Pediatrician's Role in Caring for Late Preterm and Early Term Neonates

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Objectives

- Definitions of late preterm & early term
- Magnitude of the problem
- Health problems of these infants
- General principals of management
- Prevention

Late Preterm–Definition

Gestational age 34–0/7 to 36–6/7 wk

Earlier they were known as near term

Near Term vs late Preterm

Near Term	Late Preterm
Maturity	Physiologic & metabolic immaturity
Similar risk of morbidity & mortality as in term infants	Higher risk of morbidity & mortality compared to term infants

Term Pregnancy

- Term pregnancy extends from 37-0/7 wk to 41-6/7 wk
- Earlier it was thought that that the outcome is uniform and good across 5 weeks' gestation in term pregnancy

Defining Term Pregnancy

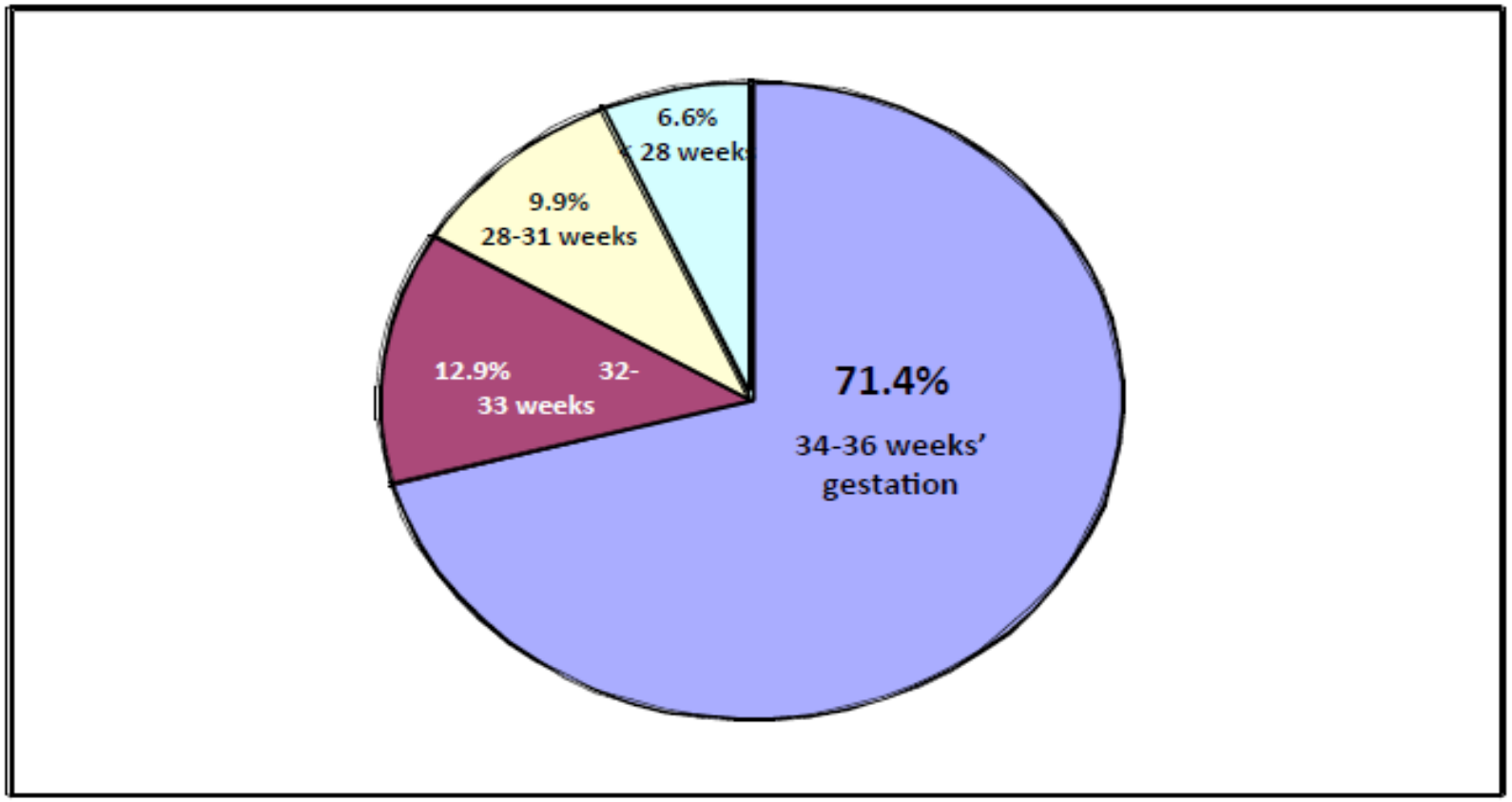
JAMA 2013; 309: 2445

- Early Term: 37 0/7 wk – 38 6/7 wk
- Full Term: 39 0/7 wk – 40 6/7 wk
- Late Term: 41 0/7 wk– 41 6/7 wk
- Post Term: 42 wk and beyond

Morbidity rate (Pediatrics 2008)

Gestation (wk)	Morbidity rate (%)
38	3.3
37	5.9
36	12.5
35	25
34	51.2

Percent distribution of preterm births: United States, 2005



CDC, NCHS final Natality Data 2005

Figure 1. Birth rates at 34, 35, 36, and total 34 to 36 weeks of gestation: United States, 1990–2006

