Additional data

- eFig 1. Search strategies
- eFig 2. Risk of Bias and quality assessment
- eFig 3. GRADE assessment
- eFig 4. Forest plots

<u>eFig 1</u>

Database: **Ovid MEDLINE(R)** and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R) <1946 to January 19, 2022> Search Strategy:

1 (t piece or t-piece or neopuff or neo tee or babypuff or neotee or tom thumb).ti,ab,kf. (675)

- 2 (((self or flow) adj3 bag*) or mask*).ti,ab,kf. (90664)
- 3 manual ventilation.ti,ab,kf. (442)

4 (positive adj3 (pressure or ventilation)).ti,ab,kf. (30797)

- 5 exp Infant/ or (infan* or Neonat* or Newborn* or Prematur* or Preterm or (low adj3 weight*)).ti,ab,kf. (1677278)
- 6 Delivery Rooms/ or (delivery room* or birth or resuscitation).ti,ab,kf. (387460)
- 7 exp Positive-Pressure Respiration/ae, is, mt, mo [Adverse Effects, Instrumentation, Methods, Mortality] (10680)
- 8 Ventilators, Mechanical/ (9422)
- 9 1 or 2 or 3 or 4 or 7 or 8 (131755)
- 10 5 and 6 and 9 (3006)

Scopus (1,384 document results)

(TITLE-ABS-KEY (manual AND ventilation) OR TITLE-ABS-

KEY (t AND piece OR neopuff OR neo AND tee OR babypuff OR neotee OR tom AND thumb) OR TITLE-ABS-KEY ((self OR flow) W/3 bag*) OR TITLE-ABS-

KEY (positive W/3 (pressure OR ventilation)) AND TITLE-ABS-

KEY (infan* OR neonat* OR newborn* OR prematur* OR preterm OR (low W/3 weigh t*)) AND TITLE-ABS-KEY (delivery AND room* OR birth OR resuscitation))

Embase

No. Query Results	Result	S
#9. #1 AND #7 AND #8		3,394
#8. #2 OR #3 OR #4 OR #5 OR #6		203,473
#7. 'delivery room' OR birth		516,157
#6. 'positive pressure ventilation'		12,839
#5. 'manual emergency ventilator'		754
#4. (self OR flow) AND inflating AND bag	324	
#3. 'ventilator'		68,006
#2. t AND piece OR 't piece' OR neopuff OR (neo AND	7,356	
tee) OR babypuff OR neotee OR (tom AND thumb)		
#1. 'infant'/exp OR 'infant' OR 'newborn'/exp OR		1,447,060
'newborn' OR 'prematurity'/exp OR 'prematurity'		

.....

		Ng 2015 [31]	Guinsburg 2018 [32]
А			
	Representativeness of the exposed cohort	+	+
	Selection of the non- exposed cohort	+	+
	Ascertainment of exposure	+	+
	Demonstration that outcome of interest was not present at start of study	+	+
В			
	Comparability of cohorts on the gestational age	NC	•
	Comparability of cohorts for any additional factor	+	•
С			
	Assessment of outcome	+	•
	Was follow-up long enough for outcomes to occur (mortality, HIE, BPD)	+	+
	Adequacy of follow up of cohorts	+	+

	Menakaya 2004 [24]	Dawson 2011 [25]	Kookna 2019 [26]	Szyld 2014 [27]	Thakur 2015 [28]	Te Pas 2007 [30]	El-Chimi 2016 [29]
Randomisation process	+	+	+	•	•	+	•
Deviations from the intended intervention	?	?	?	?	?	?	?
Missing outcome data	+	+	+	+	+	+	•
Measurement of the outcome	+	+	•	+	+	+	•
Selection of the reported result	+	+	+	+	+	+	+
OVERALL	!	!	•	-	•	!	•

eFig 3. - Question: Fixed Pressure Devices compared to Hand Driven Pressure Devices for neonatal resuscitation at birth

