Supplement File

Supplement Figure 1A- Forest plot for the outcome of change in FiO_2 after surfactant therapy

Supplement Figure 1B- Forest plot for the outcome of change in PaO_2 after surfactant therapy

Supplement Figure 2A- Forest plot for the outcome of change in after surfactant therapy

Supplement Figure 2B- Forest plot for the outcome of change in a/AO_2 after surfactant therapy

Supplement Figure 2C- Forest plot for the outcome of change in OI after surfactant therapy

Supplement Figure 3A- Risk of bias assessment of the included RCT

Supplement Figure 3B- Risk of bias assessment of the studies included in the proportion- based meta-analysis

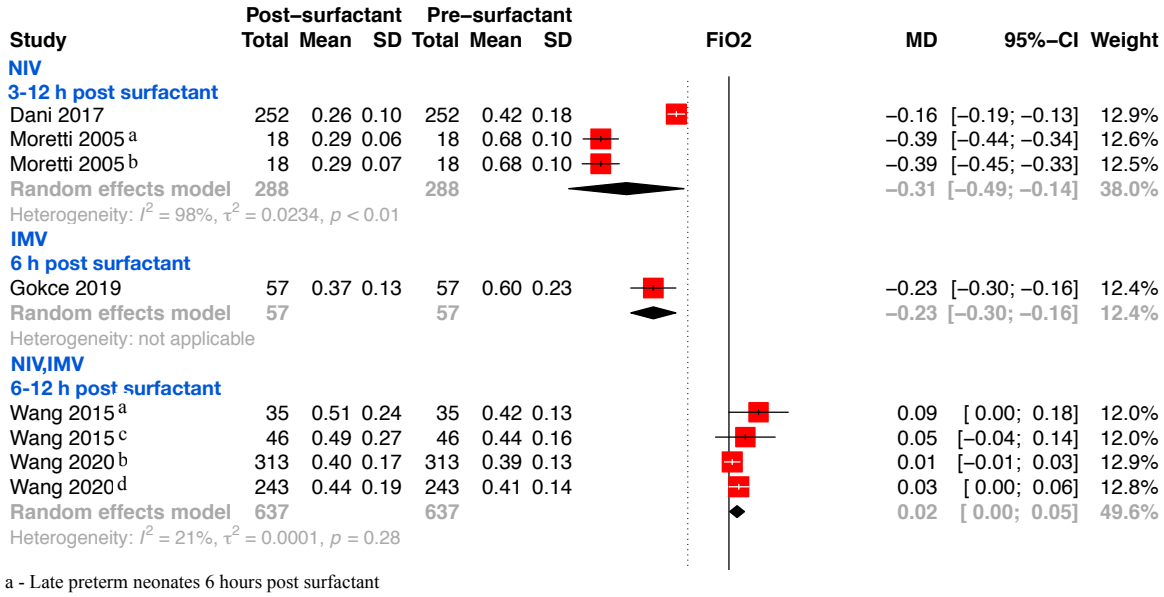
Supplement Figure 4- Risk of bias assessment of the cohort studies

Supplement File 1- Literature search strategy for all the databases

Supplement Table 1- Characteristics of included studies

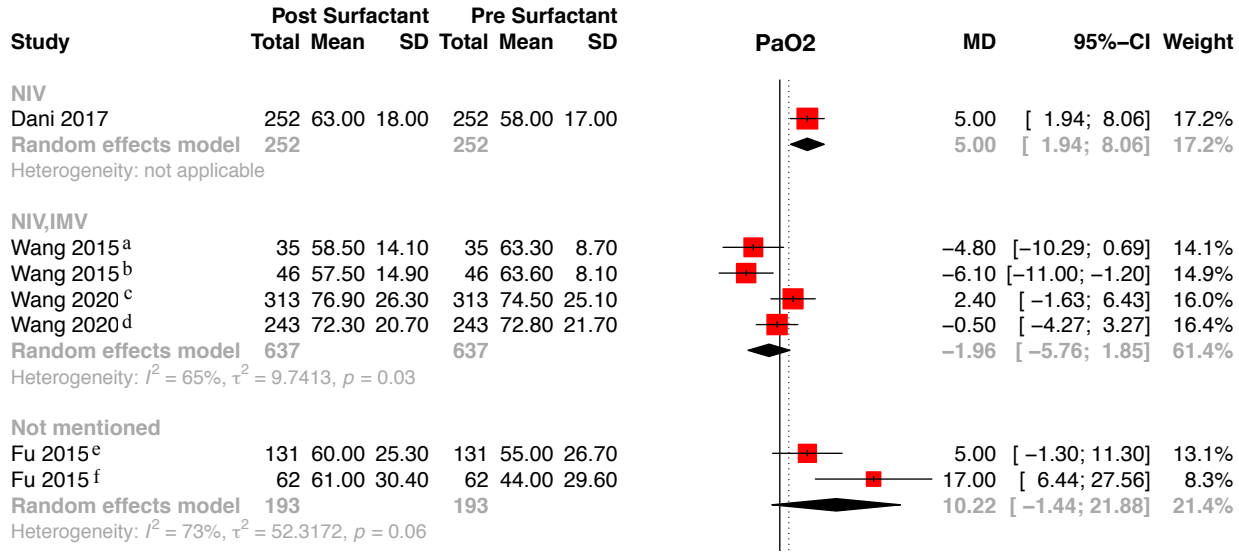
Supplement Table 2- Certainty of evidence assessment for all the outcomes