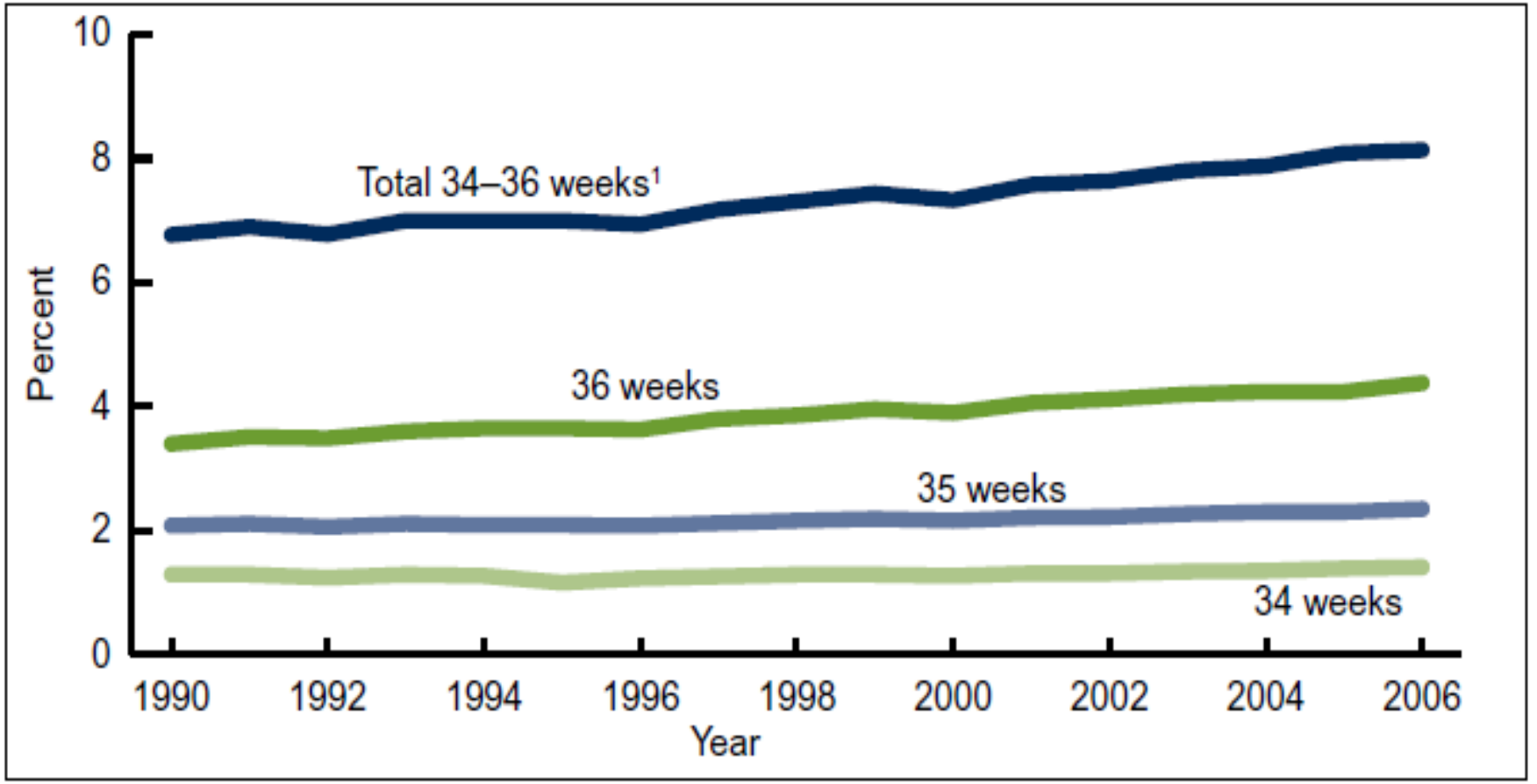


Figure 2. Late preterm birth rates by age of mother: United States, 1990, 2000, and 2006

