newborns, and should not be discharged at < 48 hours (ACOG/AAP Guidelines for Perinatal Care, 5th edition).

9. Follow-Up After Discharge:

Follow-up after discharge should occur at the primary care office within 1-3 days. Healthy LPIs with <4 days of hospital stay have had reported readmission rates of up to 4.8%, and observational visits (ED <24 hours) of 1.3%, with the two most frequent diagnoses being jaundice and infection (Escobar 2005, Shapiro-Mendoza 2006). Jaundice readmissions (63%) occurred 95% of the time at <7 days of age. Infection readmissions were 13% by day 7, and 30% by 14 days of age. Emergency department visits vary by gestational age as well: 34 weeks- 26%; 35 weeks- 21%; and 36 weeks -52%, the most frequent users of the LPI cohort (Shabnam 2006).

Guidelines for Respiratory Syncitial Virus (**RSV) prophylaxis** with Synagis (Palivizumab) may apply to some of these patients if multiple factors are present The American Academy of Pediatrics recommends prophylaxis with Synagis (Palivizumab) for infants born at 32 to less than 35 weeks' gestation (defined as 32 weeks, 0 days through 34 weeks, 6 days of gestation) as follows. (*Red Book: 2012 Report of the Committee on Infectious Diseases.* Pickering LK, ed. 29th ed. Elk Grove Village, IL.)

Limit prophylaxis to infants < 3 months of age at the start of the RSV season or who are born during the RSV season and who are likely to have an increased risk of exposure to RSV, i.e. when at least 1 of the following 2 risk factors is present:

- The infant attends child care: home or facility where care is provided for any number of infants or young toddlers; or
- One or more older siblings < 5 years of age or other children < 5 years of age lives permanently in the same household.

Multiple births younger than 1 year of age are not considered a risk factor.

> Prophylaxis may be considered for infants born at 32 through < 35 weeks' gestation who are born < 3 months before the onset of or during the RSV season and for whom at least 1 of the 2 risk factors is present. Infants in this group should receive prophylaxis only until they reach 3 months of age and should receive a maximum of 3 monthly doses; often only 1 or 2 doses will have been received before 3 months of age. Beyond 90 days of age, hospitalization risk attributable to RSV lower respiratory tract disease is reduced. Palivizumab is not recommended after 3 months of age for patients in this category.

Passive household exposure to tobacco smoke has not been associated with an increased risk of RSV hospitalization on a consistent basis. Furthermore, exposure to tobacco smoke is a risk factor that can be controlled by the family of an infant at increased risk of severe RSV disease, and preventive measures will be far less costly than Palivizumab prophylaxis. High-risk infants should not be exposed to tobacco smoke. In contrast to the well- documented beneficial effect of breastfeeding against many viral illnesses, existing data are conflicting regarding the specific protective effect of breastfeeding against RSV infection. High-risk infants should be kept away from crowds and from situations in which exposure to infected individuals cannot be controlled. Participation in group child care should be restricted during the RSV season for high-risk infants whenever feasible. Parents should be instructed on the importance of careful hand hygiene.

In addition, all high-risk infants and their contacts should be immunized against **influenza** beginning at 6 months of age (Lieberthal 2006).

10. Timing of Infant Delivery :

Prolonging the gestation of LPIs at 34 and 35 weeks may improve infant outcome and reduce costs (Elliott 2003). NICU admission and length of stay (LOS) decline by 50% with each advancing week of gestation. Determining the ideal delivery gestation age based on presenting clinical factors will require further research to avoid compromise to mother and infant Seubert 1999, Jones 2000, Jones 2002) .
Mild stable gestational hypertension, as opined by Barton in a retrospective review of 300 late preterm pregnancies, may be considered an inappropriate reason for delivery (48-2011) (50-2010) (53-ACOG). Neonatal morbidity doubles for each gestational week <38 weeks ?. 9-2010) New evidence suggests that LPI infants " without evidence-based indication for delivery" may experience more ventilator need and higher risk of major neonatal morbidity (Kuehn JAMA 2010;303(12):1129–30). LPIs with mild pre-eclampsia and mature lung profiles who were electively delivered had longer length of hospital stay and similar rates of Respiratory Distress Syndrome (RDS) compared to matched infants who were delivered spontaneously and by clinically indicated deliveries (1-2009). Evidence suggests that, for mothers with premature rupture of membranes (PROM) or placenta previa at 34 weeks gestation, delivery may benefit both mother and child(Naef 1998, Ramsey 2005).

11. Long Term Outcomes:

A growing body of literature raises concern that LPIs may experience issues in later life that may or may not be directly related to morbidity encountered in the NICU (37-2009)(38-2010) (32-2012). Mortality in early childhood and young adulthood of late preterm born infants was higher than for term infants (7-2011).

The increased likelihood of persistent asthma and need for inhaled corticosteroids was more prevalent in LPIs vs term infants (22-2010)(24-2011). One retrospective review from the Early Childhood Longitudinal Study–Birth Cohort showed that LPIs at 2 years of age have poorer neurodevelopment outcomes than term infants (35-2011). (Late preterm infants up to 7 years have poorer outcomes, as suggested by a systematic review, though this review may be compromised by not having matching infants not admitted to the NICU.(36-2011)) LPIs at school age were found to have higher numbers of Individual Education Plans at early school age than term infants (41-2008). Romeo's study (reference?) reinforces the issue that comparing LPIs and term infants at 12-18 months may still need correcting for gestational age (45-2010). A study of normal developing preterm twins identified smaller cerebellum volume trends at 9 years of age compared to term twins; however, it included 32-33 week infants in the graphic calculations. (45-2010)

12. **Practice Process and Outcomes Evaluation**

Successful achievement of multi-faceted, multidisciplinary care activities requires continuing development, education, skills enhancement, monitoring, and reporting back to all involved. Some monitors need to be used only periodically; others may need to be continually used (70-2007) (See Appendix C).

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Care and Management of the Late Preterm Infant Toolkit:

Section II: Late Preterm Infant: At Risk for Sepsis

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Provisional Best Practice Statement: Late preterm infants are at heightened risk for invasive disease with pathogenic organisms. This is due to the increased risk of Group B Streptococcus (GBS) disease with prematurity and the risk of clinical or subclinical chorioamnionitis leading to infection with other pathogens colonizing the maternal genitourinarytract.

1. Known risk factors have been reported that increase the likelihood of invasive infection with pathogenic organisms in this population.
2. Evolving obstetrical management has resulted in a greater awareness and prevalence of late preterm gestation infants.
3. The evaluation of possible sepsis needs to be modified for this population of infants.

I. Risk Factors for Sepsis

Infection is a known factor associated with the increased risk of mortality in late preterm infants. [1, 2, 3] The immunological immaturity of this population of infants is well known. Any pathogenic organism is more likely to cause clinical symptoms and result in more evidence of invasive disease in preterm infants. The early onset sepsis rate in late preterm infants is 4.4 per 1000 live births compared to 0.5-1 per 1000 live births in all infants. [4, 5, 6] Other factors often contribute to the late preterm birth: Preterm Premature Rupture of Membranes (PPROM), chorioamnionitis and potential subclinical intra-amniotic infection responsible for preterm labor with intact membranes.[7, 8, 9]

GBS in Late Preterm Infants

Prematurity has been clearly shown to be a risk factor for early onset GBS disease. Benitz et al[10, 11, 12] showed that this increased risk is progressive with decreasing gestational age. [13] A complicating factor with late preterm infants is that many mothers have not yet had GBS recto-vaginal cultures performed when their late preterm gestation infant is delivered. The revised CDC Guidelines for Prevention of Perinatal GBS Disease provide algorithms for management of mothers with threatened preterm delivery andPPROM. [14]

Recent data still show poor compliance with the Centers for Disease Control and Prevention (CDC) recommendations for managing mothers in preterm labor without GBS cultures on presentation. [15] The important points emphasized in the most recent Guidelines are to obtain a GBS culture at the time of admission, initiate GBS prophylaxis while awaiting the results, and to provide intrapartum antibiotic prophylaxis (IAP) to mothers whose GBS cultures come back positive if they have not yet delivered after the initial acute course of antibiotics. Treatment with ampicillin for PPROM is not a substitute for intrapartum prophylaxis when the delivery occurs after discontinuation of the initial antibiotic course.