Supplement Figure 1A- Forest plot for the outcome of change in FiO2 after surfactant therapy



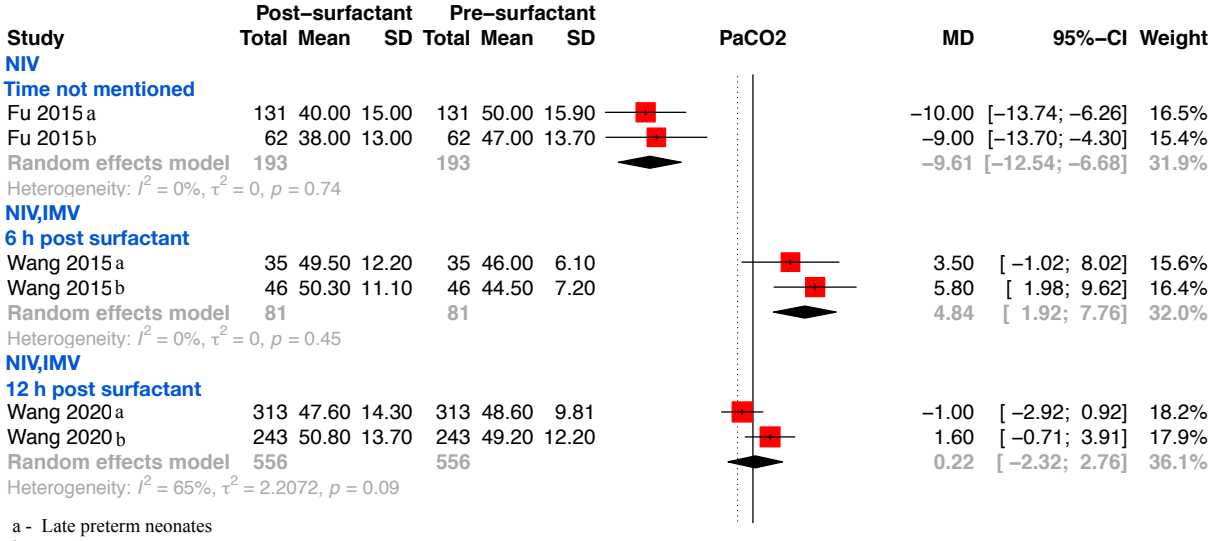
a - Late preterm neonates 6 hours post surfactant
b - Late preterm neonates 12 hours post surfactant
c - Term neonates 6 hours post surfactant
d - Term neonates 12 hours post surfactant

Supplement Figure 1B- Forest plot for the outcome of change in PaO2 after surfactant therapy



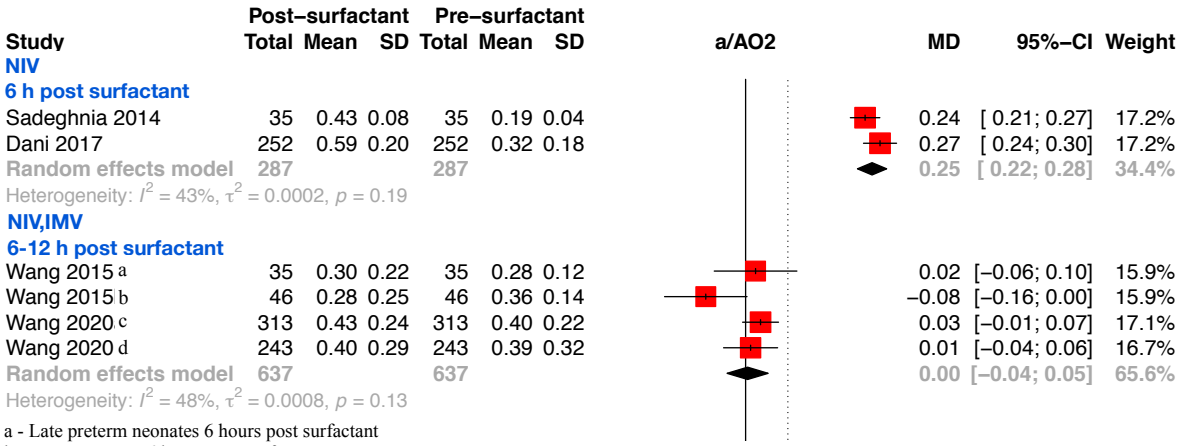
a - Late preterm neonates 6 hours post surfactant
b - Term neonates 6 hours post surfactant
c - Late preterm neonates 12 hours post surfactant
d - Term neonates 12 hours post surfactant
e - Late preterm neonates, time cut-off not mentioned
f - Term neonates, time cut-off not mentioned

Supplement Figure 2A- Forest plot for the outcome of change in PaCO2 after surfactant therapy