			Certainty as	sessment			Nº of p	atients		Effect		1
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fixed Pressure Devices	Hand Driven Pressure Devices	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality i	n all studies											
9	observational studies and RCTs	serious	not serious	not serious	not serious	none	490/2270 (21.6%)	282/1332 (21.2%)	OR 0.57 (0.47 to 0.69)	79 fewer per 1 000 (from 100 fewer to 55 fewer)	⊕⊖⊖⊖ Very low	CRITICAL
BPD in RC	Ts or quasi-RCT	s	<u>.</u>			•	Ļ	Ļ	•	•		<u>.</u>
5	randomised trials	serious	not serious	not serious	serious (a)	none	43/627 (6.9%)	64/641 (10.0%)	RR 0.68 (0.48 to 0.96)	32 fewer per 1 000 (from 52 fewer to 4 fewer)	⊕⊕⊖⊖ Low	IMPORTANT
Intubation	in delivery room	in RCTs or quas	i-RCTs			•	Ļ	Ļ	•	•		<u>.</u>
4	randomised trials	serious	not serious	not serious	not serious	none	119/625 (19.0%)	171/641 (26.7%)	RR 0.72 (0.58 to 0.88)	75 fewer per 1 000 (from 112 fewer to 32 fewer)	⊕⊕⊕⊖ Moderate	IMPORTANT
Mechanica	al ventilation repo	orted in RCTs or	quasi-RCTs			<u>!</u>	ļ	ļ	ļ	1		<u>ļ</u>
3	randomised trials	serious	not serious	not serious	not serious	none	149/592 (25.2%)	188/605 (31.1%)	RR 0.81 (0.67 to 0.96)	59 fewer per 1 000 (from 103 fewer to 12 fewer)	⊕⊕⊕⊖ Moderate	IMPORTANT
Airleaks in	n RCTs or quasi-F	RCTs				L	I	I	I	I		I
5	randomised trials	serious	not serious	not serious	not serious	none	15/628 (2.4%)	16/643 (2.5%)	RR 0.98 (0.50 to 1.95)	0 fewer per 1 000 (from 12 fewer to 24 more)	⊕⊕⊕⊖ Moderate	IMPORTANT
Need for s	surfactant in RCT	s or quasi-RCTs										
3	randomised trials	serious	not serious	not serious	serious (a)	none	70/137 (51.1%)	103/158 (65.2%)	RR 0.78 (0.64 to 0.96)	143 fewer per 1 000 (from 235 fewer to 26 fewer)	⊕⊕⊖⊖ Low	NOT IMPORTANT(b)
cPVL in al	l studies									•		
3	observational studies	serious	not serious	not serious	not serious	none	97/1353 (7.2%)	51/526 (9.7%)	OR 0.59 (0.41 to 0.85)	37 fewer per 1 000 (from 55 fewer to 13 fewer)	⊕⊖⊖⊖ Very low	CRITICAL

(a) Number of patients below the optimal information size.(b) Important in low resources settings

CI: confidence interval; OR: odds ratio; RR: risk ratio; RCT: randomized controlled trials, BPD bronchopulmonary dysplasia; cPVL: cystic periventricular leukomalacia.

RCTs and qRCTs analysis

Mortality^{24–28}

	FPC)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
3.1.1 RCT							
Dawson 2011	2	41	6	39	22.0%	0.32 [0.07, 1.48]	
Kookna 2019	1	25	0	25	1.8%	3.00 [0.13, 70.30]	
Menakaya 2014	1	11	4	13	13.1%	0.30 [0.04, 2.27]	
Szyld 2014	11	511	15	516	53.5%	0.74 [0.34, 1.60]	
Thakur 2015	3	40	3	50	9.6%	1.25 [0.27, 5.86]	
Total (95% CI)		628		643	100.0%	0.68 [0.38, 1.20]	•
Total events	18		28				
Heterogeneity: Chi ² =	= 3.08, df	= 4 (P	= 0.54);	$I^2 = 0\%$	6		0.01 0.1 1 10 100
Test for overall effect	t: Z = 1.34	4 (P = 0)).18)				Favours FPD Favours HDPD
Test for subgroup dif	fferences:	Not ap	plicable				

HIE^{26,27}

	FPD)	HDP	D		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M–H, Fixed, 95% Cl
3.8.1 RCTs								
Kookna 2019	4	25	2	25	6.7%	2.00 [0.40, 9.95]		
Szvld 2014	21	511	28	516	93.3%	0.76 [0.44, 1.32]		
Total (95% CI)		536		541	100.0%	0.84 [0.50, 1.41]		•
Total events	25		30					
Heterogeneity: Chi ² =	= 1.26, df	= 1 (P)	= 0.26);	$I^2 = 21$	%			
Test for overall effect	: Z = 0.66	6 (P = 0).51)				0.01	0.1 1 10 100 Favours FPD Favours HDPD
Test for subgroup dif	ferences:	Not ap	plicable					

BPD²⁴⁻²⁸

	Experim	ental	Cont	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
2.1.1 RCT							
Dawson 2011	15	41	11	39	17.6%	1.30 [0.68, 2.47]	- +
Kookna 2019	0	25	1	25	2.3%	0.33 [0.01, 7.81]	
Menakaya 2014	7	10	8	11	11.9%	0.96 [0.56, 1.66]	_
Szyld 2014	21	511	44	516	68.2%	0.48 [0.29, 0.80]	
Thakur 2015	0	40	0	50		Not estimable	
Total (95% CI)		627		641	100.0%	0.68 [0.48, 0.96]	\bullet
Total events	43		64				
Heterogeneity: Chi ² =	= 7.45, df =	= 3 (P =	• 0.06); l ²	$^{2} = 60\%$			
Test for overall effect							0.01 0.1 1 10 100 Favours FPD Favours HPDP
Test for subgroup dif	ferences: I	Not app	licable				Favours FPD Favours HPDP

