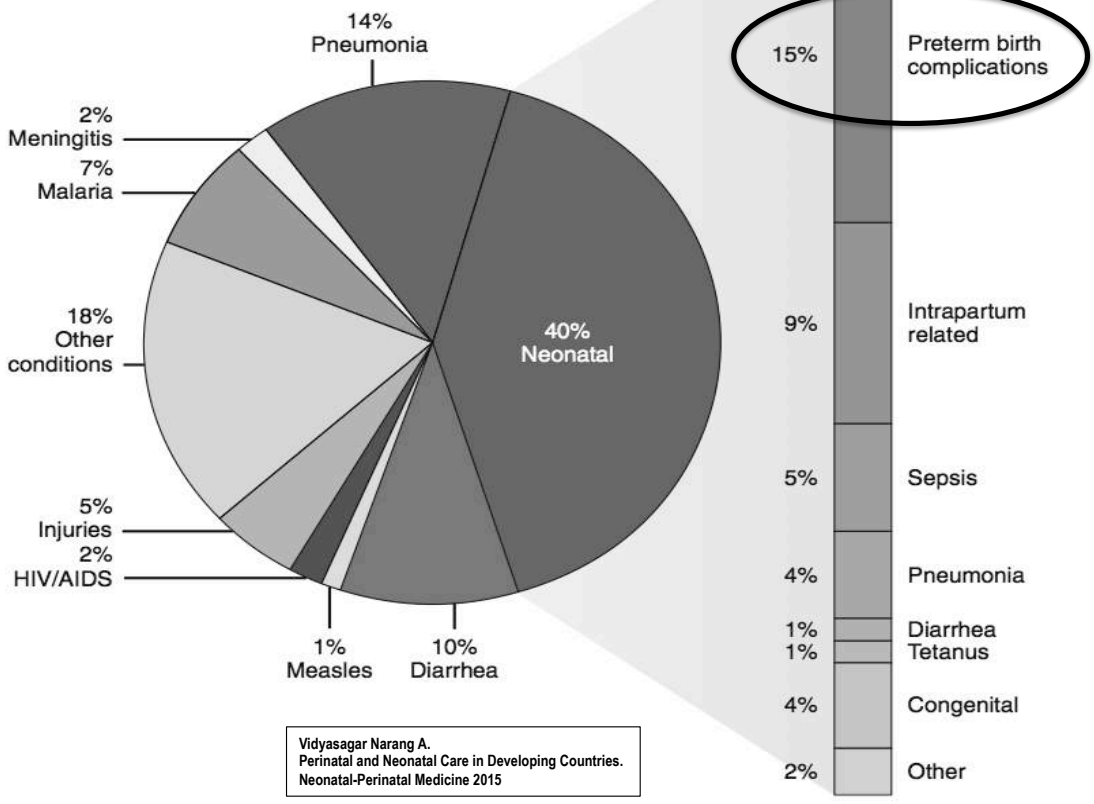
MANAGEMENT OF PRETERM INFANTS

Aris Primadi
IDAI Jawa Barat

DISTRIBUTION OF CHILD AND NEONATAL DEATHS BY CAUSE



Vidyasagar Narang A.
Perinatal and Neonatal Care in Developing Countries.
Neonatal-Perinatal Medicine 2015

WHO RECOMMENDATIONS ON INTERVENTIONS TO IMPROVE PRETERM BIRTH OUTCOMES

OVERVIEW

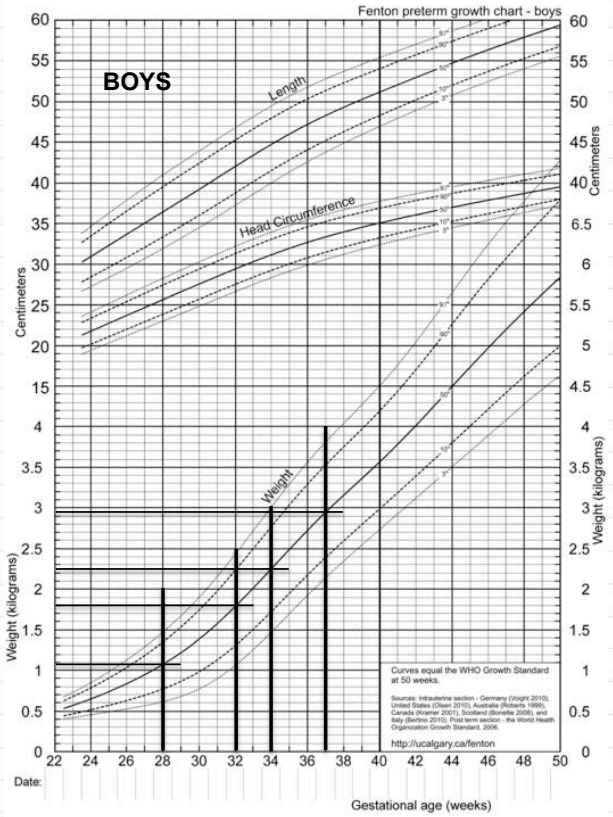
Preterm is defined as babies born alive before 37 weeks of pregnancy are completed.

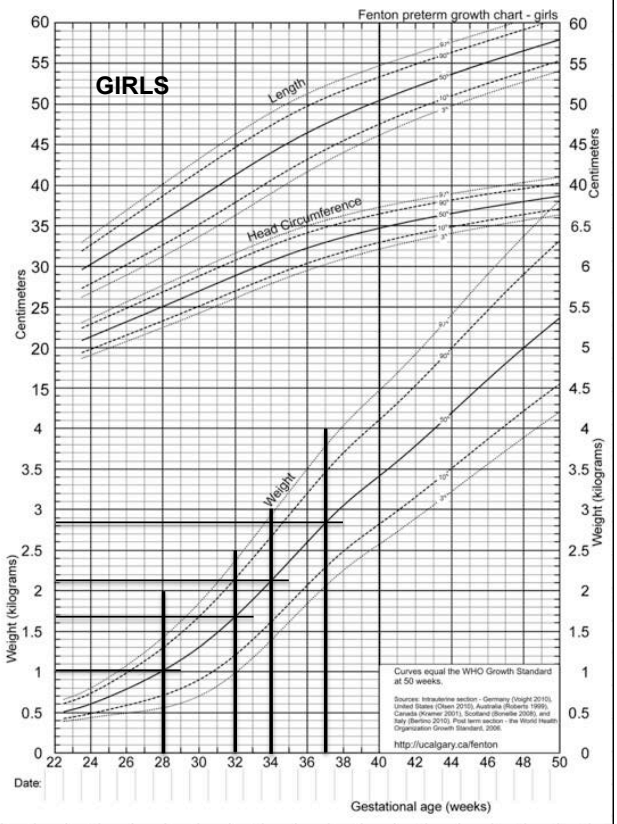
There are sub-categories of preterm birth, based on gestational age:

- Extremely preterm (<28 weeks)
- Very preterm (28 to <32 weeks)
- Moderate to late preterm (32 to <37 weeks)

Induction or caesarean birth should not be planned before 39 completed weeks unless medically indicated.

World Health Organization





A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. Fenton and Kim BMC Pediatrics 2013, 13:59

THE PROBLEM

- An estimated 15 million babies are born too early every year. That is more than 1 in 10 babies.
- Almost 1 million children die each year due to complications of preterm birth.
- Many survivors face a lifetime of disability, including learning disabilities and visual and hearing problems.
- And in almost all countries with reliable data, preterm birth rates are increasing..

World Health Organization

THE PROBLEM

There is a dramatic difference in survival of premature babies depending on where they are born

- More than 90% of extremely preterm babies (< 28 weeks) born in low-income countries die within the first few days of life; yet < 10% of babies of this gestation die in high-income settings
- In low-income settings, half of the babies born at or below 32 weeks (2 months early) die; in high-income countries, almost all of these babies survive.

World Health Organization

Why does preterm birth happen?

- Most preterm births happen spontaneously, but some are due to early induction of labour or caesarean birth, whether for medical or non-medical reasons.
- Common causes of preterm birth include multiple pregnancies, infections and chronic conditions such as diabetes and high blood pressure; however, often no cause is identified.
- There could also be a genetic influence.
- Better understanding of the causes and mechanisms will advance the development of solutions to prevent preterm birth.

World Health Organization

Where and when does preterm birth happen?

- More than 60% of preterm births occur in Africa and South Asia

- The 10 countries with the greatest number of preterm births:

1. India: 3 519 100
2. China: 1 172 300
3. Nigeria: 773 600
4. Pakistan: 748 100
5. **Indonesia: 675 700**
6. The United States of America: 517 400
7. Bangladesh: 424 100
8. The Philippines: 348 900
9. The Democratic Republic of the Congo: 341 400
10. Brazil: 279 300

World Health Organization

Where and when does preterm birth happen?