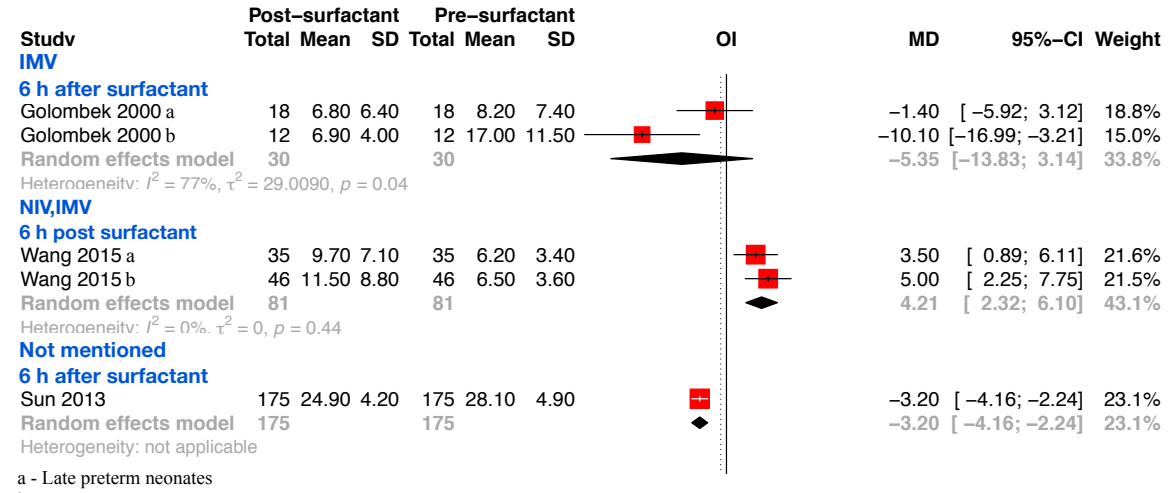
a - Late preterm neonates
b - Term neonates

Supplement Figure 2B- Forest plot for the outcome of change in a/AO2 after surfactant therapy



a - Late preterm neonates 6 hours post surfactant
b - Term neonates 6 hours post surfactant
c - Late preterm neonates 12 hours post surfactant
d - Term neonates 12 hours post surfactant

Supplement Figure 2C- Forest plot for the outcome of change in OI after surfactant therapy



a - Late preterm neonates
b - Term neonates

Supplement Figure 3A- Risk of bias assessment of the included RCT

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall bias
Zhou 2014	Some concerns	Some concerns	Low risk	Some concerns	Some concerns	High risk

Supplement Figure 3B- Risk of bias assessment of the studies included in the proportion-based meta-analysis

Study	Study Participation (Study sample adequately represents the population of interest – Late preterm and/or Term neonates with RDS included, sampling frame and recruitment explained, inclusion/ exclusion criteria specified)	Design (Prospective, retrospective analysis of prospectively collected multicentric electronic data or retrospective)	Prognostic Factor Measurement (Definition of RDS adequately stated, Severity of RDS or threshold for surfactant administration specified)	Outcome Measurement (Surfactant administration in neonates with RDS specified clearly)	Study Confounding (Gender, singleton/ multiple, Antenatal steroid use, stabilisation on CPAP or NIPPV, Mode of delivery, Time of admission to the NICU specified)	Attrition (Significant lost to follow up?)	Overall Assessment
Dani 2017	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk
Debillon 2021	Moderate risk	Low risk	High risk	Moderate risk	Low risk	Low risk	High risk
Fu 2015	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High risk
Golombek 2000	Moderate risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Jackson 2020	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk
Roth-Kleiner 2003	High risk	High risk	Low risk	Low risk	Low risk	Low risk	High risk
Sun 2013	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Wu 2013	Moderate risk	High risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk

Supplement Figure 4- Risk of bias assessment of the cohort studies

Study	Confounding	Selection	Classification of interventions	Deviation from intended intervention	Missing data	Measurement of outcomes	Selective reporting	Overall
Chen 2008	Low risk	NI	NI	Low risk	Low risk	Low risk	NI	Moderate
Dani 2017	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk	NI	Moderate
Fu 2015	Low risk	Moderate risk	Serious risk	Low risk	Low risk	Low risk	NI	Serious
Golombek 2000	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Gokce 2020	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Jasani 2015	Moderate risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Moretti 2005	Low risk	Serious risk	Moderate risk	Low risk	Low risk	Low risk	NI	Serious
Sadeghnia 2014	Low risk	Serious risk	Low risk	Low risk	Low risk	Low risk	NI	Serious
Sun 2013	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Wang 2015	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Wang 2017	NI	Serious risk	Serious risk	Low risk	Low risk	Low risk	NI	Serious
Wang 2020	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	NI	Moderate
Wu 2013	Serious risk	Low risk	Serious risk	Low risk	Low risk	Low risk	NI	Serious

Supplement Table 1- Literature search strategy for all the databases

MEDLINE

1	(""near term"" or ""late preterm"" or ""late pre-term"" or (matur* adj5 (preterm or prematur* or gestation*))).ti,ab.	(10156)
2	(34 week* or 35 week* or 36 week* or thirty four week* or thirty five week* or thirty six week*).ti,ab.	(25060)
3	Respiratory Distress Syndrome, Newborn	(13112)
4	(respiratory distress syndrome or RDS).ti,ab.	(32094)
5	Hyaline Membrane Disease	(2593)
6	(Hyaline membrane disease or HMD).ti,ab.	(2430)
7	1 or 2 or 3 or 4 or 5 or 6	(75307)
8	Surface-Active Agents	(30242)
9	surfactant*.ti,ab.	(60870)
10	8 or 9	(75602)
11	7 and 10	(4609)
12	exp animals/ not humans.sh.	(4796084)
13	11 not 12	(4108)