Intubation in DR^{25–28}

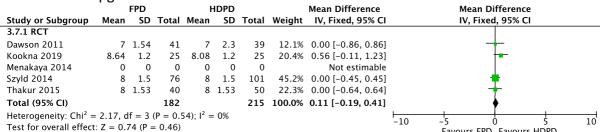
	FPD)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
1.1.1 RCT							
Dawson 2011	26	49	19	50	11.2%	1.40 [0.90, 2.17]	
Kookna 2019	1	25	1	25	0.6%	1.00 [0.07, 15.12]	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	86	511	134	516	79.2%	0.65 [0.51, 0.83]	
Thakur 2015	6	40	17	50	9.0%	0.44 [0.19, 1.01]	
Total (95% CI)		625		641	100.0%	0.72 [0.58, 0.88]	•
Total events	119		171				
Heterogeneity: Chi ² =	10.82, d	f = 3 (I	P = 0.01)	; $I^2 = 7$	2%		0.01 0.1 1 10 100
Test for overall effect Test for subgroup dif			,				Favours FPD Favours HDPD
rescror subgroup un	rerences.	not ap	pricable				

5

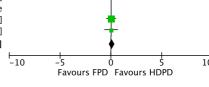
Need for advanced resuscitation ^{25–27}

	FPC)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M–H, Fixed, 95% Cl
1.6.1 RCT							
Dawson 2011	0	40	0	50		Not estimable	
Kookna 2019	1	25	1	25	5.6%	1.00 [0.07, 15.12]	
Szyld 2014	8	511	17	516	94.4%	0.48 [0.21, 1.09]	
Total (95% CI)		576		591	100.0%	0.50 [0.23, 1.11]	•
Total events	9		18				
Heterogeneity: Chi ² =	= 0.26, df	= 1 (P)	= 0.61);	$I^2 = 0\%$	6		
Test for overall effect	Z = 1.70) (P = 0	0.09)				0.01 0.1 1 10 100 Favours FPD Favours HDPD
Test for subgroup dif	ferences:	Not ap	plicable				

Five minutes Apgar score^{25–28}



Test for subgroup differences: Not applicable



Occurrences of heart rate >100 bpm at 2 minutes of life^{26,27}

	FPD)	HDP	Ď		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M–H, Fix	ed, 95% CI	
Kookna 2019	25	25	25	25	5.2%	1.00 [0.93, 1.08]			+	
Szyld 2014	479	511	466	516	94.8%	1.04 [1.00, 1.08]				
Total (95% CI)		536		541	100.0%	1.04 [1.00, 1.07]			,	
Total events	504		491							
Heterogeneity: Chi ² = Test for overall effect	,			$I^2 = 0\%$	6		0.01	0.1 Favours FPD	1 10 Favours HDPD	100

Air leaks^{24–28}

	FPD)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
3.2.1 RCT							
Dawson 2011	1	41	2	39	12.9%	0.48 [0.04, 5.04]	
Kookna 2019	0	25	0	25		Not estimable	
Menakaya 2014	1	11	5	13	28.8%	0.24 [0.03, 1.73]	
Szyld 2014	13	511	8	516	50.0%	1.64 [0.69, 3.93]	-+∎
Thakur 2015	0	40	1	50	8.4%	0.41 [0.02, 9.91]	
Total (95% CI)		628		643	100.0%	0.98 [0.50, 1.95]	•
Total events	15		16				
Heterogeneity: Chi ² =	3.94, df	= 3 (P	= 0.27);	$1^2 = 24$	%		0.01 0.1 1 10 100
Test for overall effect	Z = 0.05	5 (P = 0)).96)				Favours FPD Favours HDPD
Test for subgroup dif	ferences:	Not ap	plicable				

Surfactant needs 25,27,28

	FPD)	HDP	D		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95%	CI	
1.2.1 RCT										
Dawson 2011	25	41	26	39	28.1%	0.91 [0.66, 1.27]				
Kookna 2019	0	0	0	0		Not estimable				
Menakaya 2014	0	0	0	0		Not estimable				
Szyld 2014	39	77	68	101	62.1%	0.75 [0.58, 0.97]				
Thakur 2015	6	19	9	18	9.8%	0.63 [0.28, 1.42]				
Total (95% CI)		137		158	100.0%	0.79 [0.64, 0.96]		•		
Total events	70		103							
Heterogeneity: Chi ² =	1.20, df	= 2 (P	= 0.55);	$I^2 = 0\%$	6		0.01	0.1 1	10	100
Test for overall effect	: Z = 2.36	5 (P = 0).02)				0.01	Favours FPD Favour	s HDPD	100
Test for subgroup dif	ferences:	Not ap	plicable							