In the lower-income countries, on average, 12% of babies are born too early compared with 9% in higher-income countries.

The 10 countries with the highest rates of preterm birth per 100 live births:

1. Malawi: 18.1 per 100
2. Comoros: 16.7
3. Congo: 16.7
4. Zimbabwe: 16.6
5. Equatorial Guinea: 16.5
6. Mozambique: 16.4
7. Gabon: 16.3
8. Pakistan: 15.8
9. **Indonesia: 15.5**
10. Mauritania: 15.4

World Health Organization

Angka Kejadian BBLR

di RS Hasan Sadikin Bandung

	2001	2010	2013
BBLASR	2,84%	1,8%	0,02%
BBLSR	3,27%	4,2%	3,58%
BBLR	22,7%	23,27%	21,50%

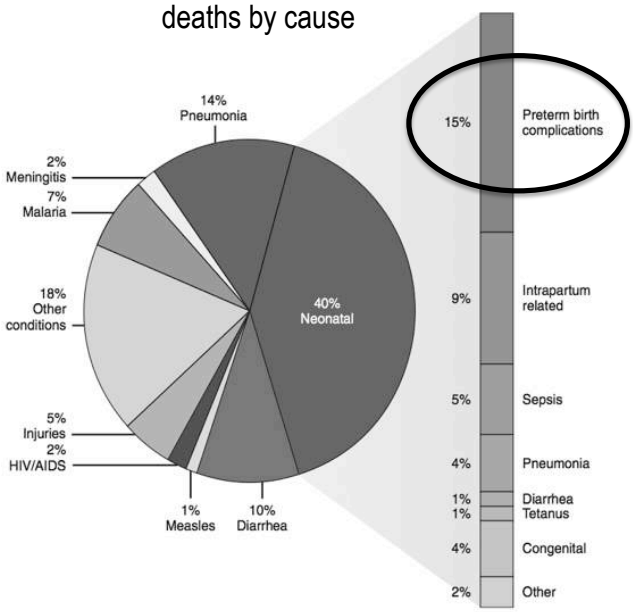
KELAHIRAN PREMATUR RS DR. HASAN SADIKIN
TAHUN 2017

		Januari	Februari	Maret	April	Mei	Juni	Juli	Agustus	September	Oktober	November	Desember
	∑Kelahiran	203	166	176	227	256	287	239	243	255	260	232	265
Extremly Preterm	< 28 minggu	3	3	7	10	13	8	9	4	3	9	4	5
Very Preterm	28-31 minggu	19	12	12	8	12	11	19	9	7	14	14	14
Moderate Preterm	32-33 minggu	14	12	8	13	17	28	9	11	10	24	23	29
Late Preterm	34-36 minggu	35	28	39	52	60	48	43	61	78	59	66	70
		71	**55**	**66**	**83**	**75**	**95**	**79**	**85**	**60**	**106**	**107**	**118**

KELAHIRAN PREMATUR RS DR. HASAN SADIKIN
TAHUN 2018

		Januari	Februari	Maret	April	Mei	Juni	Juli	Agustus	September	Oktober	November	Desember
	∑Kelahiran	255	210	266	294	297	293						
Extremly Preterm	< 28 minggu	8	0	5	6	9	9						
Very Preterm	28-31 minggu	12	17	23	23	18	14						
Moderate Preterm	32-33 minggu	15	22	26	20	31	20						
Late Preterm	34-36 minggu	69	38	61	78	71	77						
		104	**77**	**122**	**127**	**129**	**120**						

Distribution of child and neonatal deaths by cause



Vidyasagar Narang A. Perinatal and Neonatal Care in Developing Countries. Neonatal-Perinatal Medicine 2015

THE MOST COMMON COMPLICATIONS OF PREMATURE BIRTHS:

- Respiratory Distress Syndrome (RDS)
- Apnea and Bradycardia
- Pneumonia
- Inability to maintain body heat
- Jaundice
- Infection – Sepsis
- Intraventricular hemorrhage (IVH)
- Immature gastrointestinal and digestive system
- Necrotizing Enterocolitis (NEC)
- Patent Ductus Arteriosus (PDA)
- Retinopathy of Prematurity (ROP)
- Bronchopulmonary Dysplasia (BPD)

HMD → RDS

- Hyaline Membrane Disease (HMD): A respiratory disease of the newborn, especially the premature infant
- The word "hyaline" comes from the Greek word "hyalos" meaning "glass or transparent stone such as crystal"
- HMD is now commonly called Respiratory Distress Syndrome (RDS)
- It is caused by a deficiency of a molecule called surfactant

Original article SWISS MED WKLY 2003;133:283–288 · www.smw.ch 283

Respiratory distress syndrome in near-term babies after caesarean section

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Summary

Objective: Severe respiratory distress syndrome (RDS) caused by surfactant deficiency is described not only in preterm infants but also in (near-) term babies after caesarean section (CS), especially when carried out before the onset of labour. The aim of the present study was to document the severity of this theoretically avoidable entity in order to improve obstetric and perinatal care.

Patients: All neonates admitted to the paediatric intensive care unit of the University Hospital of Bern between 1988 and 2000 with RDS on the basis of hyaline membrane disease (HMD) needing mechanical ventilation (MV) after CS and with a birthweight ≥ 2500 g were analysed. HMD was diagnosed when respiratory distress and the typical radiological signs were present. Patients were grouped into elective CS before onset of labour and before rupture of membranes (group 1, n = 34) and patients delivered by emergency CS or CS after onset of labour or rupture of membranes (group 2, n = 22). Analysed indices for severity of illness were duration of stay in intensive care unit and MV, ventilation mode, worst oxygenation index (OI), presence of pulmonary air leak, and systemic hypotension.

Results: Mean gestational age (GA) was 37 2/7 weeks in group 1 and 36 2/7 weeks in group 2; no patient had a GA of ≥ 39 0/7 weeks. Duration of MV was 4.4 days in group 1 and 3.9 days in group 2. Thirteen patients (38%) of group 1 and 7 (32%) of group 2 had to be managed by rescue high-frequency ventilation. A total of 7 patients had an OI >40. Eight patients (24%) in group 1 and 4 (18%) in group 2 developed a pulmonary air leak. Four- teen neonates (41%) in group 1 had to be supported by catecholamines versus 5 (22%) in group 2. There was one death in group 1.

Conclusion: Severe RDS on the basis of HMD can also occur in near-term babies after CS; even a fatal outcome can not be excluded. The severity of illness in elective CS without labour may be quite high and is comparable to newborns delivered by CS (after onset of labour and/or rupture of the membranes) who were 1 week younger. No case of HMD was found in our population when CS was carried out after completion of 39 postmenstrual weeks of gestation.

Key words: *respiratory distress syndrome; term and near-term newborns; Caesarean section; hyaline membrane disease*

Original article SWISS MED WKLY 2003;133:283–288 · www.smw.ch 283

Respiratory distress syndrome in near-term babies after caesarean section

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Conclusions

- As shown by our series, **iatrogenic RDS** caused by too early elective CS before onset of labour is still a reality.
- Some of these patients are extremely ill and need invasive high-tech medical measures to save their lives.
- Even then, a fatal outcome cannot be excluded.
- Overall, iatrogenic RDS is a rare cause of RDS in neonates, but as a potentially preventable disease all possible efforts have to be undertaken to avoid it.
- As documented by our series and recent works by other authors, no case of severe HMD has been observed after completion of 39 weeks of GA.

Pirjani *et al. BMC Pregnancy and Childbirth* (2018) 18:140
https://doi.org/10.1186/s12884-018-1785-2

BMC Pregnancy and Childbirth

RESEARCH ARTICLE Open Access

Elective caesarean section at 38–39 weeks gestation compared to > 39 weeks on neonatal outcomes: a prospective cohort study

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Abstract

Background: This study was conducted to compare neonatal complications in scheduled cesarean sections (CS) between 38 and 39 gestational weeks with CS performed after 39 gestational weeks in Iranian low -risk pregnant women.

Methods: In this cohort study, 2086 patients were enrolled based on the inclusion and exclusion criteria. The neonates were evaluated in terms of the following items: transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), sepsis, need for NICU hospitalization, birth weight, birth height, head circumference, and the first minute and fifth minute Apgar score. Several multiple logistic regression models were performed for each response variable (adverse outcome) separately.

Results: The incidence of NICU admission was significantly higher in neonates born at 38–39 gestational weeks than those who were born after 39 gestational weeks. No significant differences were found in the incidence of neonatal sepsis, TTN, and RDS between the two groups.

Conclusion: According to our study results, elective CS at 38–9 weeks' gestation is associated with a higher rate of TTN and NICU admission in comparison with elective CS performed after 39 completed gestational weeks.