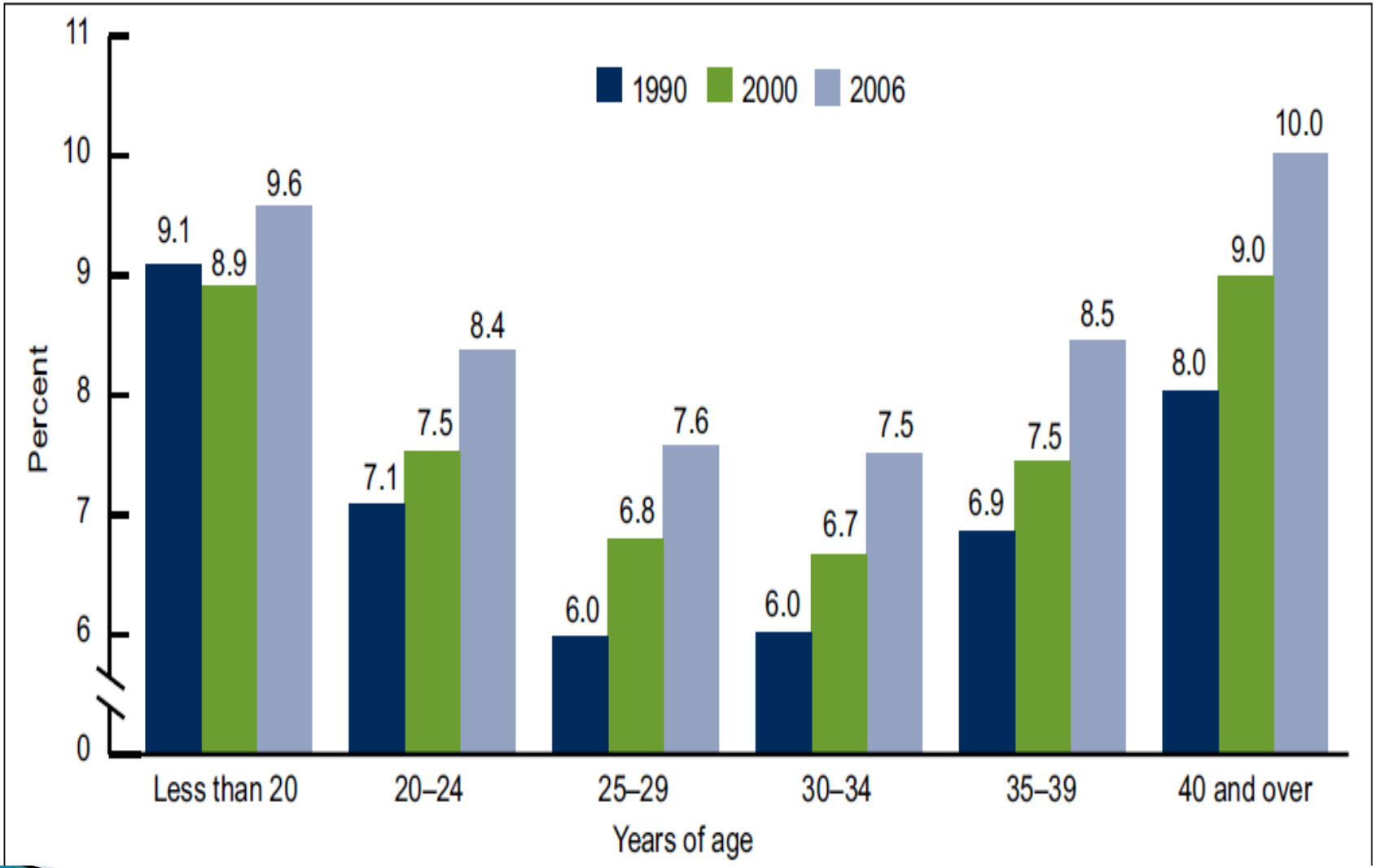
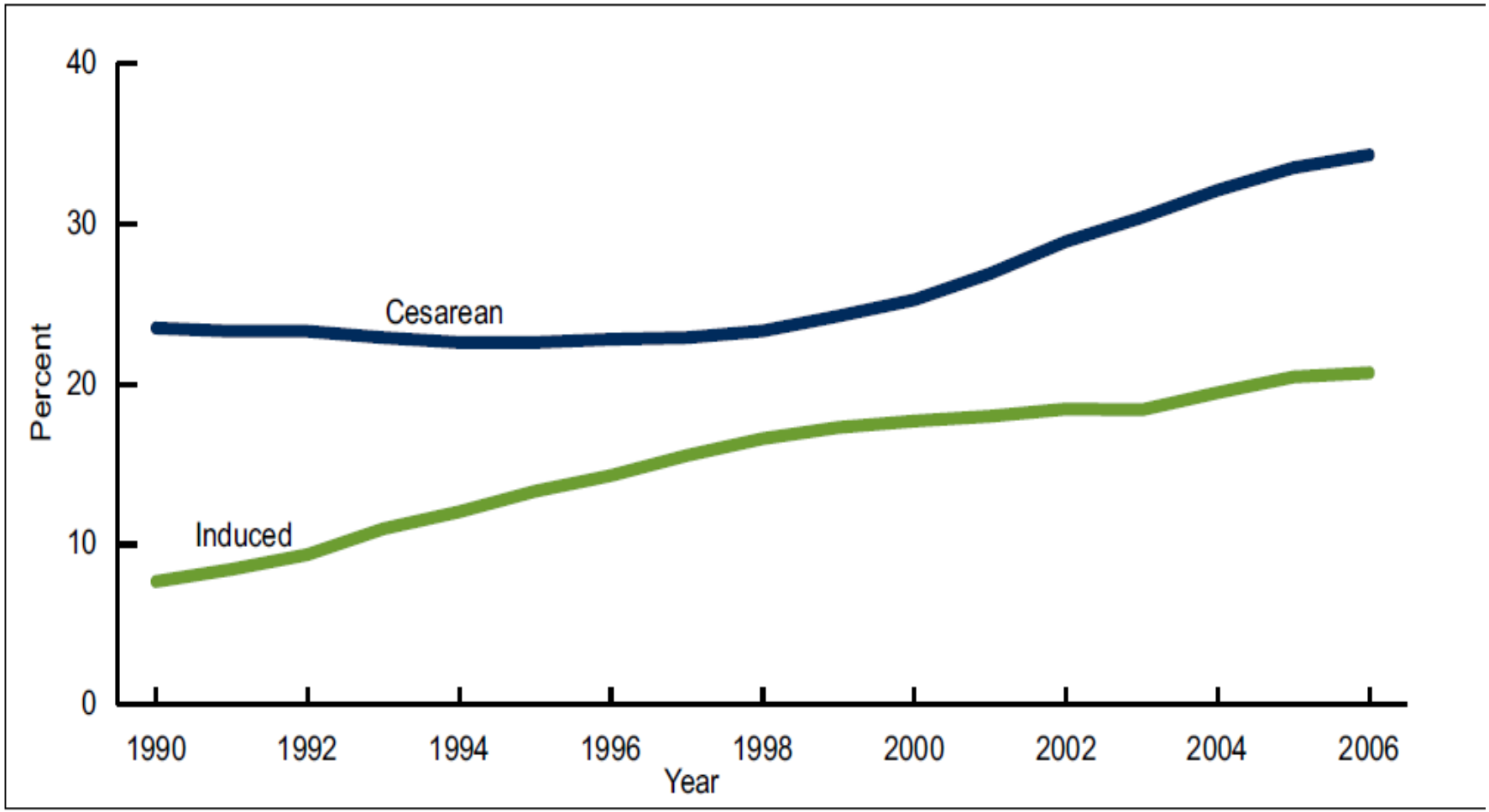


Figure 5. Induction of labor and cesarean delivery rates among late preterm births: United States, 1990–2006



Etiology of Late Preterm and Early Term Births (*Pediatrics 2006;118;1207-14)*

- Increasing maternal age
- Fertility treatment
- Multiple births
- C-section
- Increasing maternal obesity
- Maternal comorbid conditions
- Non medical reasons
- Inaccurate gestational age

Risks of Late Preterm & Early Term Births

NICU admission	Excessive weight loss
Respiratory morbidities- TTN/RDS/Apnea/Respiratory failure	Sepsis
Temperature instability	Neurological morbidities
Hypoglycemia	Longer hospital stay
Hyperbilirubinemia	Hospital readmission
Feeding difficulties	Neonatal and infant mortality

Respiratory Morbidity (JAMA 2010; 304; 423)

aOR

Gest. wk	RDS	TTN	Pneumonia	Resp Failure	Surfactant	Ventilator	Oscillator
39–40	1	1	1	1	1	1	1
38	1.1	1	0.9	1.4	1.1	1.2	0.9
37	3.1	2.5	1.7	2.8	4.8	2.8	2.8
36	9.1	6.1	3.6	6.2	16.1	7.3	7.1
35	21.9	11.1	6.6	4.9	35.2	9.8	12.3
34	41.1	14.7	7.6	10.5	58.5	13.9	18.8