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II. Perinatal Management Issues Related to the Late Preterm Gestation Infant

The increase in late preterm births has been shown to be related to several important factors, some resulting from evolving changes in routine obstetrical management. PPROM and the presence of chorioamnionitis are the most import of these factors contributing to the risk of sepsis in the late preterm gestation infant. There are numerous studies and systematic reviews addressing the obstetrical management of these gestations. Common scenarios are:

1. *Preterm labor with intact membranes.* The ORACLE trial[16] and Cochrane Database of Systematic Reviews[17] show a reduction of maternal infection but no benefit and possible increased mortality associated with treatment of this population with prophylactic antibiotics. The evidence in the literature does not support this practice.

2. *PPROM.* The Cochrane Database of Systematic Reviews[18] includes 22 RCTs. The use of antibiotics following PPROM is associated with a reduction of chorioamnionitis, prolongation of gestation up to at least 7 days and the reduction of neonatal morbidity, including infection, use of surfactant, oxygen treatment and abnormal head ultrasound. Antibiotics have a beneficial effect in this scenario.

3. *Induction at 32-34 weeks.* Elective induction for PPROM will theoretically reduce the risk of infection in infants by preventing frank chorioamnionitis. Other risks to the fetus and mother may also be avoided: maternal infection and cord prolapse, along with neonatal morbidity from chorioamnionitis, including Bronchopulmonary Dysplasia (BPD), Cerebral Palsy (CP) and Periventricular Leukomalacia (PVL). These theoretical advantages may be outweighed by complications of prematurity. The question of elective induction versus expectant management has been studied extensively.[19, 20, 21, 22,23] The evidence suggests the timing of elective induction in this population to be optimal at 32-34 weeks, when risks associated with prematurity are minimized relative to those associated with continuation of the pregnancy.

4. *Emergence of Resistant Organisms.* Ampicillin-resistant E. coli has been shown to be an emerging pathogen in the era of widespread intrapartum antibiotic use. Most studies show that the phenomenon is prevalent only in preterm infants, thus the late preterm gestation infant may be at risk. In data from the CDC Emerging Infections Network, Schrag et al showed the increased prevalence of Ampicillin-resistant E. coli in Early Onset Sepsis.[24] In case control analysis, gestation $\leq$ 33 weeks, presence of intrapartum fever and ROM $\geq$ 18 hr were associated with resistant E. coli. Puopolo and Eichenwald, in a retrospective single center cohort study, reported no overall increase in Ampicillin-resistant pathogens causing early

onset sepsis, but the overall incidence of early onset sepsis decreased and the incidence of ampicillin-resistant organisms remained the same, thus the proportion of ampicillin resistant organisms increased. [25] Ampicillin resistance was associated with preterm labor, premature rupture of membranes, and intrapartum antibiotic therapy with ampicillin. These data point to a concern regarding the use of intrapartum antibiotics in preterm infants (especially ampicillin) that must also be taken into consideration when late preterm infants are exposed to antibiotic regimens prenatally.

III. Neonatal Management-Treatment Scenarios

A. *Low Risk.* In asymptomatic newborns, regardless of gestational age, there is insufficient evidence to support the use of empiric or prophylactic antibiotics in asymptomatic newborns. (The only exception is the subgroup of newborns with chorioamnionitis.) Regarding the risk of GBS disease, the CDC recommends that a sepsis evaluation is not indicated when the mother's GBS status is known to be negative or when she has received appropriate prophylaxis for a positive culture. These recommendations do not specify a difference in approach for preterm infants as long as the infant is asymptomatic. [14] (See Figure)

B. *Moderate Risk.* Some moderate-risk situations involving asymptomatic newborns where initiation of antibiotics is not indicated still warrant a higher index of suspicion. These include GBS positive mothers without adequate intrapartum antibiotic prophylaxis or mothers with GBS status unknown. This scenario of unknown GBS status is commonly encountered in the late preterm gestation infant when delivery occurs before the maternal GBS specimen was obtained. Other historical factors are useful in identifying asymptomatic at- risk infants. In a recent nested case-control study of a large cohort of births from California and Massachusetts, Puopolo et al [3] have developed a predictive model of risk for early onset infection based on gestational age, highest maternal temperature and duration of ROM, illustrating the importance of these prenatal factors.

Close clinical observation with frequent physical assessments and vital signs is the most reliable means of detecting the presence of infection in a septic neonate.(Ottolini) Serial CBCs and other ancillary tests, such as C-reactive protein (CRP) may be useful adjuncts in the ongoing evaluation of neonates suspected of or at risk for infection, although these tests have been shown to have limited value in identifying the presence of infection due to the high rate of false positives. They have been shown to be much more useful in documenting the absence of infection in neonates. (Engle 1997, Jackson, Rodwell) The initial CBC and blood culture can also be obtained from cord blood which has been shown in two recent small studies to be a substitute for the CBC and blood culture

obtained from venipuncture in the newborn after birth. [26,27] With further validation of such cord blood studies, there may be a role for such recommendations in the future.

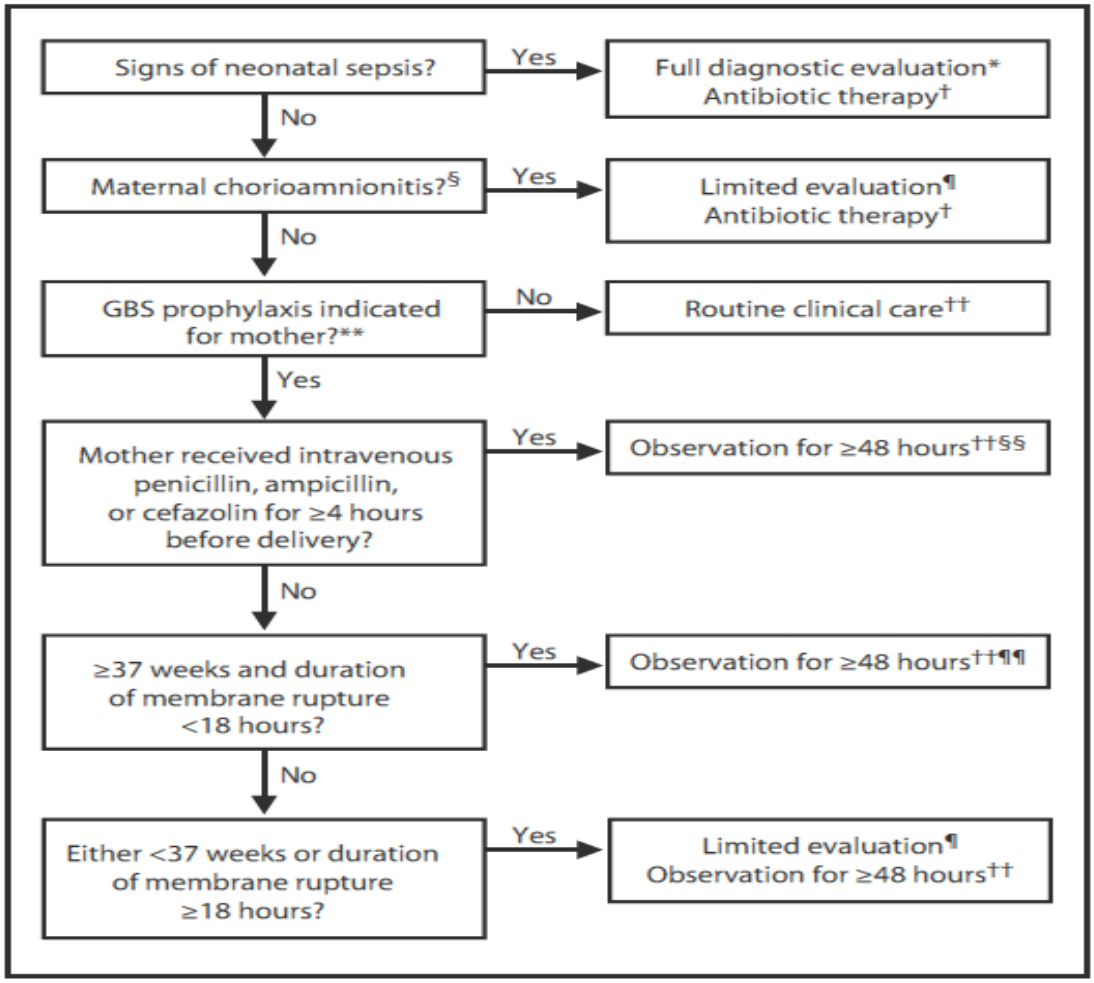
In the scenario when a blood culture is obtained in an asymptomatic infant, and the infant subsequently becomes symptomatic, a blood culture should also be obtained at the time that symptoms appear. Due to numerous retrospective studies showing the incidence of meningitis occurring in the absence of bloodstream infection, a lumbar puncture should be considered when previously asymptomatic infants show symptoms consistent with infection. [28, 29,30] Close observation for the first 24 hours is essential in asymptomatic newborns with risk factors for infection, whether or not antibiotics are started empirically.