Mechanical ventilation requirements^{25,27,28}

	FPD)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
3.9.1 RCT							
Dawson 2011	25	41	24	39	13.2%	0.99 [0.70, 1.40]	-
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	116	511	147	516	78.6%	0.80 [0.65, 0.98]	
Thakur 2015	8	40	17	50	8.1%	0.59 [0.28, 1.22]	— • +
Total (95% CI)		592		605	100.0%	0.81 [0.67, 0.96]	•
Total events	149		188				
Heterogeneity: Chi ² =	2.08, df	= 2 (P	= 0.35);	$I^2 = 4\%$,		0.01 0.1 1 10 100
Test for overall effect	: Z = 2.36	5 (P = 0)).02)				0.01 0.1 1 10 100 Favours FPD Favours HDPD
Test for subgroup dif	ferences:	Not ap	plicable				

Mechanical ventilation duration^{27,28}

		FPD		- I	HDPD			Mean Difference		Mea	an Differer	ice	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95%	CI	
1.3.1 RCT													
Dawson 2011	0	0	0	0	0	0		Not estimable					
Menakaya 2014	0	0	0	0	0	0		Not estimable					
Szyld 2014	5	7.6	116	8.3	13.3	147	33.9%	-3.30 [-5.86, -0.74]					
Thakur 2015	1.53	1.6	8	2.17	3.06	17	66.1%	-0.64 [-2.47, 1.19]		-	──■┼──		
Total (95% CI)			124			164	100.0%	-1.54 [-3.03, -0.05]		-			
Heterogeneity: Chi ² =	= 2.75, d	f = 1	(P = 0.)	10); I ² =	= 64%				+10		<u> </u>	<u> </u>	10
Test for overall effect									-10	-5 Favours	FPD Favor	ہ urs HDPD	10

Test for subgroup differences: Not applicable

Non-invasive ventilation duration^{27,28}

		FPD		H	IDPD			Mean Difference		Mean I	oifference	e	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% C	1	
1.4.1 RCTs													
Szyld 2014	7.83	11.3	511	7.96	10.1	516	98.9%	-0.13 [-1.44, 1.18]		_	-		
Thakur 2015	27.1	30.76	40	29.15	28.6	50	1.1%	-2.05 [-14.45, 10.35]	←		Ŧ		
Total (95% CI)			551			566	100.0%	-0.15 [-1.46, 1.15]		-			
Heterogeneity: Chi ² =	= 0.09, d	If = 1 (F	P = 0.76	5); $I^2 = 0$	%				-10	<u> </u>			10
Test for overall effect	: Z = 0.2	23 (P =	0.82)						-10	-5 Favours FPI) Favour	s HDPD	10
Test for subgroup dif	ferences	s: Not a	pplicab	le						, arours , i	, intour	511212	

Mortality in preterm infants^{24,25,28}

	FPC)	HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M–H, Fixed, 95% Cl
3.10.1 RCTs							
Dawson 2011	2	41	6	39	47.7%	0.32 [0.07, 1.48]	
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	1	11	4	13	28.4%	0.30 [0.04, 2.27]	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015	3	19	3	18	23.9%	0.95 [0.22, 4.10]	
Total (95% CI)		71		70	100.0%	0.46 [0.18, 1.15]	
Total events	6		13				
Heterogeneity: Chi ² =	1.34, df	= 2 (P	= 0.51);	$I^2 = 0\%$,		0.01 0.1 1 10 100
Test for overall effect Test for subgroup diff		,	,				0.01 0.1 1 10 100 Favours FPD Favours HDPD

DR intubation in preterm infants^{25,27,28}

	' FPC)	HDP	D		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M–H, Fixed, 95% Cl	
1.9.1 RCTs									
Dawson 2011	26	49	19	50	19.3%	1.40 [0.90, 2.17]		+	
Szyld 2014	45	85	76	110	68.0%	0.77 [0.61, 0.97]			
Thakur 2015	5	19	12	18	12.7%	0.39 [0.17, 0.90]			
Total (95% CI)		153		178	100.0%	0.84 [0.69, 1.03]		•	
Total events	76		107						
Heterogeneity: Chi ² =	= 8.93, df	= 2 (P	= 0.01);	$l^2 = 78$	\$%				100
Test for overall effect	t: Z = 1.63	8 (P = 0	0.09)				0.01	0.1 1 10 Favours FPD Favours HDPD	100
Test for subgroup dif	fferences:	Not ap	plicable					Favours FFD Favours HDFD	

MV requirements in preterm infants(RR 0,89[0,76-1,03)^{25,27,28}.