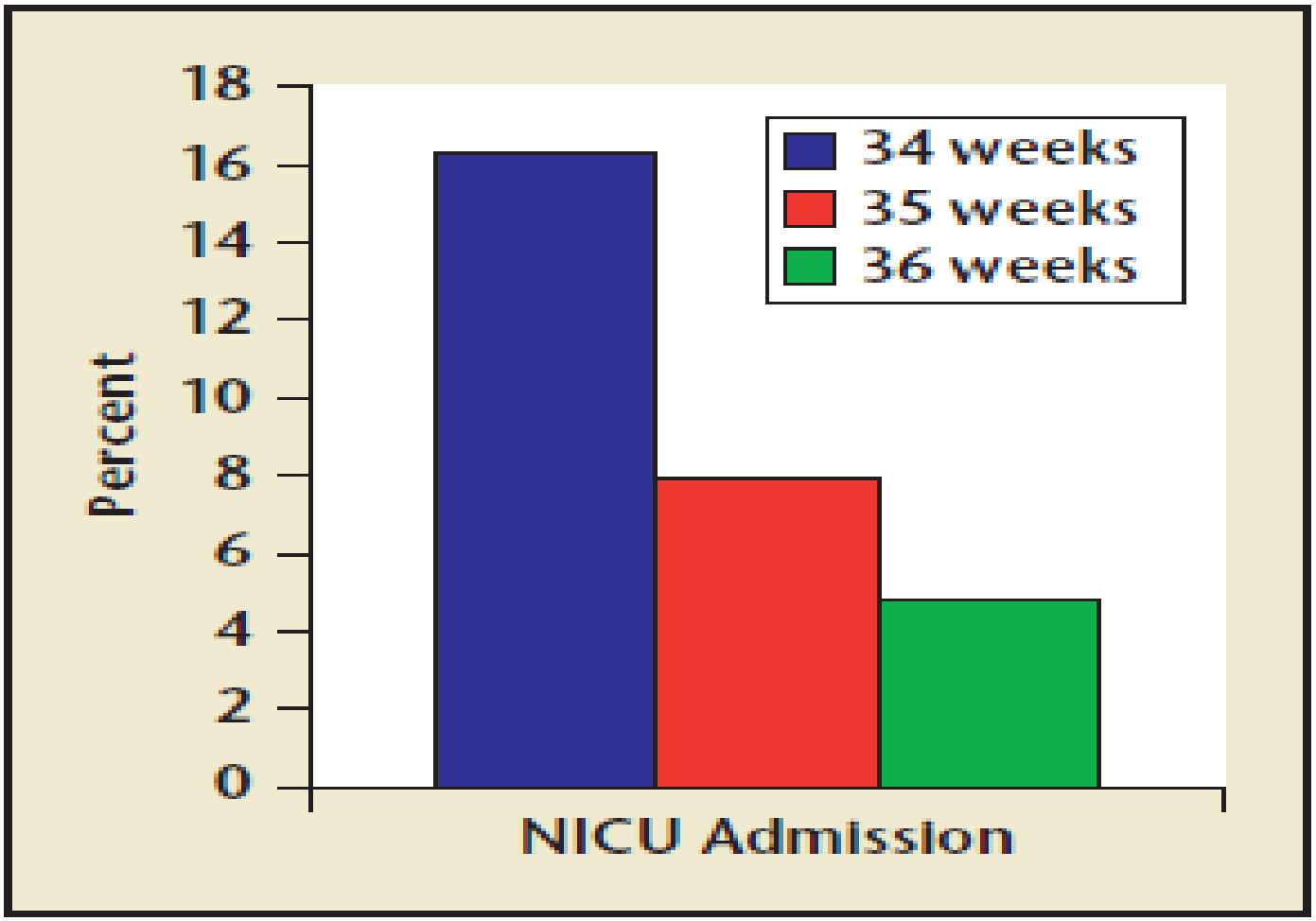


Figure 2. *Rate of neonatal intensive care unit (NICU) admission by gestational age.*