C. *High Risk for Sepsis*

1. *Chorioamnionitis* In patients with clinical chorioamnionitis empiric antibiotic therapy is recommended, due to the increased risk of neonatal infection associated with chorioamnionitis.[14, 31] Since initiation of a course of antibiotics will be based on the presence of clinical chorioamnionitis, the diagnosis of this condition should be established upon specific clinical criteria. [32] These usually include maternal temperature > 38.0 C, plus 2 of the following:
    a. WBC count greater than 15,000 cells/mm^3
    b. Maternal tachycardia >100 bpm
    c. Fetal tachycardia > 160 bpm
    d. Tender uterus
    e. Foul-smelling discharge.
2. *Symptoms at birth or developing soon after birth.* Due to the physiologic immaturity of the late preterm birth infant, many symptoms of extra-uterine transition may be exaggerated and raise the suspicion of sepsis. Late preterm birth infants have been shown to have an overall increase in sepsis evaluations due to this immaturity. [33] These infants also have an increased risk of invasive infection with pathogenic organisms justifying the higher index of suspicion for sepsis.[4] Symptomatic late preterm birth infants, even when the symptoms are mild or nonspecific, should be evaluated closely and clinicians should have a low threshold for starting antibiotics after a sepsis evaluation. Again, the role of a lumbar puncture is important to consider in the assessment of these infants when symptomatic, even in the absence of negative blood cultures.

An additional complicating factor is that many of these symptomatic infants are exposed to intrapartum antibiotics due to unknown GBS status of the mother or the presence of chorioamnionitis. The blood culture is often negative in this scenario, making the duration of antibiotics an empiric decision based on the initial degree and duration of symptoms, and ancillary laboratory results. [30] Ongoing surveillance with close clinical observation and frequent vital signs to document resolution of the initial symptoms is critical in identifying deterioration in the infant's status or in making the decision about duration of antibiotic therapy.

Figure: Algorithm for secondary prevention of early onset GBS disease in newborns. (MMWR Recommendations and Reports 2010;59(RR-10): 1-31)



*Full diagnostic evaluation includes a blood culture, a complete blood count and platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

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[†]Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (indluding E. Coli and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

[§]Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

[¶]Limited evaluation includes blood culture (at birth) and CBC with diff and platelets (at birth and/or at 6-12 hours of life).

[**]See Table 3 of CDC 2010 guideline for indications for intrapartum GBS prophylaxis.

[††]If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

[§§]If >37 weeks gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶Some experts recommend a CBC with differential and platelets at age 6-12 hours.

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Care and Management of the Late Preterm Infant Toolkit:

Section II: Late Preterm Infant: At Risk for Sepsis

Richard Powers, MD

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At Risk for Sepsis References

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CPQCC

Care and Management of the Late Preterm Infant Toolkit:

Section III: The Late Preterm Infant: Respiratory Compromise of the Late Preterm Infant

Richard Bell, MD

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Best Practice Statement #1: The team should anticipate the enhanced risks for respiratory compromise in the LPI population.

Physiologic Explanation for Respiratory Compromise with LPI:

Raju et al recently reviewed the multiple physiologic explanations for the increased risk of respiratory morbidities in the LPI. From a structural standpoint, alveolarization occurs progressively during gestation. Beginning at 32 weeks gestation, pulmonary saccules begin to mature into alveoli with dramatic weekly increments so that by term, the number of mature alveoli is nearly 80% of the adult alveolar count. Lung surface area also increases dramatically during the last weeks of gestation. At 30-32 weeks the surface area is 1-2 M^2, increasing to 3-4 M^2 at term (Colin).

Surfactant deficiency is common in the LPI. Around 32 weeks gestation, the surfactant pool begins to increase, followed by a surge in surfactant production at about 35 weeks. During labor, there is a surge in catecholamine levels and endogenous steroids which enhance release of surfactant from the Type II alveolocytes. In late preterm births, these processes are often interrupted, leading to frank surfactant deficiency and clinical RDS.

Clearing of fetal lung fluid is the result of a complex cascade of hormonally mediated physiologic events which begin in the days prior to onset of labor. In the final weeks of gestation, fetal lung fluid production begins to decrease. With the surge in endogenous hormones associated with the spontaneous onset of labor, fetal lung fluid is cleared by both Type I and Type II alveolocytes into the pulmonary vasculature and lymphatic spaces. Because LPIs are often delivered without the benefit of spontaneous onset of labor, this clearance of fetal lung fluid may be delayed and result in Transient Tachypnea of the Newborn (TTN) (Jain, Eaton).

TTN is usually thought of as a benign, short-lived process. It may delay feedings and result in antibiotic exposure, but usually is easily treated with supplemental oxygen without the need for positive pressure ventilation. A small minority of cases, however, may progress to severe, progressive hypoxic respiratory failure requiring inhaled nitric oxide and/or extracorporeal membrane oxygenation (ECMO) treatment. This group of patients was first described in 1992 (Keszler, et al). More recently, a review of the national ECMO registry (Ramachandrappa, et al) documented that the incidence of persistent pulmonary hypertension of the newborn (PPHN) was almost five times higher in LPIs compared to term infants. Furthermore, of those infants who went on to require ECMO, LPIs had a higher mortality rate than term infants requiring the same intervention (OR=2.81, with 95% CI of 2.50-3.16).

Apnea is more common in LPIs compared to term infants. The increased compliance of upper airways and chest wall leads to their collapse with contraction of the diaphragm. This is

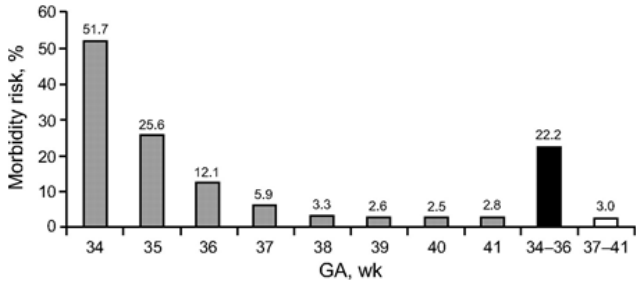
especially true during rapid eye movement (REM) sleep which dominates the total sleep time of LPIs (60%). LPIs also have immature responses to both hypoxia and hypercarbia. Thus, there is a measurable increase in the risk of significant apnea, apparent life-threatening events, and SIDS with decreasing gestational age (Raju).

Incidence of Respiratory Compromise in LPI:

There is irrefutable evidence that late preterm delivery is associated with an increased risk of respiratory morbidity of all levels of severity. A consistent pattern in published data shows that respiratory compromise approximately doubles with each decreasing week of gestation below 39 weeks.

Colin et al recently reviewed published studies between 2000 and 2009 which addressed respiratory morbidities seen in infants between 34 and 36 weeks gestation. Twenty-four papers met their inclusion criteria. The figure below summarizes their cumulative findings on the risk of any respiratory compromise at these gestational ages.

Proportion of infants with neonatal morbidity as a function of GA. Newborn morbidity was assessed by using a combination of indicators on infants' hospital discharge record and mortality data available from death certificates.