Keywords: Caesarean section, Intensive care units, Neonate, Transient tachypnea of the newborn, Respiratory distress syndrome

Guidelines to improve preterm birth outcomes

- WHO has developed new guidelines with recommendations for improving outcomes of preterm births.
- The guidelines include interventions provided to the mother – for example steroid injections before birth, antibiotics when her water breaks before the onset of labour.
- As well as interventions for the newborn baby – for example thermal care (e.g. kangaroo mother care when babies are stable), safe oxygen use, and other treatments to help babies breathe more easily.

World Health Organization

Quality of the evidence and Strength of the recommendations

Recommendation 1:

Antenatal corticosteroid therapy is recommended for women at risk of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met:

- Gestational age assessment can be accurately undertaken;
- Preterm birth is considered imminent;
- There is no clinical evidence of maternal infection;
- Adequate childbirth care is available (including the capacity to recognize and safely manage preterm labour and birth);
- The preterm newborn can receive adequate care if needed (including resuscitation, thermal care, feeding support, infection treatment & safe oxygen use).

Antenatal corticosteroid therapy

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate (newborn) ☒ Low (mother) ☐ Very low	Based on the main analysis, the overall quality of evidence for maternal outcomes was mostly rated as low, whereas for newborn severe morbidity and mortality outcomes it was rated as moderate or high. Long-term outcomes during childhood and adulthood were rated as low. The quality of evidence from the subgroup analyses based on gestational age at first dose was rated low for most newborn morbidity and mortality outcomes due to few trials and small sample sizes. However, it was rated as moderate or high for categories between 26 and 34+6 weeks for respiratory distress syndrome (RDS). The quality of evidence from the subgroup analyses based on gestational age at birth was quite variable, ranging from low to high across the different age categories for severe neonatal morbidity and mortality outcomes. However, it was moderate to high for RDS for babies born < 30 weeks, < 32 weeks, < 34 weeks and < 36 weeks. The Guideline Development Group (GDG) acknowledged the differences in the quality of evidence between maternal and early newborn critical outcomes and between early and late newborn critical outcomes. The panel interpreted the overall quality of evidence within the context of the recommendation question and the main review findings, and favoured a distinction between the quality of evidence for the mother and the newborn. Thus, the overall quality of evidence was rated as moderate for newborn outcomes and low for maternal outcomes.
Values and preferences	☒ No significant variability ☐ Significant variability	Health-care providers, policy-makers, and pregnant women and their families in all settings are likely to place a high value on the survival of a preterm newborn without residual morbidity. The GDG is confident that there is no variation in this value among mothers, health-care providers and policy-makers in low-, middle- and high-income settings.
Balance of benefits versus disadvantages	☒ Benefits outweigh disadvantages ☐ Benefits and disadvantages are balanced ☐ Disadvantages outweigh benefits	Antenatal corticosteroid reduces the risk of death and serious short-term morbidities and is probably beneficial in reducing long-term adverse neurological outcomes for preterm infants. For the mother, there is no evidence of benefits or harms. While the Cochrane systematic review demonstrated these benefits across a broad range of gestational ages (largely from 24 to 36 weeks), the subgroup analyses for the most part lack sufficient power to show consistent statistically significant results for specific gestational age categories. These inconsistencies were more pronounced at the two extremes of prematurity (< 26 weeks and > 34 weeks) because the sample sizes were even smaller. Nevertheless, the subgroup analyses showed consistent evidence of reduction in neonatal death when the infant is born before 34 weeks of gestation. Likewise, the data indicated that corticosteroid does not reduce infant mortality when born after 34 weeks and there is an increasing likelihood of fetal and newborn death when born at 36 weeks or after. With regard to the lower end of gestational age limit, corticosteroid may likely reduce neonatal mortality for infants born as early as 23 weeks of gestation, but the overall rate of survival without residual morbidity is generally low among infants born before 24 weeks. Overall, the desirable consequences for preterm infants whose mothers receive antenatal corticosteroid between 24 and 34 weeks are substantial (including reduction in the risks of death and serious short-term morbidities and possibly better long-term neurological outcomes) and highly valued. For eligible mothers, these benefits are achievable without increased harm to mother and baby. Beyond this gestational age range, the undesirable consequences for the preterm infant (including survival with residual long-term morbidity and increased risk of death) outweigh the potential benefits.
Resource use	☒ Less resource intensive ☐ More resource intensive	Antenatal corticosteroids are relatively cheap, easy to administer, and readily available in at least one preparation in all settings. It is feasible to include antenatal corticosteroid therapy into existing health structures and protocols that are designed to manage women at imminent risk of preterm birth with minimal costs.
Recommendation direction	☒ In favour of the intervention ☐ Against the intervention	The moderate-to-high confidence in the magnitude of effects of a relatively cheap intervention on highly valued critical newborn outcomes favoured the intervention.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the benefits to the preterm infants in terms of reducing severe morbidity and mortality outcomes, the low cost and wide availability of corticosteroid globally, the feasibility of implementing the intervention and the potential impact on health-care resource use across settings, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 1:

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate (newborn) ☒ Low (mother) ☐ Very low	Based on the main analysis, the overall quality of evidence for maternal outcomes was mostly rated as low, whereas for newborn severe morbidity and mortality outcomes it was rated as moderate or high. Long-term outcomes during childhood and adulthood were rated as low. The quality of evidence from the subgroup analyses based on gestational age at first dose was rated low for most newborn morbidity and mortality outcomes due to few trials and small sample sizes. However, it was rated as moderate or high for categories between 26 and 34+6 weeks for respiratory distress syndrome (RDS). The quality of evidence from the subgroup analyses based on gestational age at birth was quite variable, ranging from low to high across the different age categories for severe neonatal morbidity and mortality outcomes. However, it was moderate to high for RDS for babies born < 30 weeks, < 32 weeks, < 34 weeks and < 36 weeks. The Guideline Development Group (GDG) acknowledged the differences in the quality of evidence between maternal and early newborn critical outcomes and between early and late newborn critical outcomes. The panel interpreted the overall quality of evidence within the context of the recommendation question and the main review findings, and favoured a distinction between the quality of evidence for the mother and the newborn. Thus, the overall quality of evidence was rated as moderate for newborn outcomes and low for maternal outcomes.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the benefits to the preterm infants in terms of reducing severe morbidity and mortality outcomes, the low cost and wide availability of corticosteroid globally, the feasibility of implementing the intervention and the potential impact on health-care resource use across settings, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 2:

Tocolytic treatments (acute and maintenance treatments) are not recommended for women at risk of imminent preterm birth for the purpose of improving neonatal outcomes.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☐ Low ☒ Very low	There were design limitations and insufficient data on critical maternal and neonatal outcomes for many of the studies comparing first-line tocolytic or maintenance therapy with placebo.
Overall strength of the recommendation	☐ Strong recommendation ☒ Conditional recommendation	The GDG considered the quality of the evidence and the variability in values and preferences of mothers, health-care providers and policy-makers across different settings, and chose to make a conditional recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 3:

The use of magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 weeks of gestation for prevention of cerebral palsy in the infant and child.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The quality of the evidence was moderate to high for critical outcomes relating to infant mortality and serious morbidity and maternal outcomes. Overall, the quality of evidence was rated as moderate.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the considerable short- and long-term harm this intervention could cause to the preterm infant, and the need to curb the widespread use of routine antibiotic prophylaxis globally, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 4:

Routine antibiotic administration *is not* recommended for women in preterm labour with intact amniotic membranes and no clinical signs of infection.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The overall quality of the evidence was graded as moderate for newborn and maternal outcomes.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the considerable short- and long-term harm this intervention could cause to the preterm infant, and the need to curb the widespread use of routine antibiotic prophylaxis globally, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 5:

Antibiotic administration is recommended for women with preterm prelabour rupture of membranes.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The overall quality of the evidence for the main comparison was graded as moderate for newborn and maternal outcomes.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the short-term benefits to the mother and preterm infants in terms of reducing infection without evidence of harm, the moderate quality of evidence, an even stronger argument for antibiotic use in low-income settings, and wide availability of the recommended antibiotics globally, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 6:

Routine delivery by caesarean section for the purpose of improving preterm newborn outcomes *is not* recommended, regardless of cephalic or breech presentation.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☐ Low ☒ Very low	The overall quality of evidence was rated as very low for maternal and newborn critical outcomes mainly because of the small sample sizes of the studies in the review.
Overall strength of the recommendation	☐ Strong recommendation ☒ Conditional recommendation	The GDG considered the very low confidence in the quality of evidence and the variations in values and preferences relating to the interventions across settings, and therefore chose to make a conditional recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 7.0:

Kangaroo mother care is recommended for the routine care of newborns weighing 2000 g or less at birth, and should be initiated in health-care facilities as soon as the newborns are clinically stable.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The quality of evidence for most of the critical outcomes, including that for mortality, neonatal infections and hypothermia, was high. However, the GDG decided to rate the overall quality of evidence as moderate because the quality of evidence was moderate for hyperthermia and re-admission to hospital.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	The GDG made a strong recommendation considering the moderate- to high-quality evidence, the benefits outweighing the risks, the lack of variability in the values and preferences which were all in favour of the intervention, the low cost, the feasibility of implementing the intervention and the potential impact on health-care resource use across all settings.