	FPD		HDP	D		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.7.1 RCT							
Dawson 2011	25	41	24	39	21.8%	0.99 [0.70, 1.40]	- + -
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	62	85	85	110	65.5%	0.94 [0.80, 1.11]	· · · · · · · · · · · · · · · · · · ·
Thakur 2015	6	19	14	18	12.7%	0.41 [0.20, 0.82]	
Total (95% CI)		145		167	100.0%	0.89 [0.76, 1.03]	♦
Total events	93		123				
Heterogeneity: $Chi^2 =$	5.66, df	= 2 (P	= 0.06);	$l^2 = 65$	%		
Test for overall effect:							0.01 0.1 1 10 100 Favours FPD Favours HDPD

Test for subgroup differences: Not applicable

Overall analysis, including RCTs with bundle interventions and cohort studies

Mortality^{24–32}

	FPD	,	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.1.1 RCT							
Dawson 2011	2	41	6	39	1.3%	0.28 [0.05, 1.49]	
Kookna 2019	1	25	0	25	0.3%	3.12 [0.12, 80.39]	
Menakaya 2014	1	11	4	13	0.6%	0.23 [0.02, 2.40]	
Szyld 2014	11	511	15	516	5.8%	0.73 [0.33, 1.62]	
Thakur 2015	3	40	3	50	1.3%	1.27 [0.24, 6.66]	
Subtotal (95% CI)		628		643	9.3%	0.68 [0.36, 1.25]	
Fotal events	18		28				
Heterogeneity: Tau ² =	= 0.00; Cł	$1i^2 = 3.$	34, df =	4 (P =	0.50); I ² =	= 0%	
Test for overall effect	: Z = 1.24	$\downarrow (P = C)$).21)				
3.1.2 RCT with bund							
I-Chimi 2017	12	57	19	55	5.0%	0.51 [0.22, 1.18]	
Fe Pas 2007	2	104	4	103	1.2%	0.49 [0.09, 2.71]	
Subtotal (95% CI)		161		158	6.2%	0.50 [0.23, 1.07]	
Fotal events	14	2	23				
Heterogeneity: Tau ² =				1 (P =	0.97); l4 =	= 0%	
Test for overall effect	Z = 1.78	3 (P = C)).07)				
3.1.3 cohort studies							
Guinsburg 2018	456	1456	224	506	83.2%	0.57 [0.47, 0.71]	
Ng 2015	2	25	7		1.3%	0.22 [0.04, 1.21]	
Subtotal (95% CI)	2	1481		531	84.4%	0.53 [0.31, 0.89]	
Total events	458		231				•
Heterogeneity: Tau ² =		$1i^2 = 1$		1 (P =	$(0.28) \cdot 1^2 =$	= 15%	
5 ,	,		,	- () -	0.20), 1 -	- 1570	
	. 2 - 2.50	, (i – t					
est for overall effect							• 1
Test for overall effect Fotal (95% CI)		2270		1332	100.0%	0.57 [0.47, 0.69]	\bullet
	490	2270	282	1332	100.0%	0.57 [0.47, 0.69]	•
Fotal (95% CI) Fotal events						. , .	• · · · · · · · · · · · · · · · · · · ·
Total (95% CI)	= 0.00; Cł	ni² = 4.	92, df =	8 (P =		. , .	0.01 0.1 1 10 10 Favours FPD Favours HDPD

Bronchopulmonary dysplasia^{24–30}

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
2.1.1 RCT							
Dawson 2011	15	41	11	39	11.7%	1.47 [0.57, 3.77]	
Kookna 2019	0	25	1	25	1.3%	0.32 [0.01, 8.25]	
Menakaya 2014	7	10	8	11	3.6%	0.88 [0.13, 5.82]	
Szyld 2014	21	511	44	516	23.5%	0.46 [0.27, 0.78]	
Thakur 2015 Subtotal (95% CI)	0	40 627	0	50 641	40.1%	Not estimable 0.71 [0.34, 1.47]	
Total events	43		64				-
Heterogeneity: Tau ² =	= 0.19; Ch	$i^2 = 4.6$	9, $df = 3$	(P = 0)	20); $I^2 =$	36%	
Test for overall effect	,			,			
2.1.2 RCT with bund	le interve	ntions					
El-Chimi 2017	1	57	4	55	2.7%	0.23 [0.02, 2.10]	
Te Pas 2007	22	104	34	103	20.0%	0.54 [0.29, 1.02]	
Subtotal (95% CI)		161		158	22.7%	0.51 [0.28, 0.93]	\bullet
Total events	23		38				
Heterogeneity: Tau ² =	= 0.00; Ch	$i^2 = 0.5$	5, df = 1	(P = 0)	.46); I ² =	0%	
Test for overall effect	: Z = 2.19	(P = 0.0)	03)				
2.1.3 cohort studies							
Guinsburg 2018	254	1456	95	506	37.2%	0.91 [0.70, 1.19]	
Na 2015	0	0	0	0	57.12/0	Not estimable	
Subtotal (95% CI)	, i i i i i i i i i i i i i i i i i i i	1456	· ·	506	37.2%	0.91 [0.70, 1.19]	
Total events	254		95				
Heterogeneity: Not ag							
Test for overall effect		(P = 0.1)	50)				
		·	/				
Total (95% CI)		2244		1305	100.0%	0.70 [0.48, 1.02]	\blacklozenge
10tal (95% CI)			197				
Total events	320		197				
Total events Heterogeneity: Tau² =	= 0.08; Ch		6, df = 6	(P = 0)	.14); I ² =	38%	
Total events	= 0.08; Ch : Z = 1.85	(P = 0.0)	6, df = 6 06)	·	.,	0	0.01 0.1 1 10 100 Favours FPD Favours HPDP