EMBASE

Database: Embase 1974 to present

Search Strategy:

1	(""near term"" or ""late preterm"" or ""late pre-term"" or (matur* adj5 (preterm or prematur* or gestation*))).ti,ab.	(13129)
2	(34 week* or 35 week* or 36 week* or thirty four week* or thirty five week* or thirty six week*).ti,ab.	(38340)
3	neonatal respiratory distress syndrome	(7831)
4	(respiratory distress syndrome or RDS).ti,ab.	(43333)
5	hyaline membrane disease	(3598)
6	(Hyaline membrane disease or HMD).ti,ab.	(2762)
7	1 or 2 or 3 or 4 or 5 or 6	(99896)
8	surfactant/	(40977)
9	surfactant*.ti,ab.	(75039)
10	8 or 9	(84550)
11	7 and 10	(6145)

CENTRAL

ID	Search	Hits
#1	""("near term"" or ""late preterm"" or ""late pre-term"")"	960
#2	(matur* NEAR/5 (preterm or prematur* or gestation*))	283
#3	(34 week* or 35 week* or 36 week* or thirty four week* or thirty five week* or thirty six week*)	125833
#4	"MeSH descriptor: [Respiratory Distress Syndrome, Newborn] explode all trees"	1634
#5	MeSH descriptor: [Hyaline Membrane Disease] explode all trees	98
#6	respiratory distress syndrome or RDS	6789
#7	Hyaline membrane disease or HMD	350
#8	#1 OR #2 OR #3 OR #4 OR #5 or #6 OR #7	131711
#9	MeSH descriptor: [Surface-Active Agents] explode all trees	744
#10	MeSH descriptor: [Pulmonary Surfactants] explode all trees	549
#11	surfactant*	2251
#12	#9 OR #10 OR #11	2896
#13	#8 AND #12	1433
#14	Trials subset	1230

CINAHL

#	Database	Search term	Results
1	CINAHL	""("near term"" OR ""late preterm"" OR ""late pre-term"" OR (matur* ADJ5 (preterm OR prematur* OR gestation*))).ti,ab"	3008
2	CINAHL	"(34 week* OR 35 week* OR 36 week* OR thirty four week* OR thirty five week* OR thirty six week*).ti,ab"	39035
3	CINAHL	"""RESPIRATORY DISTRESS SYNDROME""/ OR ""HYALINE MEMBRANE DISEASE""/"	3453
4	CINAHL	"(respiratory distress syndrome OR RDS).ti,ab"	9368
5	CINAHL	"(Hyaline membrane disease OR HMD).ti,ab"	299
6	CINAHL	(1 OR 2 OR 3 OR 4 OR 5)	52435
7	CINAHL	"""SURFACE-ACTIVE AGENTS""/"	1026
8	CINAHL	"""PULMONARY SURFACTANTS""/"	1592
9	CINAHL	"(surfactant*).ti,ab"	2805
10	CINAHL	(7 OR 8 OR 9)	3863
11	CINAHL	(6 AND 10)	1273

Web of Science

"TI=(""near term"" OR ""late preterm"" OR ""late pre-term"" OR ""mature preterm"" OR ""respiratory distress syndrome"" OR ""hyaline membrane disease"") AND TI=surfactant*

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years"

Supplement Table 1- Characteristics of the included studies

Author / Year / Country	Study design	Study population	Severity of RDS, threshold for surfactant	Intervention / Exposure / Risk factor	Comparator	Comments
Studies on proportion of late preterm and term neonates with RDS treated with surfactant						
Debillon 2021 France	Prospective cohort	- All neonates of 30-36 w (subgroups – 30-33 w; 34-36 w) gestation with respiratory distress of varying etiologies were studied - ANS: 44.4% - Inborn: n/a - Multiple pregnancy: 34.8% - LGA: n/a - C-Section: 56.9%	- 97.8% of the LPT neonates (including non-RDS neonates) were on NIV. - Mortality: 0% - No threshold mentioned for surfactant administration	- 31.8% of LPT neonates (n=89, total n=281) were diagnosed with RDS	-	- 28/89 (31.4%) of the LPT neonates with RDS received surfactant. - TTNB and RDS were the most common causes of respiratory distress in LPT neonates - RDS diagnosis: Physician discretion - Pre-post surfactant analysis of surrogate markers: No
Roth-Kleiner 2003 Switzerland	Retrospective cohort	- LPT and near term neonates with RDS - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: 19.6% - C-Section: 100%	- All the enrolled neonates were on IMV - Mortality: 1.8% - No threshold mentioned for surfactant administration	- Delivered through elective C-section prior to onset of labour or rupture of membranes (n=34)	Delivered through emergency C-section after onset of labour or rupture of membranes (n=22)	- There was a statistically significant difference between the gestational age and birth weight of neonates between the two groups with those delivered through emergency C-section being more immature. - 8/34 (23.5%) in the first group and 7/22 (31.8%) in second group received surfactant.