Quality of the evidence and Strength of the recommendations

Recommendation 7.1:

Newborns weighing 2000 g or less at birth should be provided as close to continuous Kangaroo mother care as possible.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The quality of evidence for most of the critical outcomes, including that for mortality, neonatal infections and hypothermia, was high. However, the GDG decided to rate the overall quality of evidence as moderate, because the quality of evidence was moderate for hyperthermia and re-admission to hospital.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	The GDG emphasized the moderate- to high-quality evidence, the benefits outweighing the risks, the lack of variability in the values and preferences which were all in favour of the intervention, the fact that there will be no additional costs in implementing continuous compared to intermittent KMC, the feasibility of implementing the intervention and the potential impact on health-care resource use across settings, and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 7.2:

Intermittent Kangaroo mother care, rather than conventional care, is recommended for newborns weighing 2000g or less at birth, if continuous Kangaroo mother care is not possible.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The quality of evidence was moderate for neonatal mortality and hyperthermia, but high for all other critical outcomes. The GDG rated the overall quality of evidence as moderate because of imprecision around the mortality effect estimates.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	The GDG made a strong recommendation, based on the moderate- to high-quality evidence suggesting that the benefits to the preterm newborn in terms of reducing morbidity and mortality outcomes outweighs the risks. The group also considered the low cost and feasibility of implementing the intervention, as well as the lack of suitable alternatives, across many low- and middle-income settings.

Quality of the evidence and Strength of the recommendations

Recommendation 7.3:

Unstable newborns weighing 2000g or less at birth, or stable newborns weighing less than 2000g who cannot be given Kangaroo mother care, should be cared for in a thermo-neutral environment either under radiant warmers or in incubators.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☐ Low ☒ Very low	The evidence was from only one study conducted in a high-income setting and the mortality effect estimates were imprecise. The overall quality of evidence was rated very low.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	Based on the benefits to sick or unstable preterm newborns, even though the quality of the evidence was very low, the GDG made a strong recommendation. The group considered that the benefits outweigh the risks and the intervention will be valued in all settings because KMC cannot be practised for these babies.

Quality of the evidence and Strength of the recommendations

Recommendation 7.4:

There is insufficient evidence on the e effectiveness of plastic bags/wraps in providing thermal care for preterm newborns immediately after birth. However, during stabilization and transfer of preterm newborns to specialized neonatal care wards, wrapping in plastic bags/wraps may be considered as an alternative to prevent hypothermia.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☒ Low ☐ Very low	The evidence was derived from component studies that had methodological biases, with inconsistent and imprecise effect estimates or were conducted in high-income settings; hence the GDG graded the overall evidence quality as low.
Overall strength of the recommendation	☐ Strong recommendation ☒ Conditional recommendation	The GDG could not make a recommendation for the routine use of the plastic bags/wraps. It did, however, make a conditional recommendation for the use of the plastic bags and wraps within hospitals to prevent hypothermia in situations where KMC cannot be applied.

Quality of the evidence and Strength of the recommendations

Recommendation 8.0:

Continuous positive airway pressure therapy is recommended for the treatment of preterm newborns with RDS

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☒ Low ☐ Very low	The GDG rated the quality of evidence as low because of methodological biases and imprecise effect estimates in the component studies. The studies were also conducted mainly in high-income settings.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	The GDG acknowledged the low quality of evidence for this recommendation, but considered that the potential for the intervention to improve newborn outcomes was substantial and outweighs the risks. The group felt that though the costs may be high, the intervention will be highly valued in settings where it can be implemented, and were unanimous in making a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 8.1:

CPAP therapy for newborns with respiratory distress syndrome should be started as soon as the diagnosis is made.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☐ Low ☒ Very low	The GDG rated the overall quality of evidence as very low because there were only few trials conducted in high-income settings which had methodological biases and their effect estimates were imprecise.
Overall strength of the recommendation	☒ Strong recommendation ☐ Weak recommendation	In spite of the very low quality of evidence, the GDG considered the potential for the intervention to improve newborn outcomes and the fact that, if CPAP can be administered, there will be no additional cost in starting it early or late and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 9.0:

Surfactant replacement therapy is recommended for intubated and ventilated newborns with respiratory distress syndrome.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The GDG rated the overall quality of evidence as moderate. The evidence quality was moderate for the mortality outcomes, but low for morbidity outcomes. The trials either were conducted mainly in high-income settings or had imprecise effect estimates.
Overall strength of the recommendation	☐ Strong recommendation ☒ Conditional recommendation	The GDG considered the potential for the intervention to improve newborn outcomes, and the value that health-care providers and policy-makers will place on its use, to make recommendation conditional on the availability of the right environment and resources (human and other) for implementation.

Quality of the evidence and Strength of the recommendations

Recommendation 9.1:

Either animal-derived or protein-containing synthetic surfactants can be used for surfactant replacement therapy in ventilated preterm newborns with RDS

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☒ Moderate ☐ Low ☐ Very low	The GDG rated the overall quality of evidence as moderate because all the evidence was derived from trials conducted solely in HICs.
Overall strength of the recommendation	☐ Strong recommendation ☒ Conditional recommendation	The GDG considered the potential for the intervention to improve newborn outcomes and placed emphasis on the basic requirements in any setting that will enable the use of SRT. The group thought the recommendation should be conditional and should only be implemented in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available.

Quality of the evidence and Strength of the recommendations

Recommendation 9.2:

Administration of surfactant before the onset of respiratory distress syndrome (prophylactic administration) in preterm newborns *is not* recommended.

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☒ Low ☐ Very low	The GDG considered there were methodological biases in the studies and many were conducted in HICs, and therefore rated the overall quality of evidence as low.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG considered the potential for harm from the intervention and the resource considerations, and thought the recommendation against prophylactic use should be strong.

Quality of the evidence and Strength of the recommendations

Recommendation 9.3:

In intubated preterm newborns with respiratory distress syndrome, surfactant should be administered early (within the first 2 hours after birth) rather than waiting for the symptoms to worsen before giving rescue therapy.

FACTOR	DECISION	EXPLANATION
Quality of the Evidence	☐ High ☐ Moderate ☒ Low ☐ Very low	There was a lack of studies from LMICs and the included studies had methodological limitations. The GDG rated the overall quality of evidence as low.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG placed its emphasis on the added benefits of early SRT within 2 hours of onset of RDS and therefore made a strong recommendation.

Quality of the evidence and Strength of the recommendations

Recommendation 10.0:
During ventilation of preterm babies born at or before 32 weeks of gestation, it is recommended to start O_2 therapy with 30% oxygen or air (if blended oxygen is not available), rather than with 100% O_2

Recommendation 10.1:
The use of progressively higher concentrations of oxygen should only be considered for newborns undergoing O_2 therapy if their heart rate is less than 60 beats per minute after 30 seconds of adequate ventilation with 30% O_2 or air

FACTOR	DECISION	EXPLANATION
Quality of the evidence	☐ High ☐ Moderate ☐ Low ☒ Very low	There was a paucity of evidence from trials specifically addressing this question. Effect estimates could not be directly assessed or were imprecise, and the trials were all conducted in HICs. The GDG rated the overall quality of evidence as very low.
Overall strength of the recommendation	☒ Strong recommendation ☐ Conditional recommendation	The GDG acknowledged the paucity of evidence, but made a strong recommendation considering that the demonstrated benefits outweigh the harms for an intervention which will be valued in all settings partly because it is also easy to use.