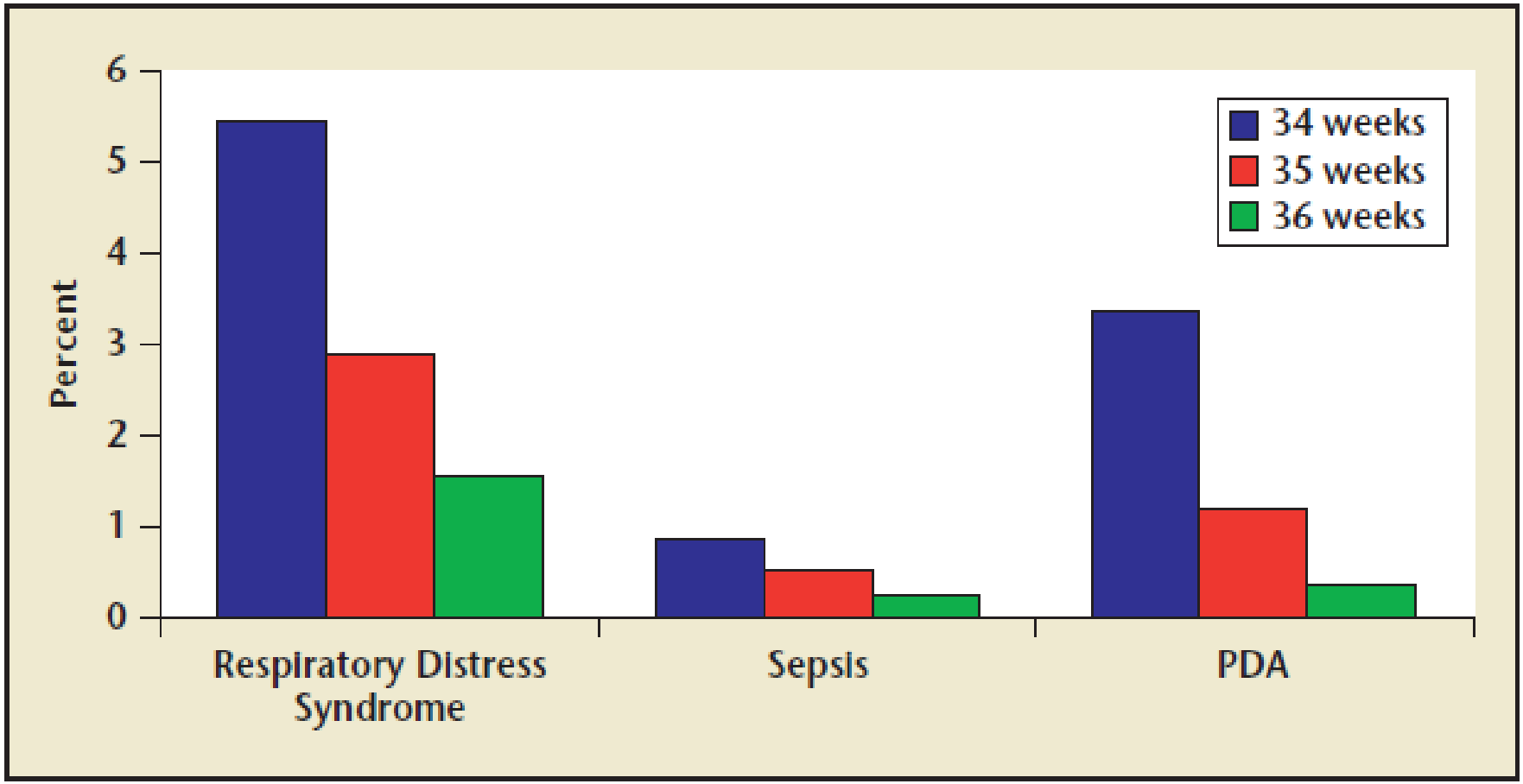
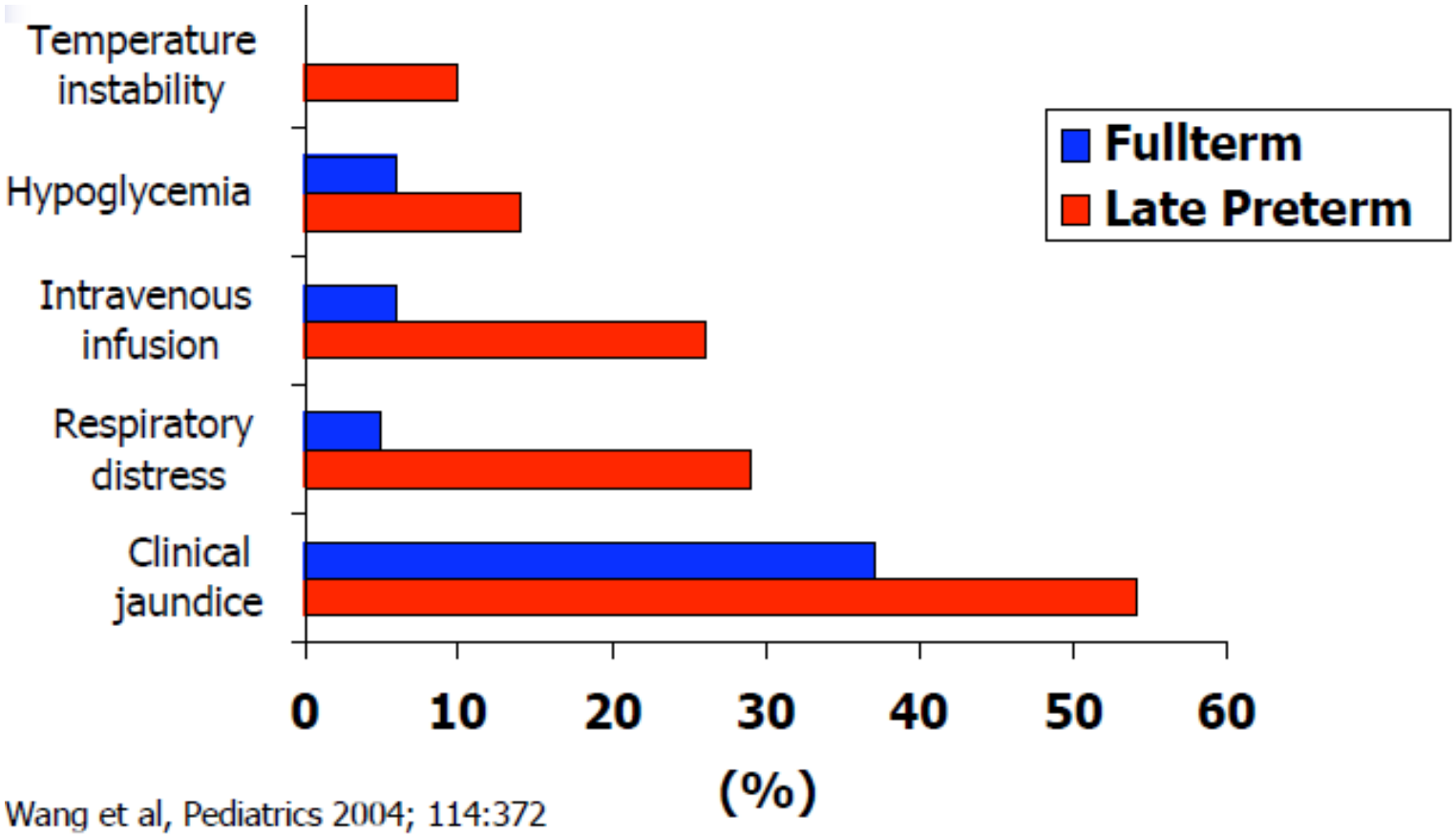


Figure 1. *Rate of respiratory distress, sepsis, and patent ductus arteriosus (PDA) by gestational age.*

Morbidity in Late Preterm



Wang et al, Pediatrics 2004; 114:372

Mortality Rates in Late Preterms & Early Term

Gestational Age, Weeks	Neonatal Mortality Rate	Neonatal Mortality RR (95% CI)	Infant Mortality Rate	Infant Mortality RR (95% CI)
34	7.1	9.5 (8.4-10.8)	11.8	5.4 (4.9-5.9)
35	4.8	6.4 (5.6-7.2)	8.6	3.9 (3.6-4.3)
36	2.8	3.7 (3.3-4.2)	5.7	2.6 (2.4-2.8)
37	1.7	2.3 (2.1-2.6)	4.1	1.9 (1.8-2.0)
38	1.0	1.4 (1.3-1.5)	2.7	1.2 (1.2-1.3)
39	0.8	1.00 (reference)	2.2	1.00 (reference)
40	0.8	1.0 (0.9-1.1)	2.1	0.9 (0.9-1.0)

Pediatrics 124:234–240, 2009

Infection

- Innate immunity is not well developed
- Higher risk of infections

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PLOS ONE

Decreased Pattern Recognition Receptor Signaling, Interferon-Signature, and Bactericidal/Permeability-Increasing Protein Gene Expression in Cord Blood of Term Low Birth Weight Human Newborns