						- RDS diagnosis: CXR confirmed by Pediatric Radiologist - Pre-post surfactant analysis of surrogate markers: No
Jackson 2020 USA	Retrospective cohort	- Preterm neonates of 30-36 w gestation and birth weight of >2000 g with RDS - ANS: IG: 30%, CG: 33% - Inborn: IG: 81%, CG: 87% - Multiple pregnancy: n/a - LGA: IG: 17%, CG: 15% - C-Section: IG: 66%, CG: 63%	- 52% of the neonates who received surfactant were on IMV, 48% on NIV - Mortality: IG: 0.4%, CG: 0.1% - Though no threshold for surfactant administration was indicated, max FiO_2 on day 0-2 was median (IQR): 0.35 (0.30-0.50) in those who received surfactant	- Neonates who were treated with surfactant (Total n=25,278; 34-36w n= 19,211)	Neonates who were not treated with surfactant (Total n=29,686; 34-36w n= 22,858)	- 19211/42069 (46%) of LPT were treated with surfactant - RDS diagnosis: Clinical judgement by treating neonatologist - Pre-post surfactant analysis of surrogate markers: No - Baseline characteristics and adjusted odds ratio for the outcomes in LPT neonates were not exclusively reported.
Observational studies evaluating the efficacy of surfactant in late preterm and term neonates						
Chen 2008 China	Observational study. Not mentioned if it was prospective	- All neonates with RDS - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: n/a	- Most of the neonates receiving surfactant had severe RDS requiring IMV - Mortality: n/a - No uniform threshold used for	Group I comprising of neonates born < 35 weeks' gestation (n=103)	Group II comprising of neonates born ≥ 35 weeks' gestation (n=74)	- 63/74 (85.1%) neonates with RDS in Group II required mechanical ventilation. - RDS diagnosis: Respiratory distress and CXR

	or retrospective		surfactant administration			- Pre-post surfactant analysis of surrogate markers: Yes The decrease in OI after surfactant administration at 2h, 8-12h and 20-24h was much lesser in group II compared to group I - Most of the neonates with RDS in group II were delivered through elective C-section before the onset of labour
Dani 2017 Italy	Retrospective cohort	- LPT neonates with RDS - ANS: IG: 35%, CG: 35% - Inborn: IG: 81%, CG: 87% - Multiple pregnancy: IG: 28%, CG: 37% - LGA: n/a - C-Section: IG: 78%, CG: 87%	- 45% of neonates with RDS who required surfactant required IMV - Mortality: IG: 0%, CG: 0% - Mean FiO_2 (SD) at the time of surfactant administration was 0.42 (0.18)	Surfactant therapy (n=252)	No surfactant therapy (n=310)	- Those who received surfactant were sicker compared to those who did not - RDS diagnosis: Respiratory distress, increasing respiratory requirement in first 24 h of life, consistent CXR findings and exclusion of other causes of respiratory distress - Pre-post surfactant analysis of surrogate markers: Yes - There was significant improvement in FiO_2, PaO_2 and a/APO_2 post surfactant therapy when compared to baseline - The adjusted odds ratio for clinical outcomes such as need for mechanical ventilation, mean duration of respiratory support and hospital stay were comparable between the two

						groups. Since there was no mortality in either of the groups, adjusted odds ratio for the mortality was not calculated.
Fu 2015 China	Retrospective cohort	- All neonates with RDS - ANS: 15.3% - Inborn: n/a - Multiple pregnancy: 14.7% - LGA: n/a - C-Section: 75.1%	- Use of IMV or threshold for surfactant administration not mentioned - Mortality: n/a	LPT neonates (n=131) and term neonates (n=62) were studied as subgroups	Early preterm (defined as <34 weeks' gestation) evaluated as a separate subgroup	-41/107 (38.3%) of LPT and 19/52 (36.5%) of term neonates were given surfactant - RDS diagnosis: Respiratory distress, increasing respiratory requirement in first 6 h of life, consistent CXR findings, requiring assisted ventilation and not improving by oxygen inhalation and exclusion of other causes of respiratory distress - Pre-post surfactant analysis of surrogate markers: Yes - pH, PaO_2, $PaCO_2$ before and after surfactant therapy were studied. No time cut-off when post-surfactant blood gas parameters were studied mentioned. All the parameters post surfactant were non-significant between all the three subgroups
Golombek 2000 USA	Retrospective cohort	- Neonates 35-39 weeks' gestation with RDS. - ANS: n/a - Inborn: 0% - Multiple pregnancy: n/a	- All the enrolled neonates were on IMV - Mortality: 3.3%	Neonates 35-36 weeks' (n=18)	Neonates 37-39 weeks' (n=12)	- 30/54 (55.6%) neonates with RDS were given surfactant - RDS diagnosis: Respiratory distress, impaired gas exchange, consistent CXR findings, and