World Health Organization

For more information, please contact:

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Department of Maternal, Newborn, Child and Adolescent Health
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www.who.int/maternal_child_adolescent

World Health Organization
Avenue Appia 20, CH-1211 Geneva 27
Switzerland

cover photo: UNICEF/Asselin

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Airway

- ***Respiratory distress*** → most common reason for referral to intensive care nursery
- Deciding best method to support breathing and when to support is often challenging

RESPIRATORY EMERGENCY
IN LATE PRETERM INFANTS

- Late preterm delivery is a strategic term used in the definition of infants born at $34^{0/7}$ - $36^{6/7}$ gestational week or between the 239^{th}-259^{th} postconceptional days
- "near-term" → "late preterm infant (LPI)"
- Late preterms constitute approximately 75% of premature babies and approximately 9% of all deliveries
- 30% of all late preterm infants are hospitalized & approximately 50-80% of these babies are treated for respiratory problems

LATE PRETERM INFANTS

$34^{0/7}$ - $36^{6/7}$ gestational week

34 week

35 week

36 week

37 week

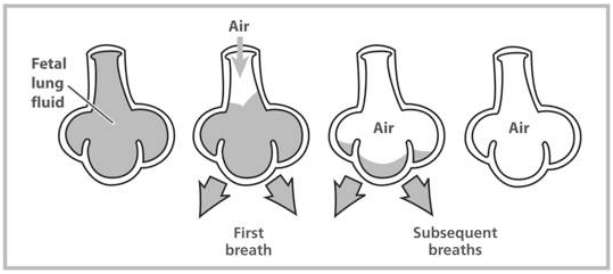
Lung Development - Late Preterm Labor

- Born at late saccular or early alveolar stages of development
- The surfactant and antioxidant systems are still relatively immature (or are still developing)
- Compared to a term infant; preterm infants at 34^{th} gestational week had:
  - 40 times more RDS risk
  - 15 times more chance of TTN
  - 10.5 times more respiratory failure
  - 14 times more risk of mechanical ventilation support
  - 59 times more surfactant application frequency

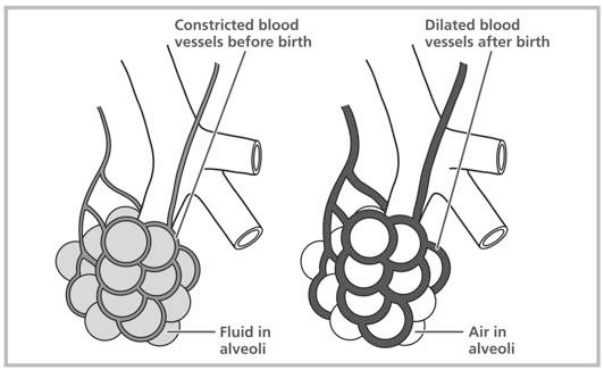
Mechanisms Leading to Respiratory Problems in Late Preterm Infants

- **Delayed Clearance of Fetal Lung Fluid**
- **Disturbance in Lung Mechanics**
- **Surfactant Deficiency**
- **Tendency to Infection and Pneumonia**
- **Apnea and Impairment in Respiratory Control**
- **Disturbance in Pulmonary Vascular Adaptation**
- **???**

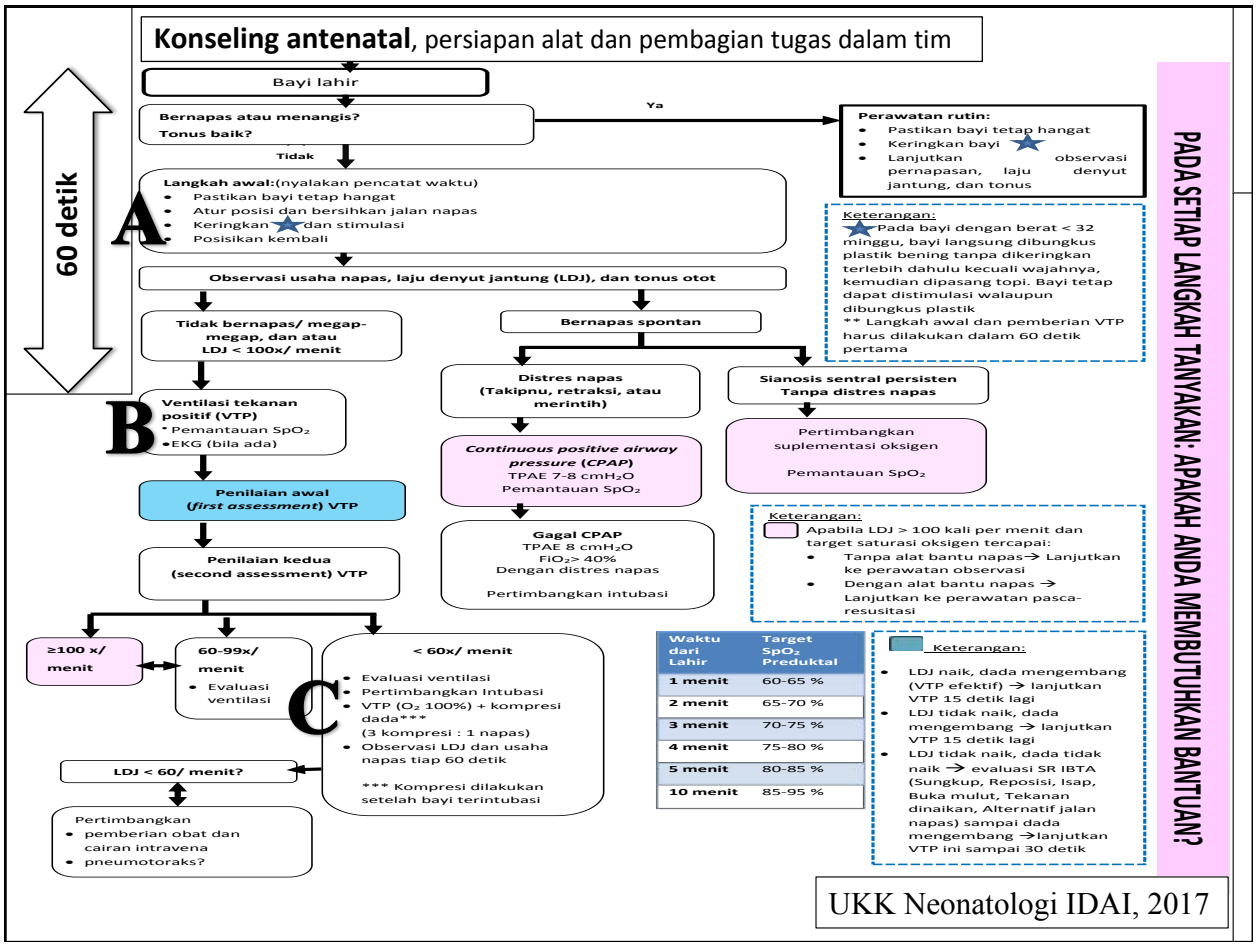
The Medical Bulletin of Sisli Etfal Hospital, Volume: 51, Number 3, 2017



Air replaces fluid in the alveoli



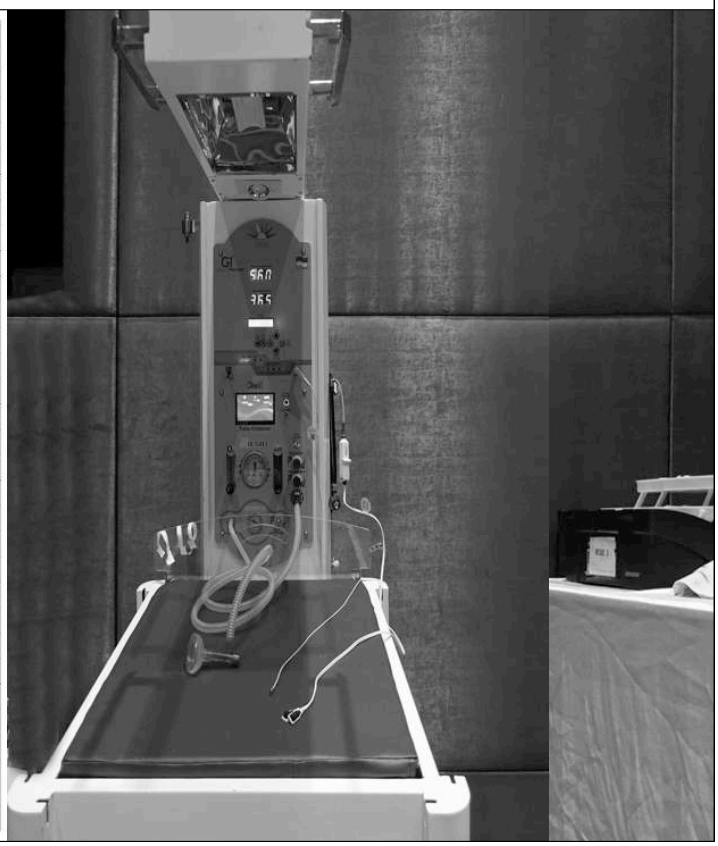
Pulmonary blood vessels dilate



Resusitasi Neonatus - - - Standar Alat-alat Utama

Resusitasi Neonatus - - - Daftar Alat-alat

Warm	• Preheated warmer
	• Warm towels or blankets
	• Temperature sensor and sensor cover for prolonged resuscitation
	• Hat
	• Plastic bag or plastic wrap (<32 weeks' gestation)
	• Thermal mattress (<32 weeks' gestation)
Clear airway	• Bulb syringe
	• 10F or 12F suction catheter attached to wall suction, set at 80 to 100 mm Hg
	• Meconium aspirator
Auscultate	• Stethoscope
Ventilate	• Flowmeter set to 10 L/min
	• Oxygen blender set to 21% *(21%-30% if <35 weeks' gestation)*
	• Positive-pressure ventilation (PPV) device
	• Term- and preterm-sized masks
	• 8F feeding tube and large syringe
Oxygenate	• Equipment to give free-flow oxygen
	• Pulse oximeter with sensor and cover
	• Target oxygen saturation table
Intubate	• Laryngoscope with size-0 and size-1 straight blades (size 00, optional)
	• Stylet (optional)
	• Endotracheal tubes (sizes 2.5, 3.0, 3.5)
	• Carbon dioxide (CO_2) detector
	• Measuring tape and/or endotracheal tube insertion depth table
	• Waterproof tape or tube-securing device
	• Scissors
	• Laryngeal mask (size 1) and 5-mL syringe
Medicate	Access to
	• 1:10,000 (0.1 mg/mL) epinephrine
	• Normal saline
	• Supplies for placing emergency umbilical venous catheter and administering medications
	• Electronic cardiac (ECG) monitor leads and ECG monitor