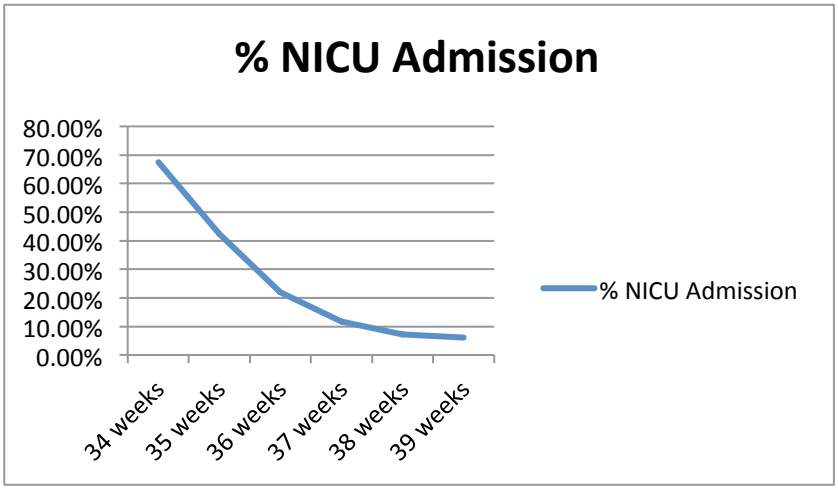


Colin A A et al. Pediatrics 2010;125:115-128

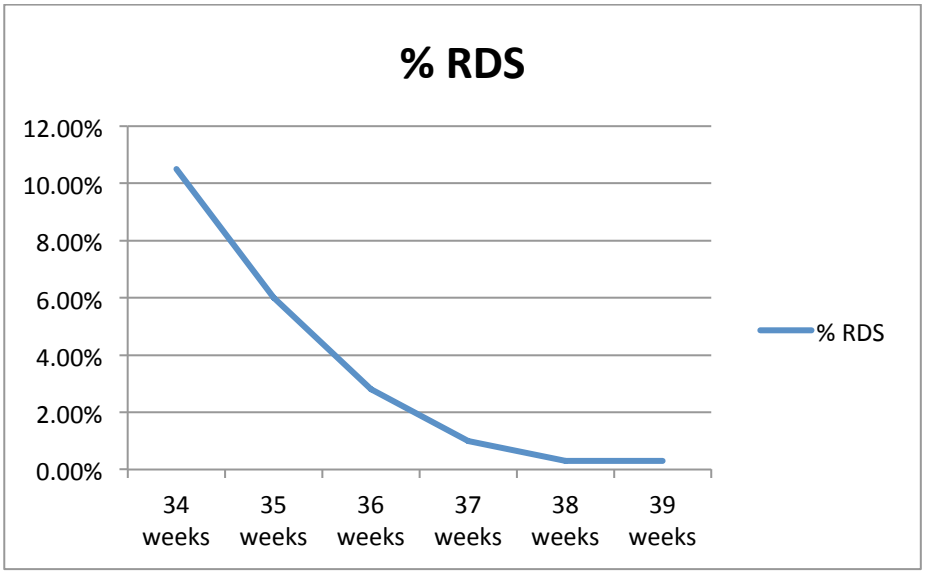
PEDIATRICS

The Consortium on Safe Labor is an initiative of the National Institute of Child Health and Human Development. Recently, the consortium published a retrospective review of the data on almost a quarter of a million deliveries at 19 institutions from 2002-2009 (Hibbard). Of these, 19,334 were late preterm births. These data help shed light on the etiology of the respiratory

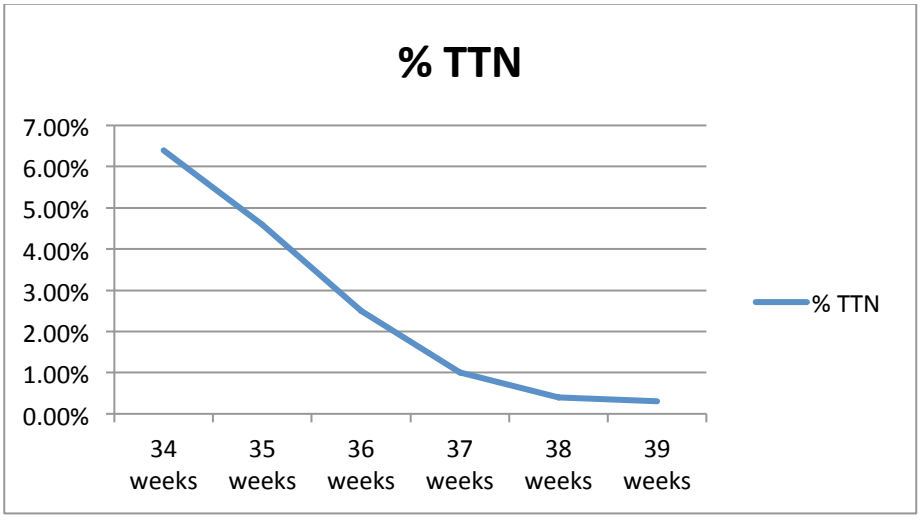
compromise seen in the LPI. While all selected morbidities decreased inversely and significantly through gestational ages 3437 compared to delivery at 39 and 40 weeks, no significant differences were shown at 38 weeks compared to 39-40 weeks. NICU admission rates increased dramatically with decreasing gestational age.



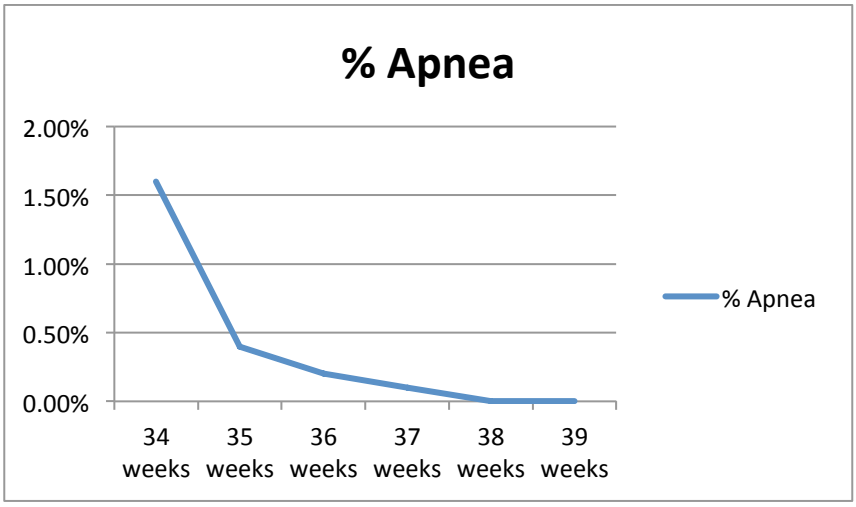
RDS was the most common respiratory morbidity at all LPI gestational ages. The adjusted odds ratio (OR) for RDS at 34 weeks was 40.1 (95% CI 32.0-50.3) compared to 1.1 (95% CI 0.8-1.4) at 38 weeks.



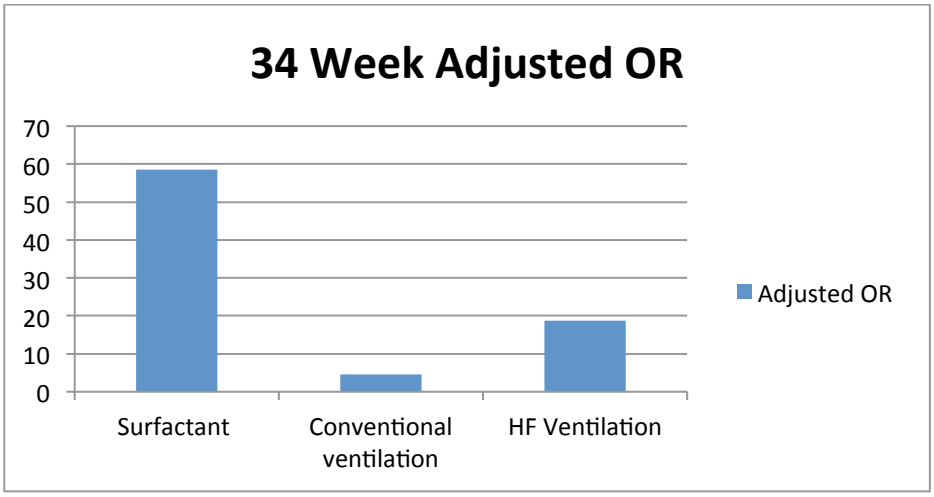
The OR for TTN likewise increased with decreasing gestational age. At 34 weeks, the adjusted OR was 14.7 (95% CI 11.7-18.4)

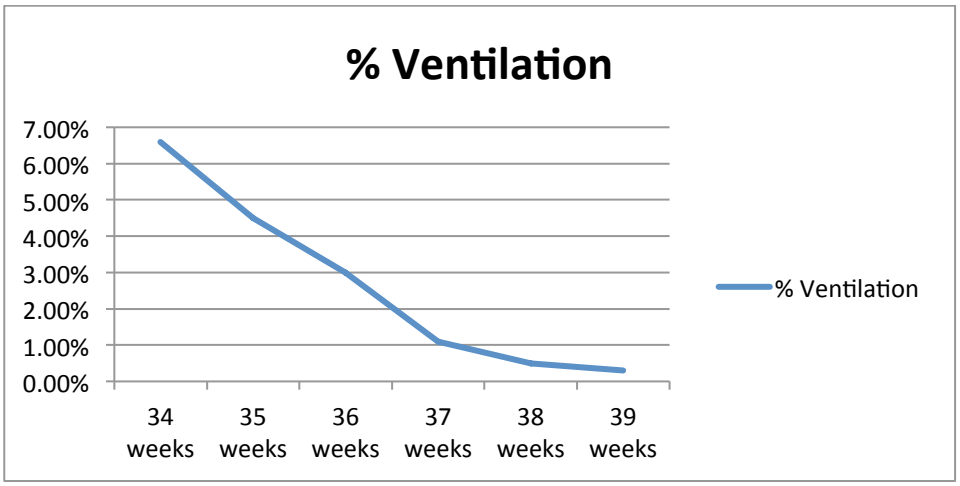


Although apnea was a distinctly uncommon event for LPI, the risk of apnea also increased with decreasing gestational age. There are wide practice variations and not enough data to recommend a universal recommendation. However, the below data suggest the need for careful monitoring of apparently well LPIs for apnea, at least at 34 weeks gestation.