		- LGA: n/a - C-Section: 75.1%	- Surfactant was administered if the neonate required IMV, the indication for which was: $FiO_2 \geq 0.8$, $PaCO_2 \geq 8$ kPa and $PaO_2 \leq 6.7$ kPa were given surfactant while on oxygen inhalation. None were treated with CPAP prior to intubation.			exclusion of other causes of respiratory distress - Pre-post surfactant analysis of surrogate markers: Yes - OI and FiO_2 significantly decreased post surfactant in all the neonates.
Gokce 2020 Turkey	Retrospective cohort	- LPT and term neonates with RDS and non-RDS disease who were treated with surfactant - ANS: IG: 36.8%, CG: 20.5% - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: IG: 82.5%, CG: 76.9%	- All the neonates were on IMV - Mortality: : IG: 5.3%, CG: 33.3% - FiO_2 threshold for surfactant administration was >0.4 on IMV. The median (IOR) at the time of surfactant administration was 0.6 (0.31)	Neonates with RDS who were treated with surfactant (n=57)	Neonates with non-RDS lung pathology who were treated with surfactant (n=78)	- The median (IQR) FiO_2, PIP and PEEP after surfactant therapy was evaluated in those with RDS and non-RDS separately - RDS diagnosis: CXR findings - Pre-post surfactant analysis of surrogate markers: Yes - FiO_2 and PIP showed a significant decrease at 1h and 6 h after surfactant therapy in those neonates with RDS.
Jasani 2015 India	Prospective cohort	- LPT neonates 34-36 weeks' with RDS - ANS: IG: 35.7%, CG: 44.4% - Inborn: n/a - Multiple pregnancy: IG: 14.3%, CG: 7.4%	- All the enrolled neonates were stabilised on CPAP – Surfactant was administered if: FiO_2	Surfactant administration via INSURE (n=28)	CPAP alone (n=27)	- Primary outcome was requirement of invasive ventilation within 72 h which was comparable between the two groups

		- LGA: n/a - C-Section: IG: 57.1%, CG: 37%	>0.30 after 1 h of CPAP - Mortality: IG: 3.6%, CG: 7.4%			- While mortality and duration of NICU stay were similar between the two groups, duration of non-invasive support and supplemental oxygen were significantly lesser in INSURE group. - RDS diagnosis: Respiratory distress with compatible CXR findings - Pre-post surfactant analysis of surrogate markers: No
Moretti 2005 Italy	Observational study. Retrospective or prospective not mentioned	- Neonates 35-39 weeks' gestation with RDS. - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: 72%	- Neonates were treated with oxygen inhalation, CPAP or NIPPV - Mortality: n/a - Surfactant was administered if FiO_2 >0.7 or >0.6 (with Silverman score ≥7) on CPAP	Surfactant given by INSURE (n=18)	-	- RDS diagnosis: Respiratory distress with compatible CXR findings - Pre-post surfactant analysis of surrogate markers: Yes - FiO_2 post surfactant at 3 h, 6 h, 12 h and 24 h significantly decreased compared to baseline. - 28% of neonates had only transient response and required invasive ventilation post surfactant. - Presence of bacterial infection and pulmonary hypertension were associated with increased failure rates of surfactant.

Sadeghnia 2014 Iran	RCT	- LPT neonates with a mean gestational age of 35 weeks and birth weight >2000 g with RDS. - ANS: IG: 65.7% CG: 51.4% - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: IG: 78%, CG: 87%	- Neonates were stabilised on CPAP of 5 cm H2O - Mortality: n/a - Surfactant was administered if $FiO_2 \geq 0.3$ on CPAP.	Surfactant given via INSURE technique (n=35)	Surfactant given through LMA (n=35)	- Only those neonates who were given surfactant via INSURE technique were included in the analysis - RDS diagnosis: RDS symptoms (tachypnea, intercostal retraction, nasal flaring, and grunting) - Pre-post surfactant analysis of surrogate markers: Yes - a/AO_2 post surfactant administration via INSURE was significantly higher compared to baseline. - Though a similar response to surfactant was observed in the LMA group as well, they were not included in the analysis as LMA is still not a proven modality of surfactant delivery
Sun 2013 China	Retrospective cohort	- Neonates of all gestational ages diagnosed with RDS - ANS: LPT: 35.8%, Term: 8.3% - Inborn: n/a - Multiple pregnancy: LPT:39.3%, T: 1.4% - LGA: n/a - C-Section: LPT: 81.7%, T:87.3%	- 26% of LPT and 39.9% of term neonates required mechanical ventilation. -Mortality: LPT: 2%, T: 1.1% - No specific threshold for surfactant administration mentioned	LPT neonates (n=657) and term neonates (n=276) were studied as separate subgroups	Very preterm (n=1,922) and moderate preterm (n=892) were evaluated as separate subgroups	- Surfactant was administered in 380/657 (57.8%) of LPT and 193/276 (69.9%) of term neonates. - RDS diagnosis: RDS symptoms with typical CXR findings - Pre-post surfactant analysis of surrogate markers: Yes - OI and PaO_2/FiO_2 were evaluated post surfactant at 0 h,4 h,8 h,12 h and 24 h in ventilated