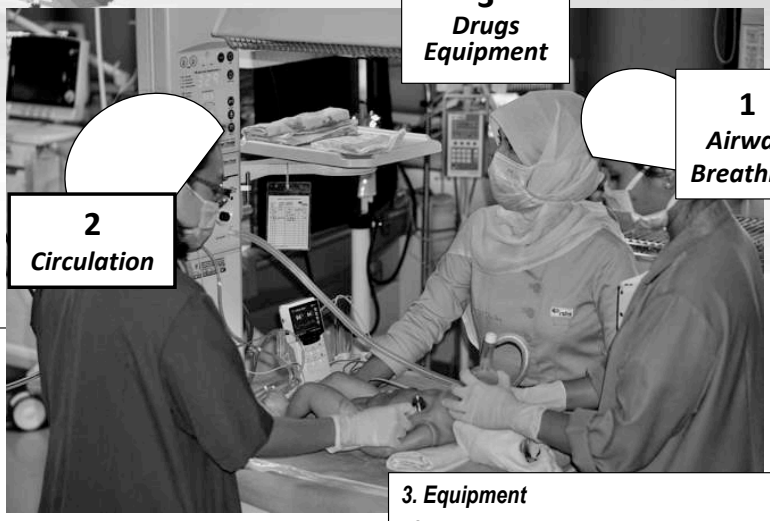


Pendidikan Berkelanjutan Ilmu Kesehatan Anak

rshs

A	***Airway*** **Langkah Awal**
B	***Breathing*** **Ventilasi Tekanan Positif**
C	***Circulation*** **Kompresi Dada + Ventilasi Tekanan Positif**

D	***Drug*** **Epinephrin**
E	***Equipment***



3
Drugs Equipment

1
Airway Breathing

2
Circulation

1. Ketua Tim
(Jalan Napas & Pernapasan)

- Ulas singkat peran, rencana dengan tim
- Hisap mulut & hidung bayi
- Jaga patensi jalan napas
- Berikan VTP
  - PEEP 5, PIP 20-25
  - RR 30-60
- Intubasi bayi & perhatikan kedalaman ET
- Beri surfaktan jika perlu
- *Thorakosintesis* jika perlu
- Nilai APGAR 1 & 5 menit
- Beri pengarahan pada tim dengan tenang

2. Sirkulasi

- Keringkan bayi
- Bekerja sama dengan sirkulasi mengeringkan & merangsang bayi, memasang plastik, mengganti linen
- Dengarkan suara jantung & napas
- Dengarkan suara napas setelah ET terpasang
- Pijat jantung

3. Equipment

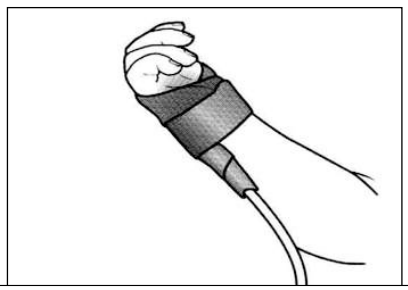
- Siapkan alat
- Aktifkan timer saat lahir
- Pasang probe suhu
- Bekerja sama dengan sirkulasi mengeringkan dan merangsang bayi, memasang plastik, mengganti linen
- Pasang sensor pulse oxymetri di tangan kanan
- Berikan pengobatan emergensi jika dibutuhkan
- Mengingatkan lama resusitasi dan mencatat tindakan dan obat-obatan yang sudah dilakukan
- Memastikan inkubator siap digunakan dan ada tempat di NICU
- Pasang kateter vena umbilikal bila diperlukan

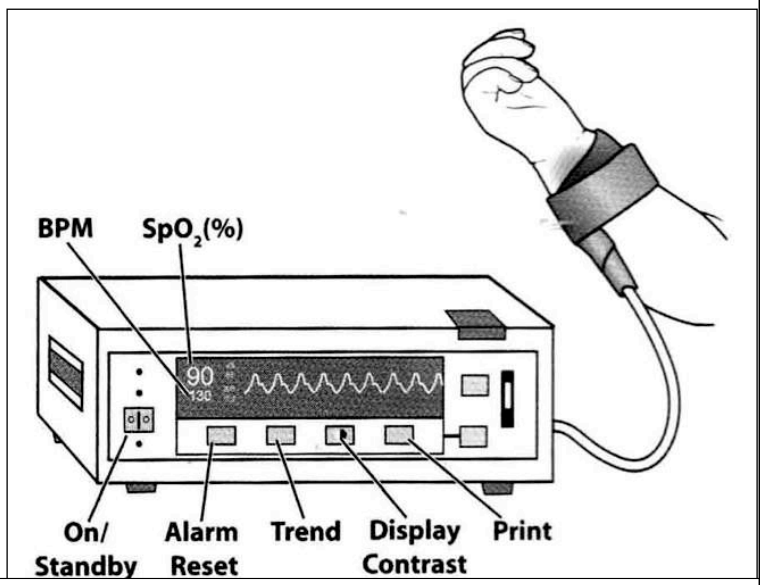
Penilaian:

1. Pernapasan …….. gerakan dada adekuat ?

2. Frekuensi jantung … hitung dalam 6 detik, kalikan 10

→ Oksigenasi …….. *pulse oxymeter*





Evaluation and Monitoring

- Vital signs
  - Temperature
  - Heart rate and rhythm
  - Respiratory rate and effort
  - Blood pressure
- Color, O_2 saturation, amount of O_2 required
- Infant well-being
  - Neurologic status
  - Skin perfusion
  - Pulses
  - Urine output

⚠ Notify medical staff provider promptly of any concerns!

Respiratory Distress Evaluation

Rate
Effort
O_2
Blood Gas

Respiratory Rate – Normal Respiratory Status

- 30 – 60 breaths per minute
- No nasal flaring, grunting, retractions
- No cyanosis
- Auscultation → clear breath sounds, equal air entry

Respiratory Distress Evaluation

Respiratory Rate > 60 per minute → Tachypnea

- Work of breathing → worsening distress
  - Flaring
  - Flaring + grunting
  - Flaring + grunting + retractions
- Evaluate
  - Color
  - O_2 requirement
  - O_2 saturation
  - Air entry
  - Blood gas

Respiratory Distress Evaluation

Respiratory Rate < 30 per minute – Bradypnea

- If labored, may be sign of exhaustion
- Apnea → frequency, duration, heart rate, O_2 saturation, self-resolved vs stimulation required
- Gasping
  - ⚠ Ominous sign of impending cardio-respiratory arrest!
  - Provide immediate positive pressure ventilation (PPV)
  - If heart rate not rising, proceed with endotracheal intubation

Respiratory Distress Evaluation

Rate
Effort
O_2
Blood Gas

Nasal Flaring

- Most often is a sign of respiratory distress but may be present at times in healthy infants
- Infants are obligate nose breathers
  - Nasal resistance contributes to total lung resistance
- Dilation of nostrils helps open up nasal passages and ↓ airway resistance

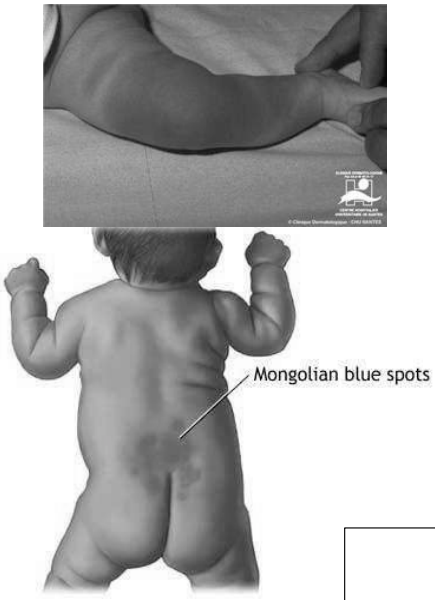
Airway Obstruction

↑RR ↑PCO_2

- Nose
- Mouth and jaw
- Larynx or trachea
- Bronchi
- Signs
  - Respiratory distress
  - Inspiratory stridor → if upper airway is narrowed or partially obstructed

Inspiratory stridor

CYANOSIS



CYANOSIS

Perioral Cyanosis

photo by Janelle Aby,MD

A blue color around the lips and philtrum is a relatively common finding shortly after birth. This is part of acrocyanosis. The skin in this infant is visibly well perfused, and the tongue and mucous membranes in the mouth were pink, a finding that assures the examiner that central cyanosis is not present. This finding resolved spontaneously over the next 48 hours.