Infants with RDS, TTN or pneumonia required increasing respiratory support . At 34 weeks, the adjusted OR for requiring surfactant administration, conventional ventilation and High Frequency ventilation are illustrated below:

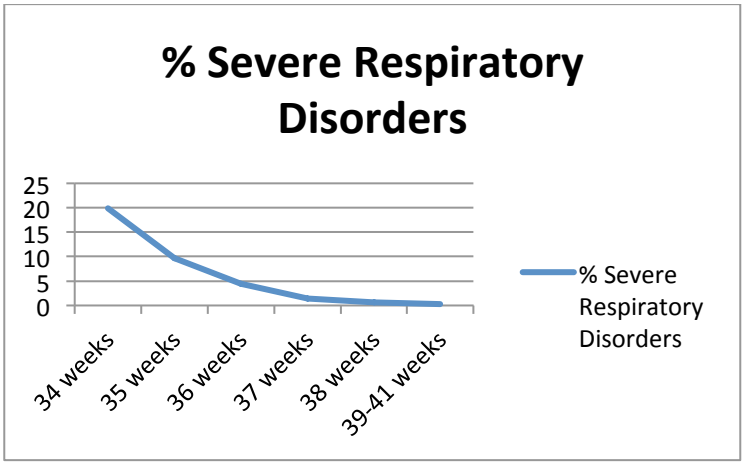




Population based data from British Columbia (Khashu) further confirm the increased relative risk of respiratory morbidities in LPI. This study included a three-year cohort of infants born between 1999-2003. Infants between 33-36 weeks were compared to those at 37-40 weeks. The relative risk of any form of respiratory morbidity was 4.4 (95% CI 4.2-4.6).

Another recent population-based study was published by the Burgundy Perinatal Network in France (Gouyon). Their data, collected from 2000-2008, show the percentage of infants with

severe respiratory disorders (those requiring either mechanical ventilation or continuous positive airway pressure [CPAP]) to increase dramatically and significantly with decreasing gestational age.



Finally, Teune et al recently published a comprehensive systematic review of the incidence of respiratory compromise in LPI. They reviewed 22 studies published from January 2000 through July 2010. These studies included over 29 million infants. As a group, the LPI risk of RDS was 17.3 (95% CI 9.8-30.6) compared to their term cohort. The risk of other morbidities including TTN, pneumothorax, PPHN, and apnea were also increased.

In summary, respiratory compromise in the LPI increases with each week of gestation below 39 weeks. Understanding these increased risks allows for better communication with parents whose infants are threatening preterm birth, and facilitated implementation of systems to recognize and support these infants once delivered.

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Care and Management of the Late Preterm Infant Toolkit:
Section III: The Late Preterm Infant: Respiratory Compromise of the Late Preterm Infant
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Tuene M: Am J Obstet Gynecol 205:374.e1-9 (2011)

Best Statement #2: The team should observe and recognize clinical signs of respiratory compromise to ensure rapid and thorough assessment, diagnosis and management, including consideration of referral to a higher level of care.

A systematic method of assessment of the respiratory status of the LPI is helpful to assure identification of infants at risk for significant respiratory compromise who may require NICU care. This systematic approach should be designed to effectively identify LPIs who require either very close physiologic monitoring or NICU intervention. The need to identify LPIs with respiratory compromise is critical to assure triage to an appropriate level of care both within an institution and between level one nurseries and their referral centers. The location of the method of assessment is not as critical as the consistency of the practice.

Examples of quantitative systematic assessment tools include the S.T.A.B.L.E. course materials (www.stableprogram.org), the Silverman-Anderson score (Askin 2001; see also Appendix D) and the Richardson score (Escobar 2004; Escobar 2006; see also Appendix E).

The Silverman-Anderson score utilizes five characteristics of the clinical respiratory exam to quantify the degree of respiratory compromise in infants (Askin 2001). This approach may be helpful in improving precision of the estimate of respiratory compromise and identifying infants whose clinical conditions warrant at least more careful monitoring, if not NICU admission.

Regardless of whether the scoring technique is used, their clinical basis should be part of nursing practice in assessing infant respiratory compromise.

Kaiser-Permanente has recently published its experience in using a modification of the SNAPII score to identify infants at risk for requiring NICU care (Escobar 2004; Escobar 2006). This tool, which uses basic information available in most nurseries, allows rapid identification of infants likely to require ventilatory intervention. The use of this tool may enable more appropriate anticipation of LPI needs for respiratory support. Because the tool has not been independently validated in NICUs other than where it was developed, CPQCC will defer recommendation at this time. Materials on its status and plans for further evaluation are noted in Appendix E.

CPQCC
Care and Management of the Late Preterm Infant Toolkit:

Section IV: Nutrition and Feeding of the Late Preterm Infant

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I. Have evidenced-based nutritional guidelines specific to the LPI

The Late Preterm Infant (LPI) has been recognized in the past 20 years as a vulnerable infant, at risk for adverse outcomes including suboptimal feeding and poor breastfeeding performance (Raju, Higgins, Stark, & Leveno, 2006). These immature infants likely benefit from the use of mother's milk even more than the term infant (Hallowell & Spatz, 2012). Outcomes such as suboptimal neurodevelopment, increased hospital readmission rates, and Sudden Infant Death Syndrome (SIDS) are more common in this group of infants and may be further compromised by the failure to breastfeed (Eidelman, 2012; Moon, 2011; Shapiro-Mendoza et al., 2006; Eidelman, 2012). Although there are no randomized controlled trials (RCTs) that assess different management strategies for LPIs, feeding should be approached cautiously during these infants' hospital course. Since the release of the 2007 CPQCC Late Preterm Infant guidelines, several studies have been published, updating the knowledge about nutrition in this group of vulnerable babies.

a. **Metabolism** It is known that the LPI is more vulnerable to cold stress and less able to generate heat than the term infant due to poor white and brown fat stores, immature hypothalamic function, a high surface area to weight ratio, and low birth weight. They are at risk for hypoglycemia due to impaired hepatic glycogenolysis and lipolysis, and immature pathways for glucose and ketone generation. These factors, combined with low enteric intake, place the LPI at high risk of hypothermia and hypoglycemia (Engle, Tomashek, & Wallman, 2007; Adamkin, 2011). A review of a cohort of 553 LPIs found that 14.3% had hypoglycemia (glucose < 45 mg%) and 2.5% had hypothermia (temperature less than 36.0°C requiring NICU transfer), 24 times and 4 times higher rate compared to term infants, respectively (Leone et al., 2012). Protecting metabolic stores and providing calories can minimize the risk of hypoglycemia and hypothermia.
   b. **Hyperbilirubinemia** A decreased ability to conjugate and eliminate bilirubin and an active enterohepatic circulation predispose the LPI to hyperbilirubinemia (Engle et al., 2007). Low caloric intake and resultant low urine and stool output further limit bilirubin excretion. Leone found that 47.7% of their group received phototherapy, a 14-fold increase over term infants (Leone et al., 2012). Adequate milk intake minimizes dehydration, reduces enterohepatic circulation of bilirubin, increases passage of meconium, improves stool transition, and minimizes the risk of excessive weight loss, all of which can decrease the likelihood of hyperbilirubinemia.
   c. **Fluid, Calorie and Protein needs** Because many LPIs are as much as one kilogram less than their term counterparts, they may not need intakes designed for term infants. However, increased metabolic needs have led many to recommend supplementation of breastfeeding until the LPI can feed effectively, empty mother's breasts, and mother's milk is abundant ("ABM clinical protocol #10: breastfeeding the late preterm infant (34(0/7) to 36(6/7) weeks gestation) (first revision June 2011)," 2011; Meier, Furman, & Degenhardt,

2007). Fortification of breast milk or use of post-discharge formula in infants >34 weeks and >1800 grams is not generally indicated for the healthy LPI, as these infants can obtain sufficient calories and protein by consuming more volume. (Cochrane review 2012) However, if an infant is very growth-restricted or not achieving adequate growth, fortification of mother's milk or use of a post-discharge preterm formula (22calories) may be indicated. After feeding is established, energy intakes of 105 – 130 Kcals/Kg/ day are usually sufficient to support the growth of a preterm infant (about 50 ml per feeding, 8 times a day for a 2.5 Kg infant). Formula-fed LPIs should receive iron-fortified term or post discharge preterm infant formula; soy formulas are not recommended for preterm or term infants (Kleinman, 2009).