DR intubation rates^{25–30,32}

	FPD		HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.1.1 RCT							
Dawson 2011	26	49	19	50	12.0%	1.84 [0.83, 4.11]	+
Kookna 2019	1	25	1	25	1.4%	1.00 [0.06, 16.93]	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	86	511	134	516	26.9%	0.58 [0.43, 0.78]	
Thakur 2015	6	40	17	50	8.3%	0.34 [0.12, 0.98]	
Subtotal (95% CI)		625		641	48.7%	0.74 [0.35, 1.56]	
Total events	119		171				
Heterogeneity: Tau ² =	= 0.33; Cł	$i^2 = 8.$	63, df =	3 (P =	0.03); I ² :	= 65%	
Test for overall effect	: Z = 0.79) (P = 0).43)				
1.1.2 RCT with bund	lle interve	ention					
El-Chimi 2017	3	57	13	55	5.7%	0.18 [0.05, 0.67]	
Te Pas 2007	18	104	37	103	15.5%	0.37 [0.20, 0.71]	_
Subtotal (95% CI)		161		158	21.2%	0.32 [0.18, 0.58]	◆
Total events	21		50				-
Heterogeneity: Tau ² =	= 0.00; Cł	$i^2 = 0.$	96, df =	1 (P =	0.33); I ² :	= 0%	
Test for overall effect	: Z = 3.80	(P = 0)).0001)				
1.1.3 cohort studies							
Guinsburg 2018	786	1456	340	506	30.1%	0.57 [0.46, 0.71]	-
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		1456		506	30.1%	0.57 [0.46, 0.71]	◆
Total events	786		340				
Heterogeneity: Not ap	oplicable						
Test for overall effect	: Z = 5.15	5 (P < 0).00001)				
Total (95% CI)		2242		1305	100.0%	0.56 [0.40, 0.79]	•
Total events	926		561				•
Heterogeneity: Tau ² =		$u^2 = 1^3$		= 6 (P =	= 0 03)· 1 ²	= 57%	
Test for overall effect	,		,	U () -	5105), 1	5.70	0.01 0.1 1 10 1
Test for subgroup dif			,	= 2 (P	= 0.14	$1^2 = 49.2\%$	Favours FPD Favours HDPD
. cot or bubgroup un	.e.ences.	-	5.5 i, ui	· • (1	0.1.1),		

Apgar scores at 5 minutes^{25–30,32}

		FPD			IDPD			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.7.1 RCT									
Dawson 2011	7	1.54	41	7	2.3	39	9.5%	0.00 [-0.86, 0.86]	+
Kookna 2019	8.64	1.2	25	8.08	1.2	25	12.1%	0.56 [-0.11, 1.23]	
Menakaya 2014	0	0	0	0	0	0		Not estimable	
Szyld 2014	8	1.5	76	8	1.5	101	15.5%	0.00 [-0.45, 0.45]	+
Thakur 2015	8	1.53	40	8	1.53	50	12.6%	0.00 [-0.64, 0.64]	+
Subtotal (95% CI)			182			215	49.8%	0.11 [-0.19, 0.41]	•
Heterogeneity: Tau ²	= 0.00;	Chi² =	2.17, 0	df = 3 (I	P = 0.	54); I ² =	= 0%		
Test for overall effec	t: $Z = 0$.	74 (P =	= 0.46)						
3.7.2 RCT with bun	dle inter	ventio	ons						
El-Chimi 2017	8	1.5	57	7	1.5	55	13.8%	1.00 [0.44, 1.56]	
Te Pas 2007	9	0.75	104	8	1.5	103	17.5%	1.00 [0.68, 1.32]	-
Subtotal (95% CI)			161			158	31.3%	1.00 [0.72, 1.28]	•
Heterogeneity: Tau ²	= 0.00;	Chi² =	0.00, 0	df = 1 (I)	P = 1.	00); I ² =	= 0%		
Test for overall effec	t: Z = 7.	01 (P ·	< 0.000	001)					
3.7.3 cohort studies	s								
Guinsburg 2018	8	1.48	1456	7	2.23	506	19.0%	1.00 [0.79, 1.21]	
Ng 2015	0	0	0	0	0	0		Not estimable	
Subtotal (95% CI)			1456			506	19.0%	1.00 [0.79, 1.21]	♦
Heterogeneity: Not a	pplicable	e							
Test for overall effec	t: Z = 9.	39 (P ·	< 0.000	001)					
Total (95% CI)			1799			879	100.0%	0.57 [0.20, 0.94]	•
Heterogeneity: Tau ²	= 0.17.0	Chi ² =	27 70	df = 6	(P = 0)				
Test for overall effect	,		,		– c		/ 0/0		-10 -5 0 5 1
Test for subgroup di		,		·	2 /D		01) 12	02.2%	Favours FPD Favours HDPD