CYANOSIS

Facial Bruising

photo byJanelle Aby, MD

Marked bruising of the face can occur during delivery. It is more common when there is a tight nuchal cord, when the delivery is precipitous or difficult, or when the infant is large. When the infant is bundled, this facial appearance could be mistaken for cyanosis, but with a quick comparison to the color of the rest of the body, the diagnosis is obvious. This type of bruising resolves over the course of several days.

Respiratory Distress Evaluation

- Hemoglobin carrying no O_2 appears **purple** = ***"reduced"*** hemoglobin
- Cyanosis is visible with 3 – 5 gm/dL ***reduced*** hemoglobin

Hb = 20 gm/dL
Hct = 60%
O_2Sat = 85%

Hb = 15 gm/dL
Hct = 45%
O_2Sat = 80%

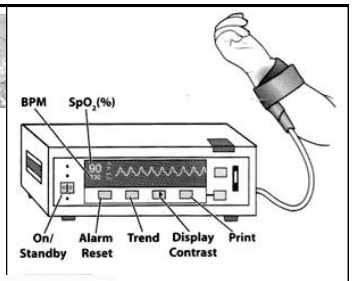
Hb = 10 gm/dL
Hct = 30%
O_2Sat = 70%

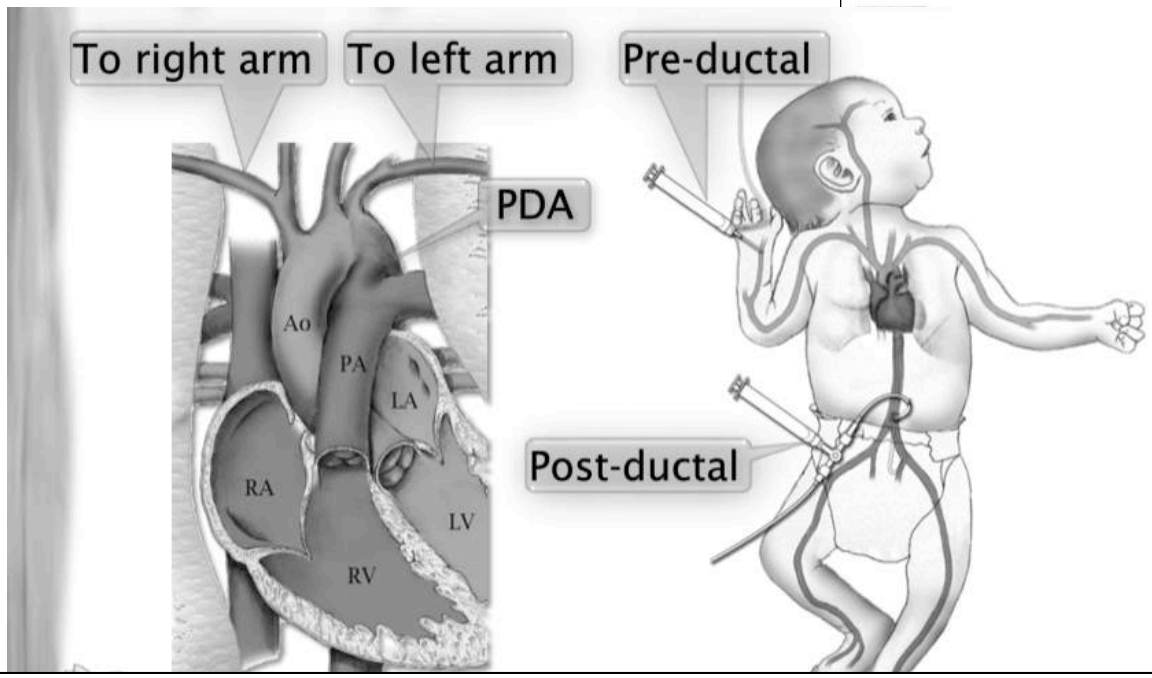
Respiratory Distress Evaluation

Oxygen Saturation (SaO_2)

- O_2 is transported to the tissues bound to hemoglobin in red blood cells
- *O_2 saturation* is the percentage of hemoglobin carrying oxygen
- Pulse oximetry estimates the O_2 saturation in the arterial blood
- Place a probe on the right palm → *pre-ductal*

Probe (sensor) oksimeter dipasang di pergelangan atau telapak tangan kanan





Maintenance of Oxygenation Target Ranges

Study	Spo_2 Target Range, %
Bhutani et al,[29] 1992	94–96
Morozoff et al,[30] 1993	90–95
Sun et al,[31] 1997	Set value ±3
Claure et al,[33] 2001	88–96
Urschitz et al,[34] 2004	87–96
Morozoff et al,[32] 2009	90–96
Claure et al,[35] 2009	88–95
Claure et al,[36] 2011	87–93[b]
Waitz et al, 2015	88–96
Hallenberger et al,[38] 2014	4 Centers 90–95 80–92 83–93 85–94
Zapata et al,[37] 2014	85–93
Lal et al,[39] 2014	90–95
Van Kaam et al,[40] 2014	89–93[b] 91–95

Oxygen Saturation Targeting by Automatic Control of Inspired Oxygen in Premature Infants, Neoreviews 2015

Respiratory Distress Evaluation

Labs and Tests

- Chest x-ray → if respiratory distress
- Abdominal x-ray → if abdominal concerns
- Blood glucose
- Blood gas → arterial or capillary
- Blood culture
- Complete blood count (CBC) with white blood cell differential







Respiratory Distress Evaluation

Rate
Effort
O_2
Blood Gas

Blood Gas Normal Values

Warm heel for 3 – 5 minutes before obtaining a CBG

		Arterial	Capillary
pH	< 48 hrs	7.30 – 7.40	Same
	> 48 hrs	7.35 – 7.45	Same
PCO_2		35 – 45	35 – 50
PO_2 on room air		60 – 80	-------
HCO_3	< 48 hrs	19 – 22	Same
	> 48 hrs	20 – 26	Same
Base Excess		– 4 to +4	Same

Use pulse oximeter for assessing oxygenation

Respiratory Distress Evaluation

Severity of Respiratory Distress

- **Mild** → rapid respiratory rate with or without need for supplemental O_2 and minimal signs of distress
- **Moderate** → cyanotic on room air and with one or more signs of respiratory distress – flaring, grunting, retractions
- **Severe** → increased work of breathing and:
  - Difficulty maintaining O_2 saturation > 90% on supplemental O_2
  - Abnormal blood gas
  - Altered mental status

Classification of breathing difficulty (WHO – Depkes)

Respiratory Rate		Additional Signs of Breathing Difficulty	Classification
More than 60 breaths per minute	WITH	Central cyanosis AND chest indrawing or grunting on expiration	**Severe breathing difficulty (page {)**
OR More than 90 breaths per minute	WITH	Central cyanosis OR chest indrawing OR grunting on expiration	
OR Less than 30 breaths per minute	WITH or WITHOUT	Any other sign of breathing difficulty	
Sixty to 90 breaths per minute	WITH but WITHOUT	Chest indrawing OR grunting on expiration Central cyanosis	**Moderate breathing difficulty (page {)**
OR More than 90 breaths per minute	WITHOUT	Chest indrawing or grunting on expiration or central cyanosis	
Sixty to 90 breaths per minute	WITHOUT	Chest indrawing or grunting on expiration or central cyanosis	**Mild breathing difficulty (page {)**
Sixty to 90 breaths per minute	WITH but WITHOUT	Central cyanosis Chest indrawing or grunting	**Congenital heart abnormality (page {)**

Silverman Anderson retraction score

Skor	Retraksi dinding dada atas	Retraksi dinding dada bawah	Retraksi epigastrium	Dilatasi cuping hidung	Merintih
0	Sinkron	Tidak ada	Tidak ada	Tidak ada	Tidak ada
1	Napas tertinggal	Agak terlihat	Agak terlihat	Minimal	Terdengar dengan stetoskop
2	*See-Saw*	Terlihat	Terlihat	Terlihat	Terdengar tanpa stetoskop

Skor > 6 menunjukkan ancaman gagal napas

Silverman WC, Anderson DH. Controlled clinical trial on effects of water mist on obstructive respiratory signs, death rate and necropsy findings among premature infants. Pediatrics 1956; 17: 1-4.