d. **Supplements** *Vitamin D supplementation* is recommended by the American Academy of Pediatrics (AAP). Breastfed infants should receive 400 IU/day of vitamin D starting soon after birth, and continue this supplement until they are weaned to 1000 ml/day of formula or fortified whole milk. Non-breastfed infants who consume less than 1000 ml/day of formula or fortified whole milk should also receive 400 IU/day of vitamin D (Wagner & Greer, 2008). *Iron supplementation* is recommended for the premature infant less than 37 weeks gestation who is human milk-fed. Breastfed LPIs, therefore, should be supplemented with 2 mg/Kg/day of elemental iron, started by one month of age and continued for 12 months. Early on, this will need to be a medicinal iron supplement, but can later be replaced by complementary food. The LPI who receives iron- fortified term infant formula (which contains 12.0 mg of elemental iron per 1000 ml) will be taking in about 2 mg/kg/day. The AAP notes however, that 14% of premature infants will still develop iron deficiency anemia at 4-8 months of age (Baker & Greer, 2010).

e. **Admission and length of stay (LOS)** A recent European study of 530 LPIs documents higher risk for in-hospital morbidity across the board, and twice the duration of hospitalization for the LPI compared to their term counterparts (Leone et al., 2012). A review of 235 LPI newborns in Utah found that only 25% received care in the well baby unit, 62% required a medical intervention, and 40% of babies had a longer hospital stay than the mother (Pulver, Denney, Silver, & Young, 2010). LOS varied by gestational age: 12.6 days for 34 weeks, 6.1 days for 35 weeks, and 3.8 days for 36 weeks. Of the 40% of infants who stayed in the hospital longer than their mothers, rates varied also by gestational age: 75% of 34 weeks, 50% of 35 weeks, and 25% of 36 weeks. A recent large Canadian series found that only 1 in 5 LPIs were stable enough to room with their mothers on the postpartum floor. In their hospital, 83.4%, 62.6%, and 32.7% of 34, 35, and 36 weeks, respectively, required NICU care (Kitsommart et al., 2009). These numbers should make hospital teams reconsider the tradition of treating the LPI as a term infant, with standard admission to the well baby service and short LOS. It is prudent for the LPI to have a period of observation after birth to assure successful transition, observation for medical complications, and demonstration of ability to take in oral feeds safely.

f. **Practical implementation:** Develop a nutrition policy for the LPI:

i. Implement observation period after birth during during skin to skin before joining mother in couplet care (with lower nurse patient ratio) with sufficient time to document physiologic stability in temperature, glucose, and oral feeding ability, as well as providing the opportunity to initiate an appropriate feeding plan
ii. Monitor infant for metabolic complications and jaundice
iii. Encourage human milk feeding and breastfeeding
iv. Provide parents with education regarding the vulnerabilities of the LPI
v. Provide vitamin D and iron supplements

II. Make a feeding plan for infant hospital stay

Several recent studies confirm that LPIs have high rates of feeding problems. Some of these infants may have had other health issues delaying their feeding capabilities, giving us additional information about how long these babies should be watched for development of safe feeding abilities. In a cohort of 235 LPIs, gavage feedings were required in: 50% of 34 weeks, 27% of 35 weeks, and 9% of 36 weeks. Feeding problems were common in another 2009 cohort of 34-40 week infants; occurring in 51% of 34 weeks, 34% of 35 weeks, and 22% of 36 weeks, compared with 2% of babies over 38 weeks (Lubow, How, Habli, Maxwell, & Sibai, 2009). The age at which LPIs reached 'full feeds' (defined as taking 120 kcal/kg/day by mouth, presumably by bottle) varies between 10 days for 34 weeks, 6 days for 35 weeks, and 3 days for 36 weeks in the NICU (Vachharajani & Dawson, 2009). Since many of these babies will be poor oral feeders, we must be careful about assuming competent feeding behavior in these infants, especially in the most immature LPI.

a. **Feeding capabilities** A third of brain growth occurs in the last 2 months of pregnancy, so not unexpectedly, the LPI may be quite immature in terms of feeding coordination.. Mature-suck-swallow-breathe patterns are not well developed until term. Breastfeeding babies depend on their ability to produce adequate suction pressures to transfer milk, and the LPI is often not capable ofdoing so (Meier et al., 2007). The LPI is therefore at increased risk for breastfeeding problems including poor intake, excessive weight loss, and dehydration (Hallowell & Spatz, 2012; Raju et al., 2006). Lastly, poor milk withdrawal from the breast may in turn lead to decreased milk production, thus putting both mother and baby at risk for problems.
b. **In-hospital support** To date, there have not been anyRCTs examining different feeding protocols for the LPI. However, a recent study of feeding data of 138,000 newborns suggested that a higher level of breastfeeding support may be beneficial in the LPI (Colaizy & Morriss, 2008). Overall, mothers of LPIs in the NICU (delivered at 35-37 weeks) were the least likely of all preterm mothers to continue breastfeeding for more than 4 weeks. However, LPIs admitted to the NICU had higher breastfeeding initiation than those who were not admitted to the NICU. The authors hypothesize that these observed effects may be due to

NICU lactation support,which assists mothers in developing an adequate milk supplyand in breastfeeding the immature infant.

c. **Excessive weight loss** Normal term infant weight loss is thought to be ≤ 7%, but little is known about norms in intake, hydration, and weight loss in the LPI. No studies have been done in a cohort of healthy, exclusively breastfed LPIs in the U.S. A recent study from India found that, although the average weight loss was 6% in 35-37-week exclusively breastfed infants, 18% of these infants had ≥ 10% weight loss (Kusuma, Agrawal, Kumar, Narang, & Prasad, 2009). Eleven percent of those with ≥ 10% weight loss were found to be hypernatremic (serum sodium ≥ 150). A recent report of weight loss norms in term infants found that 19% of exclusively breastfed infants lost ≥10% body weight by day 3 of life, a level thought to be indicative of dehydration and inadequate intake (Chantry, Nommsen-Rivers, Peerson, Cohen, & Dewey, 2011). The breastfed LPI may be at even higher risk of excessive weight loss. Recommendations regarding intakes, acceptable weight loss, and parameters for discharge should be made cautiously.

d. Practical implementation: Develop a nutrition policy for the LPI:

i. Emphasize the importance of human milk for the LPI
ii. Assess nutrition daily
    1. Calculate weight loss from birth each day
    2. Assess intake and output
    3. Jaundice assessment: The infant should have at least one bilirubin check during the hospital stay. If other risk factors for jaundice exist (Asian baby, hemolytic disease, bruising, etc.), an additional bilirubin determination prior to discharge is recommended.
iii. Initiate breastfeeding supplementation (specify what to use for supplementation and daily volume guidelines) if medically indicated, as in the following conditions:.(
    1. Hypoglycemia
    2. Hyperbilirubinemia related to poor intake
    3. Intrauterine Growth Retardation (IUGR) baby with low reserve
    4. Excessive weight loss (over 8%) with poor milk transfer
    5. Poor oral feeding before mother's milk is available

III. Encourage and support human milk feeding and goal of exclusive breastfeeding for all LPIs

The benefits of human milk to the preterm infant are impressive (Higgins et al., 2012) (Eidelman, 2012). However, breastfeeding initiation in the U.S. for the LPI is only 60-70%, with the odds of breastfeeding 4 weeks after hospital discharge much lower than their term or more premature counterparts (Radtke, 2011). The particular immaturities of the infant, combined with the risks to maternal milk supply, make this group especially vulnerable. A study of Italian mothers of LPIs found that they are much less likely (21% vs. 81%) than term mothers to exclusively breastfeed at hospital discharge; indeed, most LPIs were being formula- fed at discharge (Zanardo et al., 2011). Therefore, a supportive approach with close observation while the infant is in the hospital is optimal. Helping mother achieve a sufficient milk

supply, helping the infant obtain sufficient calories and fluid, and setting the stage for exclusive breastfeeding when the infant is able are the goals. While many maternity services are working on implementation of the Baby Friendly Hospital Initiative, one must remember that this program is for term infants. The take-home point is that both mother *and* infant have vulnerabilities that can lead to suboptimal milk supply and poor nutritional intake (Meier et al., 2007); (Hallowell & Spatz, 2012).