						neonates. The baseline OI for the combined group of LPT and term neonates were comparable to that of very and moderate preterm neonates. However, the OI at all the time cut offs post surfactant therapy was significantly higher in LPT and term neonates compared to very and moderate preterm neonates. Similarly, PaO_2/FiO_2 at all time cut offs were significantly lower in LPT and term neonates compared to very and moderate preterm neonates.
Wang 2015 China	Retrospective cohort	- All neonates with RDS of which LPT and term neonates were analysed as separate subgroups - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: LPT: 89%, T:80%	- Neonates were managed with CPAP and NIPPV if they were diagnosed to have grade I-II RDS and IMV for grade III-IV RDS. - Mortality: LPT:20%, T:11% - All infants with RDS were given surfactant as early as possible irrespective of disease severity	Neonates 35-36 weeks' gestation (n=35) and ≥37 weeks' gestation (n=46)	Neonates < 35 weeks' gestation (n=54)	- RDS diagnosis: RDS symptoms with typical CXR findings and divided into 4 grades of severity - Pre-post surfactant analysis of surrogate markers: Yes - LPT group: pH, PaO_2,a/AO_2 and $PaCO_2$ did not show any significant change at 6 h after surfactant therapy in late preterm group. FiO_2 and OI significantly increased at 6 h after surfactant therapy - Term group: There was no significant change in pH and a/AO_2. PaO_2 showed a statistically significant decrease

						and $PaCO_2$, FiO_2 and OI a statistically significant increase at 6 h after surfactant
Wang 2017 China	Retrospective cohort	- All neonates with birth weight ≥1500 g with hypoxic respiratory failure, of which LPT and term neonates were analysed as separate subgroups. - ANS: LPT: 8.7%, T: 1.7% - Inborn: n/a - Multiple pregnancy: LPT:12.8%, T: 1.4% - LGA: n/a - C-Section: LPT: 66.9%, T:65.2 %	- Hypoxic respiratory failure was defined as acute respiratory hypoxemia requiring CPAP or IMV for at least 24 h with hypoxemic status confirmed by pulse oximetry and arterial blood gas. -Mortality: LPT: IG:8%,CG: 16.8% Term: IG:11%,CG: 25.4% -16.8%- No treatment threshold for surfactant indicated	Neonates who received surfactant (LPT , n= 298; Term, n=163)	Neonates who did not receive surfactant (LPT , n= 303; Term, n=228)	- Despite non-adjustment for baseline sickness, mortality was significantly lower in surfactant group compared to non-surfactant group. - RDS diagnosis: Compatible CXR findings - Pre-post surfactant analysis of surrogate markers: No
Wang 2020 China	Retrospective cohort	- All neonates with RDS of which LPT and term neonates were analysed as separate subgroups - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: LPT: 84%, T:84%	- Neonates were managed with CPAP and NIPPV if they were diagnosed to have grade I-II RDS and IMV for grade III-IV RDS. -Mortality: LPT: 13%, T:12% - All infants with RDS were given	Neonates 34-36 weeks' gestation (n=313) and ≥37 weeks' gestation (n=243)	Neonates < 35 weeks' gestation (n=684)	- RDS diagnosis: Compatible CXR findings and blood gas findings. Severity classified into 4 grades : Grade I:IV - Pre-post surfactant analysis of surrogate markers: Yes - LPT group: There was no significant change in PaO_2, $PaCO_2$, FiO_2 and a/AO_2 12 h after surfactant therapy. pH

			surfactant as early as possible irrespective of disease severity			increased significantly 12 h post surfactant therapy. - Term group: While PaO_2, $PaCO_2$, pH and a/AO_2 did not change significantly 12 h post surfactant, FiO_2 increased significantly.
Wu 2013 China	Retrospective cohort	- LPT and term neonates with RDS - ANS: n/a - Inborn: n/a - Multiple pregnancy: n/a - LGA: n/a - C-Section: IG: 92.9%, CG: 87.8%	- All the enrolled neonates were on IMV - Mortality: IG: 15.7%; CG:19.5% - No threshold mentioned for surfactant administration	Surfactant along with standard care including invasive ventilation (n=89)	Standard care alone (n=77)	- RDS diagnosis: Symptoms of RDS within 72 h with compatible CXR findings, requiring IMV and exclusion of other diseases - Pre-post surfactant analysis of surrogate markers: No - The neonates who received surfactant were sicker and the outcomes were not adjusted for the sickness. - 89/166 (54%) of the enrolled neonates with RDS were administered surfactant. - Mortality, air leak, PPHN and pulmonary hemorrhage were comparable between the two groups even without any adjustment for baseline sickness
RCT comparing surfactant						
Zhou 2014 China	3-armed RCT	- Late preterm and term neonates with RDS	- All the neonates were on IMV at the	Group 1: Calf surfactant given at 50 mg/kg within 6 h	Group 3: Standard management	- RDS diagnosis: Symptoms of RDS within 72 h with compatible CXR findings,