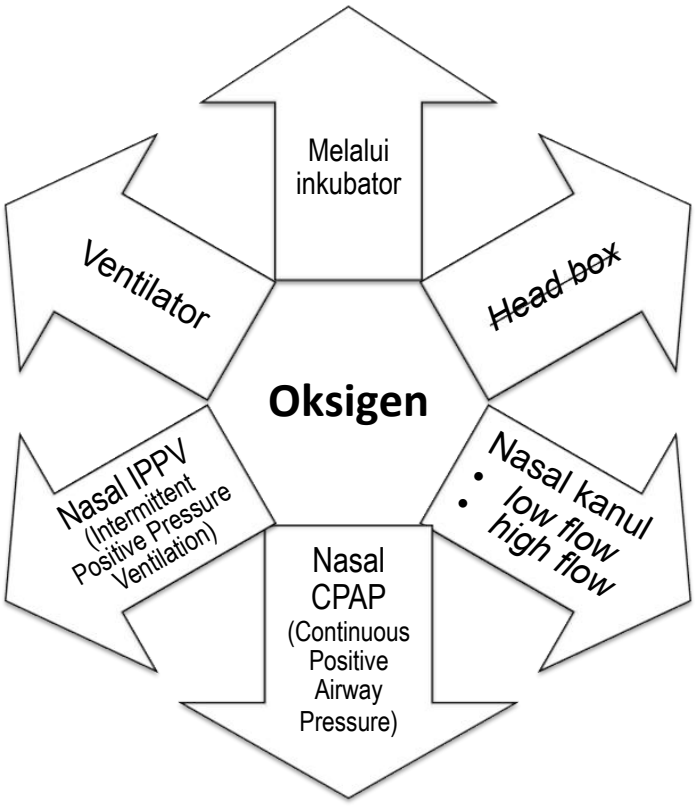
Skor Downes'

Skor	Frekuensi Napas	Sianosis	Udara Masuk	Merintih	Retraksi
0	<60/menit	Tidak sianosis	Udara masuk	Tidak merintih	Tidak ada retraksi
1	60-80/menit	Sianosis hilang dengan O_2	Penurunan ringan udara masuk	Dapat didengar dengan stetoskop	Retraksi ringan
2	>80/menit	Sianosis menetap walaupun diberi O_2	Tidak ada udara masuk	Dapat didengar tanpa alat bantu	Retraksi berat

Skor ≤ 3 Distres Napas Ringan
Skor 4 – 5 Distres Napas Sedang
Skor ≥ 6 Distres Napas Berat

Wood DW, Downes' JJ, Locks HI. A clinical score for the diagnosis of respiratory failure. Amer J Dis Child 1972; 123: 227-9.

Pemberian Oksigen



Stepwise approach towards optimal ventilation

NON-INVASIVE

Failure Criteria:
- Apneu
- Respiratory failure
  (PO_2 < 40 mmHg,
  $PaCO_2$ > 60 mmHg,
  pH < 7,25,
  BE > (-) 12)
  FiO_2 > 40%

HFN → CPAP → NIPPV → CMV → HFOV

Optimal Ventilation:

***Work of breathing* (–)**

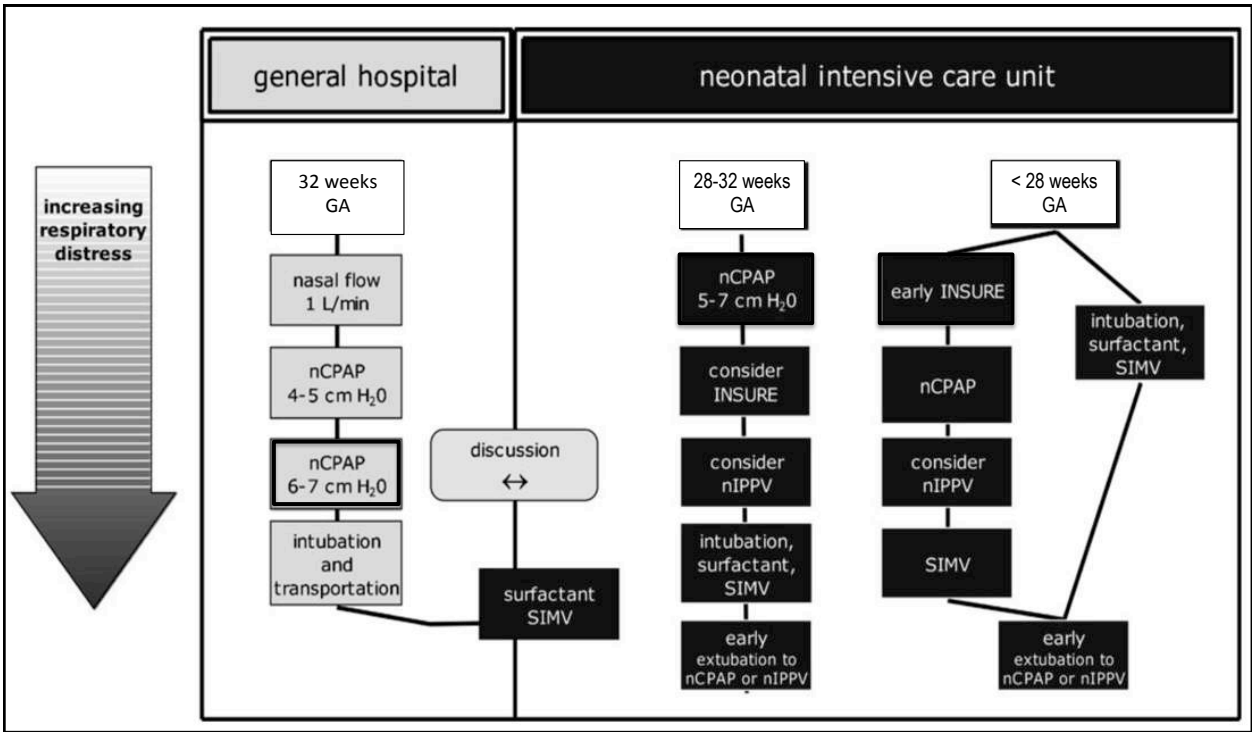
• 2 2

saturation

•Acceptable pCO_2 with pH > 7.25

• CXR- the 8th-9th ribs

Continuum of Respiratory Support



Algorithm for the treatment of RDS using NIV in PTI with increasing RDS

GA gestational age; INSURE Intubation Surfactant Extubation; nCPAP nasally delivered continuous positive airway pressure; nIPPV nasal intermittent positive pressure ventilation; SIMV synchronized intermittent mandatory ventilation

Eur J Pediatr (2010) 169:777–82

Childhood Respiratory Morbidity after Late Preterm and Early Term Delivery

Rates of respiratory morbidity diagnosed between the third and fifth year of life by gestational age category and by single week of gestational age

Gestational age	Asthma (%)	Bronchitis (%)	Asthma and bronchitis (%)
Late preterm gestation (weeks)	18.4	10.2	4.1
34	21.5	11.4	5.5
35	19.6	10.3	4.7
36	17.0	9.8	3.3
Early term gestation (weeks)	14.6	9.4	3.7
37	15.6	10.0	4.2
38	14.1	9.1	3.5
Term gestation (weeks)	12.8	8.3	3.0
39	13.4	8.2	3.0
40	12.5	8.6	3.0
41	11.5	7.6	2.6

Paediatric and Perinatal Epidemiology, 2016, 30, 67–75

Childhood Respiratory Morbidity after Late Preterm and Early Term Delivery

Bivariate comparison of neonatal and early childhood respiratory morbidity to early childhood diagnosis of asthma and bronchitis by gestational age category

	LPI		
Condition	No asthma %	Asthma %	*P*-value
Respiratory distress	4.5	5.5	0.292
Transitory tachypnea	8.9	8.7	0.869
Apnoea	7.5	10.4	**0.013**
Mechanical ventilation	4.1	5.0	0.334
Oxygen therapy	0.6	1.7	**0.004**
Sepsis	4.3	5.0	0.475
Maternal steroid injection	0.5	0.2	0.207
Respiratory syncytial virus	0.6	2.7	**<0.001**
Condition	No bronchitis %	Bronchitis %	*P*-value
Respiratory distress	4.5	6.0	0.226
Transitory tachypnea	8.9	9.1	0.903
Apnoea	8.0	7.9	0.945
Mechanical ventilation	4.2	4.8	0.604
Oxygen therapy	0.7	1.4	0.176
Sepsis	4.6	3.7	0.456
Maternal steroid injection	0.5	0.0	0.178
Respiratory syncytial virus	0.5	4.5	**<0.001**

Paediatric and Perinatal Epidemiology, 2016, 30, 67–75