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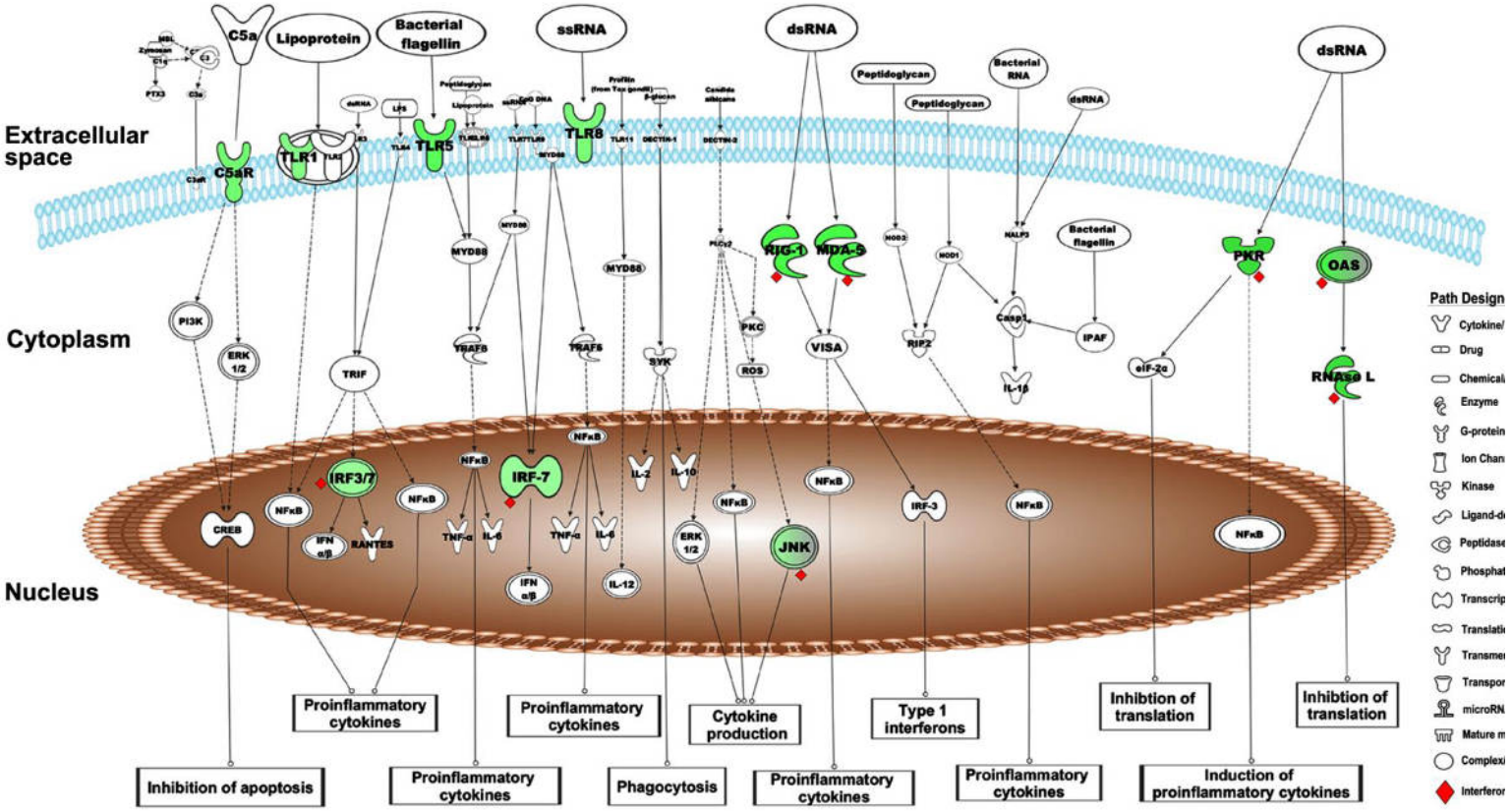
1. Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses

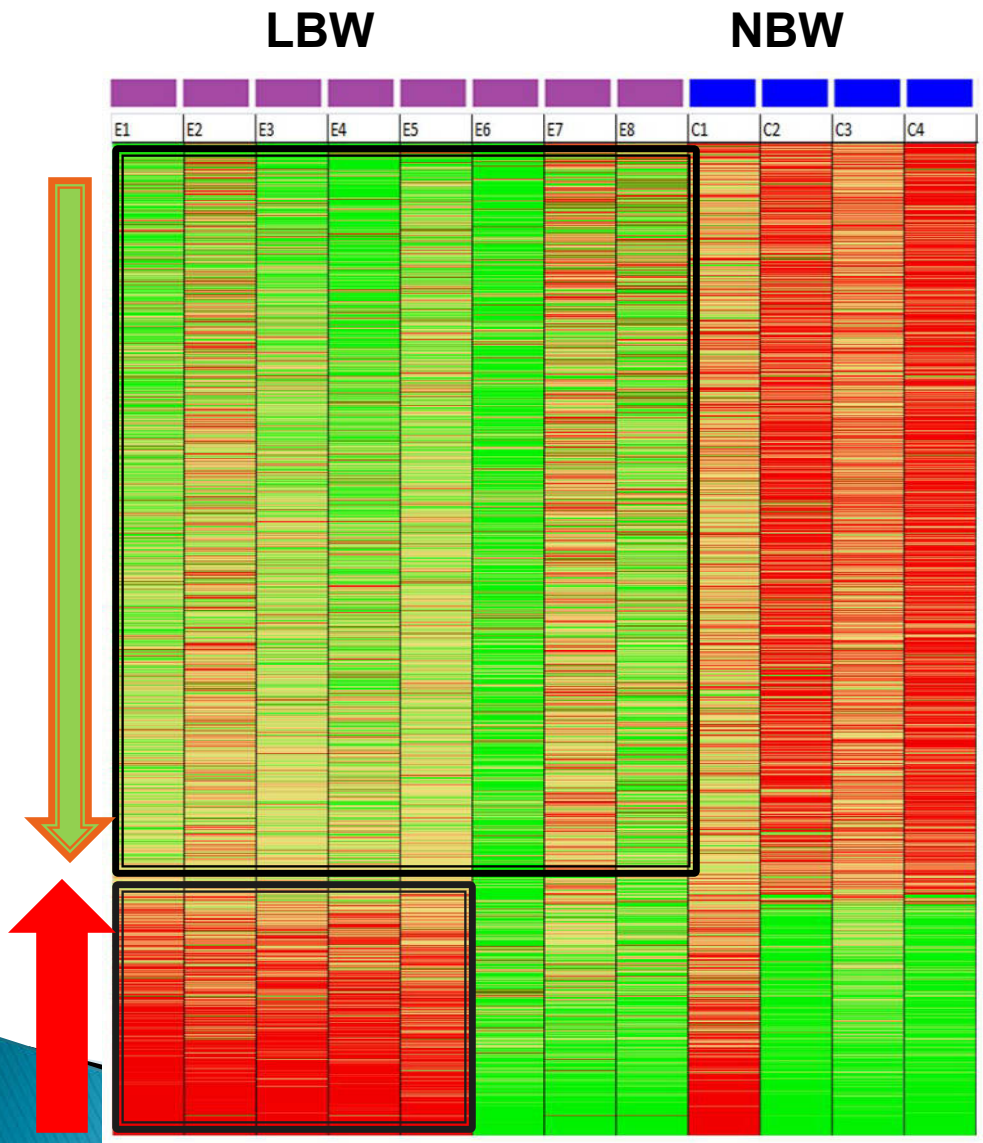
Membrane bound PRRs:
C5aR, TLRs (1, 5 and 8)