Test for subgroup differences: $Chi^2 = 25.53$, df = 2 (P < 0.00001), I² = 92.2%

Air leaks^{25–30,32}

	FPD	-	HDP	-		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.2.1 RCT							
Dawson 2011	1	41	2	39	5.7%	0.46 [0.04, 5.32]	
Kookna 2019	0	25	0	25		Not estimable	
Menakaya 2014	1	11	5	13	6.1%	0.16 [0.02, 1.66]	
Szyld 2014	13	511	8	516	24.0%	1.66 [0.68, 4.03]	
Thakur 2015 Subtotal (95% CI)	0	40 628	1	50 643	3.4% 39.2%	0.41 [0.02, 10.27] 0.73 [0.23, 2.35]	
Total events	15		16				
Heterogeneity: Tau ² =	= 0.46; Cl	hi² = 4.	29, df =	3 (P =	0.23); I ²	= 30%	
Test for overall effect	:: Z = 0.5	2 (P = 0)	0.60)				
3.2.2 RCT with bund	lle interv	ention	5				
El-Chimi 2017	4	57	6	55	15.0%	0.62 [0.16, 2.32]	
Te Pas 2007	1	104	7	100	7.3%		
Subtotal (95% CI)		161		158	22.3%	0.36 [0.08, 1.55]	
Total events	5		13				
Heterogeneity: Tau ² =	,		,	1 (P =	0.22); l ² :	= 34%	
Test for overall effect	:: Z = 1.3	8 (P = 0).17)				
3.2.3 cohort studies							
Guinsburg 2018	99	1456	28	506	38.5%	1.25 [0.81, 1.92]	-
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		1456		506	38.5%	1.25 [0.81, 1.92]	•
Total events	99		28				
Heterogeneity: Not a	oplicable						
Test for overall effect	Z = 1.0	0 (P = 0).32)				
Total (95% CI)		2245		1307	100.0%	0.82 [0.44, 1.52]	•
Total events	119		57				
2	= 0.21: C	$hi^2 = 9.$	22, df =	6 (P =	0.16); I ² :	= 35%	
Heterogeneity: Tau ² =							
Heterogeneity: Tau² = Test for overall effect	,).53)				0.01 0.1 1 10 10 Favours FPD Favours HDPD

Need for surfactant^{25,27,28,32}

	FPC)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.2.1 RCT							
Dawson 2011	25	41	26	39	5.0%	0.78 [0.31, 1.95]	
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	39	77	68	101	11.3%	0.50 [0.27, 0.92]	
Thakur 2015 Subtotal (95% CI)	6	19 137	9	18 158	2.4% 18.7%	0.46 [0.12, 1.76] 0.56 [0.35, 0.90]	•
Total events	70		103				
Heterogeneity: Tau ² =	0.00; Cł	$ni^2 = 0.$	73, df =	2 (P =	0.69); I ² :	= 0%	
Test for overall effect:	Z = 2.42	2 (P = 0)).02)				
1.2.2 RCT with bund	le interv	entions	5				
El-Chimi 2017	0	57	0	55		Not estimable	
Te Pas 2007	0	0	0	0		Not estimable	
Subtotal (95% CI)		57		55		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not app	licable					
1.2.3 cohort studies							
Guinsburg 2018	976	1456	377	506	81.3%	0.70 [0.55, 0.87]	
Ng 2015	0	0	0	0		Not estimable	_
Subtotal (95% CI)		1456		506	81.3%	0.70 [0.55, 0.87]	\bullet
Total events	976		377				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 3.12	2 (P = 0)).002)				
Total (95% CI)		1650		719	100.0%	0.67 [0.54, 0.82]	•
Total events	1046		480				
Heterogeneity: $Tau^2 =$		$ni^2 = 1.$	42. df =	3 (P =	0.70): I ² :	= 0%	
Test for overall effect:							0.01 0.1 1 10 100
Test for subgroup diff					o	2 00/	Favours FPD Favours HDPD