a. Skin-to-skin care Infant and mother will benefit from early skin-to-skin after delivery, as it leads to better breastfeeding outcomes (Moore, Anderson, Bergman, & Dowswell, 2012); (Eidelman, 2012). However, skin-to-skin care soon after delivery for the premature infant may hold additional risks due to their small size, decreased body tone, and immature protective reflexes if not closely observed. Close observation by staff and discussion with families about proper positioning and monitoring of infant during skin-to-skin care and early breastfeeding are prudent.

b. **Milk production** Recent studies have confirmed that many mothers are not experiencing milk production on what we have always considered as a normal timetable. As many as 44% of mothers experience delayed lactogenesis (Nommsen-Rivers, Chantry, Peerson, Cohen, & Dewey, 2010). Mothers may also have morbidities, which can impact their ability to make milk (Shapiro-Mendoza et al., 2008). A maternal history whichincludes adolescent breast development, breast surgery, breast changes with pregnancy, and previous breastfeeding success should be obtained, and a careful breast examination should be performed.

c. **Infant feeding capabilities** LPIs are known to have problems related to weak suction pressures. Adequate suction pressure enables the infant to stay latched on, remove milk from the breast, and achieve adequate milk volumes. Mothers may perceive the baby as slipping off the breast and not maintaining a good latch. Premature infants who have poor body tone may be difficult to position well and may not wake for feeds, further impairing their ability to transfer sufficient milk quantities (Meier et al., 2007). The LPI should have periodic observations and assessments of feeding by trained staff.

d. **Infant milk transfer** Milk transfer can be assessed by observation of a feeding, mother's pumping volumes, or by weighing the baby before and after a feeding (Kleinman, 2009). Because the LPI is prone to immature feeding behavior, a pre- and post-breastfeeding weight can provide valuable information about milk transfer (Haase, Barreira, Murphy, Mueller, & Rhodes, 2009).

e. **Supplementation** Supplementation with pumped milk or formula should be considered for the infant who is not nursing well, or has metabolic demands not being met by breastfeeding alone. Mother's own milk is always used first, and provides the infant with the benefits of active components. However, if mother's milk production is not meeting those needs, the infant should be supplemented with either pasteurized donor milk or infant formula. Volume of supplementation should be updated daily over the first days of feeding. No studies have addressed the volumes needed in the early days of life by the LPI. But practical experience suggests that, because the premature infant may obtain only small amounts of milk from the

breast, supplementation volumes of 10-20-30 ml per feeding every 3 hours for day 1-2-3, respectively, be provided. ("ABM clinical protocol #10: breastfeeding the late preterm infant (34(0/7) to 36(6/7) weeks gestation) (first revision June 2011)," 2011); (Santoro, Martinez, Ricco, & Jorge, 2010). This correlates to roughly (assuming about 5 ml of colostrum intake per feeding) 40-80-120 ml/kg/day for a 2.5 Kg infant for day 1-2-3. Thereafter, increasing daily feeding volumes by 10 ml (each feeding) may help the infant with weight gain and adequate intake. Ongoing assessment of milk transfer from mother's breast will allow discontinuation of supplementation as soon as mother's milk is abundant and the baby is nursing well.

f. **Feeding plan** The complexity of in-hospital care of mother and baby may lead to inconsistencies in LPI care. Using protocols, crib cards, or care plans to assure team members and parents are on the same page may be of benefit ("ABM clinical protocol #10: breastfeeding the late preterm infant (34(0/7) to 36(6/7) weeks gestation) (first revision June 2011)," 2011).

g. **Practical Implementation:** Develop a breastfeeding policy for the LPI:
   i. Facilitate early skin-to-skin and breastfeeding after delivery (if infant is stable)
   ii. Establish breastfeeding protocol (Meier et al., 2007)
      1. Daily breastfeeding assessment
      2. If the infant is not feeding well for at least 15 minutes every 3 hours, the mother should increase breast stimulation with double electric breast pumping
      3. Infant should breastfeed or be fed pumped milk (or formula) every 3 hours-8 feedings a day
      4. Teach parents breastfeeding positions to compensate for infant hypotonia and facilitate attachment at the breast
      5. Nipple shields may be considered to help offset the problem of weak suction pressure generation by the LPI. These shields help to keep the mother's nipple elongated in the mouth, prevent the baby from slipping off, and allow for supplementation with a tube under the shield if needed.
   iii. Assess mother for risk factors for delayed lactogenesis
   iv. Assess milk transfer (when mother's milk is in) to allow for discontinuation of supplement, formula, and pumping
   v. Address the specific concerns of multiples and feasibility of simplified feeding plan for LPI twins or triplets to prevent maternal exhaustion
   vi. Develop crib cards and/or policies to help keep parents and team members on the same page

IV. <u>Assess discharge readiness for the LPI</u>

The LPI is at increased risk for readmission. A large Kaiser cohort in 1998-2000 showed that readmission occurred in 4.4% of LPIs compared to 2.0% of term infants; 26% of the time this was due to poor feeding (Escobar et al., 2005). This study confirmed the findings of others that LPIs who spend time in the NICU have lower readmission rates. LPIs who had not spent time in the NICU had a 3 times

increased likelihood of readmission compared to those who had stayed in the NICU for more than 24 hours.It is unclear why the NICU stay is protective, but the Kaiser study suggests that close observation during the first days for feeding allows for the identification and treatment of those infants at risk.

The AAP published newborn discharge criteria in 1995 and 2004, and a clinical report regarding LPI care in 2007. However, a subsequent study found that 40% of vaginally born LPIs are still discharged early, before 48 hours of age, in contradiction to the guidelines("Hospital stay for healthy term newborns," 2004), (Engle et al., 2007)(Goyal, Fager, & Lorch, 2011). Even 'healthy' LPIs in a large Massachusetts cohort were found to have a readmission rate of 4.8%, 2/3 of which was for jaundice. These infants were more likely to be firstborn, breastfed, have labor and delivery complications, have public insurance, or to be of Asian/Pacific Island race. Eighty-nine percent of readmitted infants were breastfeeding, although only 70% of all LPIs were breastfed in this cohort (Shapiro-Mendoza et al., 2006). The same investigators found that vaginally delivered LPI (C-section babies having longer LOS) are twice as likely to be readmitted after an early discharge (< 48 hours in hospital) than their term counterparts. These data suggest that this increased risk may be present only in those infants who are breastfed (Tomashek et al., 2006). In summary, discharge of the LPI earlier than 4 days after birth has been found to result in higher readmission rates. Jaundice, suspected sepsis, and poor feeding, which are often interrelated, are the leading causes of readmission (Engle et al., 2007; Escobar et al., 1999).

a. **Discharge readiness** Assuring that the infant is feeding adequately, has sufficient intake, and that weight is stable, or that the infant has gained weight may decrease the rate of readmission in this population. Although specific RCTs do not exist, careful in-hospital observation, monitoring for poor feeding and jaundice, a discharge feeding plan, and close follow-up are prudent in light of these facts. Our 10-year experience with the LPI protocol has led us to recommend that these infants gain weight (15-30 grams) before hospital discharge.
b. **AAP discharge criteria (from 2007 Clinical Report)** Minimum discharge criteria for latepreterm infants (excerpts of feeding/nutritional/metabolic-related bullets only):
    i. Timing of discharge is individualized and based on feeding competency, thermoregulation, and absence of medical illness and social risk factors.
    ii. Latepreterm infants usually are not expected to meet the necessary competencies for discharge before 48 hours of birth.
    iii. At least 1 stool has been passed spontaneously.
    iv. Twenty-four hours of successful feeding, either at the breast or with a bottle, and the ability to coordinate sucking, swallowing, and breathing while feeding has been demonstrated.
    v. Any infant with a weight loss of more than 2% to 3% of birth weight per day or a maximum of 7% of birth weight during the birth hospitalization should be assessed for evidence of dehydration before discharge.

vi. A formal evaluation of breastfeeding, including observation of position, latch, and milk transfer, has been undertaken and documented in the chart by trained caregivers at least twice daily after birth.
vii. A feeding plan has been developed and is understood by the family.
viii. A risk assessment for the development of severe hyperbilirubinemia has been performed and appropriate follow-up has been arranged.
ix. The mother and caregivers have received information or training or have demonstrated competency in the following: expected pattern of urine and stool frequency for the breastfeeding or formula-fed neonate (verbal and written instruction is recommended) (Engle et al., 2007).