Cytoplasmic PRRs:
RIG-1, MDA5, PKR, OAS



Singh et al, PLoS ONE, 2013

Heat-Map of differentially expressed genes in LBW newborns



No. of gene down-regulated = 1065

No. of gene up-regulated = 326

Colour Range (fold change)

-2 0 2

Fold changes are represented on logarithmic scale

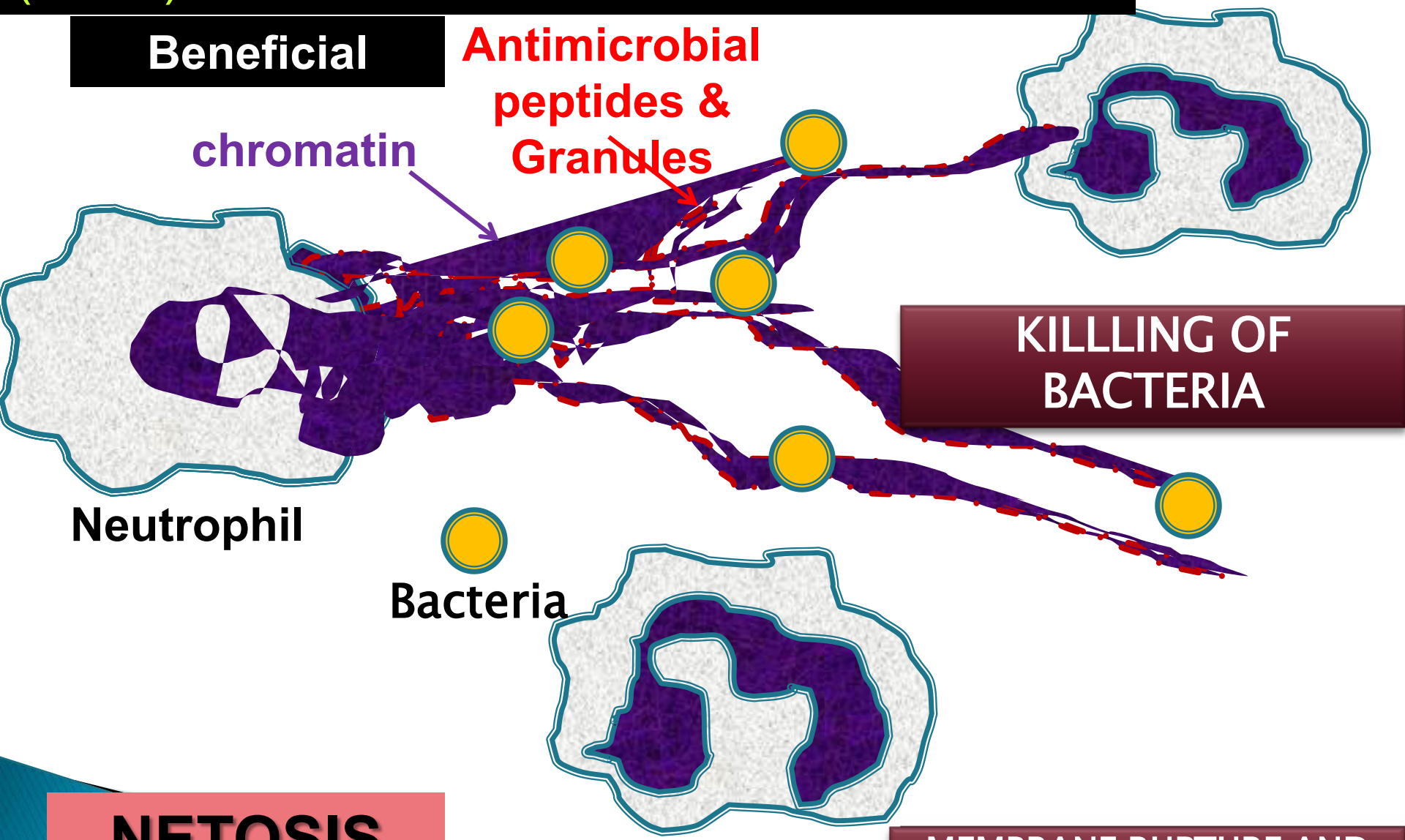
Singh et al, PLoS ONE, 2013

Neutrophil Functions-Defective

- Netosis-neutrophil extracellular trap formation

Neutrophil Extracellular Trap formation (NETs)