		- ANS: G1: 30%, G2: 33%, G3:30% - Inborn: n/a - Multiple pregnancy: G1: 3.4%, G2: 1.7%, G3:3.4% - LGA: n/a - C-Section: G1: 90%, G2: 88%, G3:88%	time of randomisation - Mortality: G1: 10.3%, G2: 8.6%, G3: 16.9% - Surfactant was given if OI was between 10-20	after admission (n=58) Group 2: Calf surfactant given at 70 m/kg within 6 h after admission (n=58)	with invasive mechanical ventilation and surfactant given after 6 h of admission if there is no improvement despite maximal medical therapy.	requiring IMV and exclusion of other diseases - Pre-post surfactant analysis of surrogate markers: No - Group 2 had lower healthcare cost and shorter duration of mechanical ventilation when compared with group 1. Group 1 had lower healthcare cost and shorter duration of mechanical ventilation compared with the group 3. - The incidence of ventilator-associated pneumonia and duration of hospital stay in Group 2 was lower than those in group 1 and group 3. - When compared with Group 3, Groups 1 and 2 had lesser requirement of additional surfactant, maximum OI, duration of CPAP, incidence of air leak and PPHN.
ANS: Antenatal corticosteroids, CG: Control group, C-section: Caesarean-section, CPAP: Continuous positive airway pressure, CXR: Chest X-ray, FiO_2: Fraction of inspired oxygen, IG: Intervention group, IMV: Intermittent mandatory ventilation, INSURE: Intubate, surfactant, extubate, IQR: Interquartile range, LGA: Large for gestational age, LMA: Laryngeal mask airway, LPT: Late preterm, NIPPV: Non-invasive positive pressure ventilation, OI: Oxygenation index, PEEP: Poitive end expiratory pressure, PIP: Peak inflation pressure, PPHN: Persistent pulmonary hypertension of the newborn, RDS: Respiratory distress syndrome, SD: Standard deviation, TTNB: Transient tachypnea of the newborn						

Supplement Table 2: Certainty of evidence assessment for all the outcomes							
Certainty of evidence for proportion based meta-analysis							
Outcome	**Effect estimate (95%CI)**	**Risk of bias**	**Inconsistency**	**Imprecision**	**Indirectness**	**Rating up the evidence (large effect, plausible confounders); Rating down the evidence (publication bias)**	**Certainty of Evidence**
Proportion of neonates with RDS treated with surfactant	0.46 [0.40; 0.51]	Not serious	Very serious	Not serious	Serious	-	Very low
Certainty of evidence for outcomes from RCTs							
Outcome	**Effect estimate OR (95%CI)**	**Risk of bias**	**Inconsistency**	**Imprecision**	**Indirectness**	**Rating down the evidence (publication bias)**	**Certainty of Evidence**
Mortality	0.51 [0.23;1.13]	Serious	Not serious	Serious	Not serious	-	Low
Pulmonary hemorrhage	0.84 [0.25; 2.86]	Serious	Not serious	Very serious	Not serious	-	Very low
Air leak	0.28 [0.13; 0.60]	Serious	Not serious	Serious	Not serious	-	Low
PPHN	0.19 [0.08; 0.45]	Serious	Not serious	Serious	Not serious	-	Low
VAP	0.54 [0.20; 1.47]	Serious	Not serious	Serious	Not serious	-	Low
Outcome	**Effect estimate MD (95%CI)**	**Risk of bias**	**Inconsistency**	**Imprecision**	**Indirectness**	**Rating down the evidence**	**Certainty of Evidence**

						(publication bias)	
Duration of invasive mechanical ventilation (hours)	-56.46 [-100.56; -12.37]	Serious	Not serious	Serious	Not serious	-	Low
Duration of respiratory support (hours)	-46.46 [-53.26; -39.67]	Serious	Not serious	Serious	Not serious	-	Low
Duration of oxygen support (hours)	2.54 [-0.80; 5.88]	Serious	Not serious	Serious	Not serious	-	Low
Duration of hospital stay (days)	-2.03 [-3.99; -0.07]	Serious	Not serious	Serious	Not serious	-	Low
Certainty of evidence for outcomes from observational studies for clinical outcomes							
Outcome	**Effect estimate OR (95%CI)**	**Risk of bias**	**Inconsistency**	**Imprecision**	**Indirectness**	**Rating up the evidence (large effect, plausible confounders)**	**Certainty of Evidence**
Mortality	0.45 [0.32;0.64]	Serious	Not serious	Not serious	Not serious	Large effect and Plausible confounder	Moderate
Requirement of invasive ventilation	1.20 [0.41; 3.46]	Not serious	Not serious	Very serious	Not serious	Not serious	Very low
Pulmonary hemorrhage	1.82 [0.59;5.59]	Serious	-	Serious	Not serious	Not serious	Very low
Air leak	1.01 [0.32; 3.15]	Serious	-	Very serious	Not serious	Not serious	Very low

PPHN	3.12 [0.83; 11.79]	Serious	-	Serious	Not serious	Not serious	Very low
Outcome	**Effect estimate MD (95%CI)**	**Risk of bias**	**Inconsistency**	**Imprecision**	**Indirectness**	**Rating up the evidence (large effect, plausible confounders)**	**Certainty of Evidence**
Duration of respiratory support (hours)	-23.60 [-42.63; -4.27]	Serious	-	Serious	Not serious	Not serious	Very low
Duration of oxygen support (hours)	-19.50 [-31.76; -7.24]	Serious	-	Serious	Not serious	Not serious	Very low
Duration of hospital stay (days)	-1.70 [-3.8; 0.4]	Serious	-	Serious	Not serious	Not serious	Very low