c. Practical implementation: Discharge feeding plan (based on AAP and ABM guidelines) to include: (Hallowell & Spatz, 2012); ("ABM clinical protocol #10: breastfeeding the late preterm infant (34(0/7) to 36(6/7) weeks gestation) (first revision June 2011)," 2011)

i. Assess infant for discharge readiness
    1. Is infant more than 48 hours old?
    2. Is infant metabolically stable?
    3. Serum or Tc bilirubin screening in an acceptable range in light of infant's risk factors?
    4. Is infant having 8 good feedings a day?
    5. Is infant taking in sufficient volumes for age?
    6. Has infant gained weight, or is weight stable?
    7. Is family competent to carry out feeding plan?
    8. Is close follow-up available within 1-2 days?
ii. Provide a discharge medical feeding plan
    1. What will the infant be fed with?
    2. How much volume to start with, and how to increase (if supplementing)?
    3. Supplementation methods, if needed, appropriate for gestational age
    4. For bottle-feeding infant (whether human milk or formula feeding), provide guidance about proper bottle-feeding technique
iii. Provide a discharge lactation feeding plan
    1. Breastfeeding assessment/observation
    2. Teach parents signs of adequate intake and milk transfer
    3. Information regarding nipple shield use and weaning
    4. Tips for improving milk transfer
    5. Provide information regarding obtaining a breast pump if needed.
    6. Lactation resources and follow-up/support group
    7. Strategies to transition infant to exclusive breastfeeding
iv. Prescribe nutritional supplements of Vitamin D and Iron; we prescribe multivitamins with iron to all breastfed LPIs to provide both needed supplements
v. Facilitate medical provider follow-up within 1-2 days
vi. Make a Women, Infants and Children Program (WIC) referral if appropriate

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V. Follow nutritional and feeding progression until infant is feeding well and growing appropriately

The reports of increased breastfeeding-related morbidities and the experience of breastfeeding specialists suggests that LPIs are at increased risk for early breastfeeding failure and are less likely to achieve exclusive breastfeeding or any breastfeeding for ≥ six months as recommended by the AAP (Meier et al., 2007) ("Breastfeeding and the use of human milk," 2012). The LPI is usually discharged before term and is often not competent at breastfeeding. It is, therefore, not surprising that most of the post-discharge morbidities in the LPI are related to problems with feeding. Since breast milk is the optimal nutrition for the preterm infant, the task of the outpatient health care provider is not merely to ensure appropriate growth and development, but to support breast milk feeding in the LPI. This requires an awareness of the LPI's specific vulnerabilities, careful monitoring, and the ability to address feeding problems, including maternal factors, that may be adversely affecting breast milk production.

a. **First follow-up appointment** The LPI should be seen by a knowledgeable health care provider within 48 hours of discharge. Current AAP policy recommends the first outpatient evaluation within 48-72 hours of discharge for all newborns; the latter may be too long for the LPI ("Hospital stay for healthy term newborns," 2004) ("ABM clinical protocol #10: breastfeeding the late preterm infant (34(0/7) to 36(6/7) weeks gestation) (first revision June 2011)," 2011). Weekly or even more frequent visits may be necessary. Evaluation in the outpatient setting should include:
    i. Review of mother's medical history, pregnancy, labor and delivery and the infant's hospital course with attention to risk factors such as maternal and infant blood type with Coombs, family history of jaundice, G6PD deficiency, phototherapy, SGA or IUGR, mode of delivery, and postpartum hemorrhage. Feeding progression after discharge should be reviewed, keeping in mind red flags such as falling asleep after a few minutes of breastfeeding, feeding for greater than 35-40 minutes and still acting hungry, less than 4-6 voids/day, and less than 3-6 good-sized transitional or yellow stools/day by 5-7 days of age.
    ii. Exam of the infant should include a naked weight with a calculation of percent of weight loss from birth and since discharge. See inpatient section regarding acceptable weight loss. If the LPI is not discharged early, there should not be significant weight loss after discharge. The infant should gain at least 25 grams per day and be satisfied after a feeding. The exam should include careful attention to jaundice, hydration, tone, level of alertness, and oral anatomy.
    iii. There should be a low threshold for checking a bilirubin (either transcutaneous or blood) and plotting the value on a nomogram with adjustments made for risk factors.

As noted above, bilirubin peaks later in the LPI and may enter a critical zone after discharge, especially if the infant is not receiving adequate enteral feeds (Maisels & Newman, 1998).

iv. Verify that the infant is receiving appropriate supplements, including Vitamin D and Iron (Berglund, Westrup, & Domellof, 2010) (Wagner & Greer, 2008).

v. Plot infant growth on the appropriate growth curve. New premature infant growth curves allow for close monitoring of growth in the important period between birth and 44 weeks, which may be difficult with the WHO curve ("Breastfeeding and the use of human milk," 2012; Olsen, Groveman, Lawson, Clark, & Zemel, 2010) (Fenton, 2003).

b. **Breastfeeding evaluation** A thorough breastfeeding evaluation is critical if the infant is failing to gain weight appropriately, is jaundiced with suboptimal weight gain, or mother is reporting breastfeeding problems. This exam may be performed by the provider , a breastfeeding medicine specialist, or a lactation consultant knowledgeable about the specific vulnerabilities of the LPI. Some LPIs are the size of full term infants and may appear to be breastfeeding well; however, they may not be effectively transferring milk from the breast. The general approach to the LPI who has suboptimal weight gain is to determine whether the problem is a baby problem (inability to transfer milk from the breast), or a mother problem (insufficient breast milk supply), or a combination of the two.

i. The first step is to assess the infant's ability to transfer milk when breastfeeding. Using an appropriate scale designed for test weights and weighing an infant with a dry diaper before and then without changing the diaper after a breastfeeding provides an accurate measure of milk transfer(Scanlon, Alexander, Serdula, Davis, & Bowman, 2002). Infants who are not transferring adequate amounts of breast milk should be carefully examined for contributing factors such as ankyloglossia.

ii. A careful assessment of mother's breast milk supply includes reviewing her medical history for previous breast surgery, breast enlargement during pregnancy and previous breastfeeding experience. If problems exist, a breast exam is needed to evaluate milk production and assess for mastitis, plugged ducts, and nipple trauma. Breast problems need to be addressed promptly. A recommendation to the mother to contact her doctor is usually not sufficient. If the infant's provider is unable to treat the mother, he or she must coordinate the mother's care with someone qualified to treat these problems. Mothers of LPIs may struggle with milk supply issues and need further assistance to develop adequate milk production.

iii. Some infants need to be supplemented via a supplemental nursing system at the breast or bottle feeds after breastfeeding. The supplements should be expressed breast milk, donor milk, or formula if breast or donor milk is not available. We do not generally limit supplement volumes after the infant is three or four days old.

iv. Teach mother techniques to increase milk transfer, such as using breast compressions or a nipple shield.

c. **Transition to breastfeeding** For the LPI, patience and referral to an experienced lactation consultant or occupational therapist may be necessary for the infant to become competent at breastfeeding. Suction pressures sufficient to extract milk are not present until approximately 36 weeks adjusted age in early preterm inifants explaining the problems LPIs have in maintaining an effective latch and slipping off the nipple even when a latch has been established. Techniques for assisting the smaller or hypotonic infant to maintain an effective latch should be taught to the mother by an experienced lactation professional (Thomas, Marinelli, & Hennessy, 2007). The LPI may also be at risk of developing abnormal feeding behaviors. A survey of mothers of late preterm infants demonstrated that 17% of LPI had oromotor dysfunction, 29% had avoidant feeding behavior at 3 months adjusted age and 12% required medical attention for feeding problems by one year of age (DeMauro, Patel, Medoff-Cooper, Posencheg, & Abbasi, 2011). Mothers of LPIs may need extra support. They are more likely to be older (NCHS Data Brief. No. 24. Nov 2009), and may have their own medical problems. Mothers who appear depressed should be referred for evaluation by a mental health provider. The primary care provider should have resources such as peer support groups, Le Leche League, and lactation consultants to whom a mother can be referred.

d. **Practical Implementation: Post-discharge nutrition assessment**

i. "LPI" should be on the top of the infant's problem list.
ii. Recognize that LPIs are at increased risk for feeding problems after discharge.
iii. Modify routine care to anticipate and address vulnerabilities.
iv. Recognize maternal and infant risk factors for suboptimal breastfeeding.
v. Recognize increased risk for hyperbilirubinemia by having a low threshold for checking bilirubin value.
vi. Perform or refer for a breastfeeding evaluation, including evaluating infant's ability to transfer breast milk and mother's ability to produce breast milk.
vii. Have strategies in place to address and treat problems detected.
viii. Ensure careful follow-up (at least weekly) until appropriate infant growth has been attained and the infant's mother is comfortable with the feeding plan.

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Care and Management of the Late Preterm Infant Toolkit:

Section IV: Nutrition and Feeding of the Late Preterm Infant

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