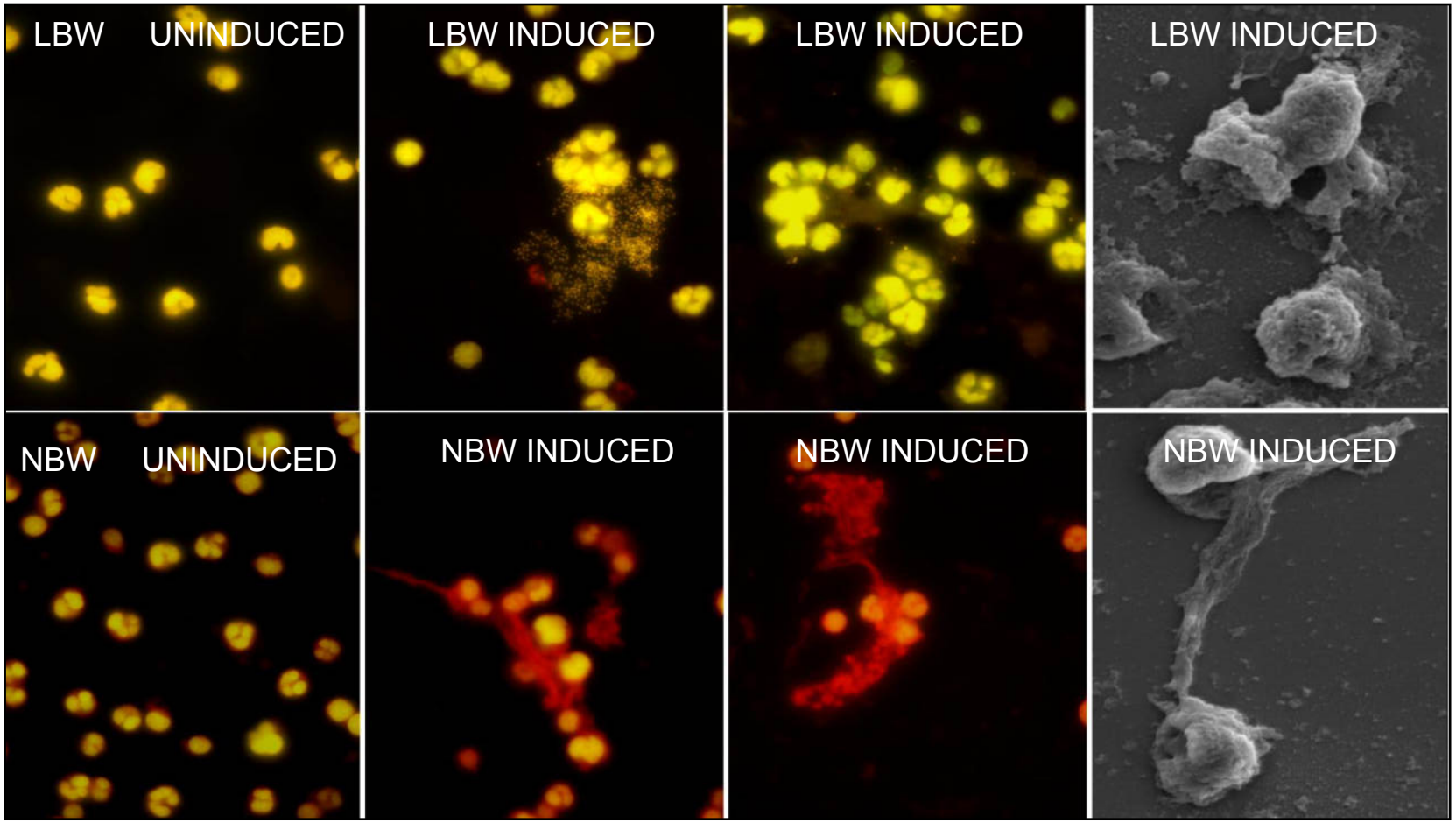
Beneficial



NETOSIS

MEMBRANE RUPTURE AND CHROMATIN RELEASE

NETOSIS in LBW Newborns



Green : Syto 13a live cell intra-nuclear DNA stain

Red : Sytox- orange a Extracellular DNA stain

- Signalling pathway which conrols Netosis is defective in LBW infants *(Singh VV, Chauhan SK, Rai R, Kumar A, Rai G: Decreased toll-like receptor-4/myeloid differentiation factor 88 response leads to defective interleukin-1beta production in term low birth weight newborn)*

  Pediatr Infect Dis J 2014, 33:1270-1276.

Management of Late Preterm and Early Term Infants

- Close monitoring
- The focus of care is individualized depending on the specific medical problems
- Counseling of parents about the possible morbidities, admission to NICU, prolonged birth hospitalization, and rehospitalization

Management Issues

- Delivery room resuscitation
- Temp maintenance
- Respiratory distress
- Feeding issues/hypoglycemia
- Hyperbilirubinemia
- Sepsis

Rehospitalization

- Hyperbilirubinemia
- Poor feeding
- Excessive weight loss
- Suspected sepsis

Long term management

- Education of mothers and families regarding long-term follow up
- Early intervention and developmental services may be indicated, especially for those who have problems with cognition, learning, and behavioral problems

Medical Outcomes in 20 to 36 Year Old Norwegian People By Gestational Age

	Gestational Age (%)					
	23-27 N=362	28-30 N=1 686	31-33 N=6 591	34-36 N=32 187	≥37 N= 853 309	Relative Risk 95% CI 34-36 vs ≥37
Cerebral Palsy	9.1	6.0	1.9	0.3	0.1	2.7(2.2-3.3)
Mental Retardation	4.4	1.8	1.0	0.7	0.4	1.6 (1.4-1.8)
Schizophrenia	0.6	0.1	0.2	0.2	0.1	1.3 (1.0-1.7)
Disorders of psychological development, behavior, and emotion	2.5	0.7	0.3	0.3	0.2	1.5 (1.2-1.8)
Other major disabilities	4.1	2.2	0.5	0.3	0.2	1.5 (1.2-1.8)
Any disability affecting working capacity	10.6	8.2	4.2	2.4	1.7	1.4 (1.3-1.5)

Moster D et al. N Engl J Med 2008;359:262-273

Prevention

- Avoidance of non-medically indicated delivery before 39 weeks
- Late preterm births have shown declining trend in recent years in US
- Early term births are continuing to rise
- Policy changes are needed to prevent early births

Policy Changes

- Hard-stop policy: hospital passes an order not to deliver early if it is not indicated
- Soft-stop policy: Obstetricians agree not to perform non-medically indicated delivery before 39 weeks
- Education program
- All 3 approaches were effective to reduce the rate but hard-stop policy was most effective (Am J Obstet Gynecol 2010)

- Documentation of fetal lung maturity does not justify early non-medically indicated delivery

Conclusions

- Late preterm and early term infants are physiologically and metabolically immature
- Higher risks of morbidity and mortality and long term health related rsiks
- Efforts are needed to reduce non-indicated early births

Thank you