Mechanical ventilation requirements ^{25,27–32}

	FPD)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
3.9.1 RCT							
Dawson 2011	25	41	24	39	9.0%	0.98 [0.40, 2.40]	
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	116	511	147	516	25.9%	0.74 [0.56, 0.98]	
Thakur 2015	8	40	17	50	8.0%	0.49 [0.18, 1.28]	
Subtotal (95% CI)		592		605	42.9%	0.73 [0.57, 0.95]	\blacklozenge
Total events	149		188				
Heterogeneity: Tau ² =	= 0.00; Cł	$ni^2 = 1.$	09, df =	2 (P =	0.58); I ² =	= 0%	
Test for overall effect	:: Z = 2.36	5 (P = C)	0.02)				
3.9.2 RCT with bund	lle intervo	entions	5				
El-Chimi 2017	17	57	25	55	11.0%	0.51 [0.23, 1.11]	_ _
Te Pas 2007	38	104	52	103	16.3%	0.56 [0.32, 0.98]	
Subtotal (95% CI)		161		158	27.3%	0.55 [0.35, 0.86]	\bullet
Total events	55		77				
Heterogeneity: Tau ² =	= 0.00; Cł	$ni^2 = 0.$	04, df =	1 (P =	0.83); I ² =	= 0%	
Test for overall effect	: Z = 2.63	B (P = C)	.009)				
3.9.3 cohort studies							
Guinsburg 2018		1456	422	506	26.6%	0.60 [0.46, 0.78]	-
Juliisburg 2018				25	3.2%	0.04 [0.01, 0.22]	
Na 2015							
Ng 2015 Subtotal (95% Cl)	2	25 1481	17				
Subtotal (95% CI)	_	25 1481		531	29.8%	0.18 [0.01, 2.47]	
Subtotal (95% CI) Total events	1096	1481	439	531	29.8%	0.18 [0.01, 2.47]	
Subtotal (95% CI) Total events Heterogeneity: Tau² =	1096 = 3.25; Cł	1481 $ni^2 = 9.$	439 73, df =	531	29.8%	0.18 [0.01, 2.47]	
Subtotal (95% CI) Total events	1096 = 3.25; Cł	1481 $ni^2 = 9.$	439 73, df =	531	29.8%	0.18 [0.01, 2.47]	
Subtotal (95% CI) Total events Heterogeneity: Tau² =	1096 = 3.25; Cł	1481 $ni^2 = 9.$	439 73, df =	531 1 (P =	29.8%	0.18 [0.01, 2.47]	•
Subtotal (95% Cl) Total events Heterogeneity: Tau ² = Test for overall effect	1096 = 3.25; Cł	1481 $ni^2 = 9.$ 3 (P = 0	439 73, df =	531 1 (P =	29.8% 0.002); I ²	0.18 [0.01, 2.47] - 90%	•
Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect Total (95% CI)	1096 = 3.25; Ch :: Z = 1.28 1300	1481 $hi^2 = 9.$ B (P = 0) 2234	439 73, df = 0.20) 704	531 1 (P = 1294	29.8% 0.002); I ² 100.0%	0.18 [0.01, 2.47] - = 90% 0.58 [0.42, 0.80]	
Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect Total (95% CI) Total events	1096 = 3.25; Cf :: Z = 1.28 1300 = 0.08; Cf	1481 $hi^2 = 9.$ B (P = 0) 2234 $hi^2 = 13$	439 73, df = 0.20) 704 8.25, df =	531 1 (P = 1294	29.8% 0.002); I ² 100.0%	0.18 [0.01, 2.47] - = 90% 0.58 [0.42, 0.80]	01 0.1 1 10 10 Favours FPD Favours HDPD

Mechanical ventilation duration

		FPD		H	IDPD			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.3.1 RCT									
Dawson 2011	0	0	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0	0	0		Not estimable	
Szyld 2014	5	7.6	116	8.3	13.3	147	19.4%	-3.30 [-5.86, -0.74]	_
Thakur 2015	1.53	1.6	8	2.17	3.06	17	37.8%	-0.64 [-2.47, 1.19]	
Subtotal (95% CI)			124			164	57.2%	-1.81 [-4.40, 0.77]	
Heterogeneity: Tau ² =	= 2.25; 0	Chi² =	2.75, c	f = 1 (P = 0.1	10); I ² =	= 64%		
Test for overall effect	Z = 1.3	37 (P =	= 0.17)						
1.3.2 RCT with bund	le inter	ventic	ons						
El-Chimi 2017	0	0	0	0	0	0		Not estimable	
Te Pas 2007	4.02	5.62	38	6	7.5	52	17.2%	-1.98 [-4.69, 0.73]	
Subtotal (95% CI)			38			52	17.2%	-1.98 [-4.69, 0.73]	
Heterogeneity: Not ap	plicable	2							
Test for overall effect	: Z = 1.4	43 (P =	= 0.15)						
1.3.3 cohort studies									
Guinsburg 2018	11.6	19.6	1094	13.8	19.9	422	25.6%	-2.20 [-4.43, 0.03]	
Ng 2015	0	0	0	0	0	0		Not estimable	
Subtotal (95% CI)			1094			422	25.6%	-2.20 [-4.43, 0.03]	
Heterogeneity: Not ap	plicable								
Test for overall effect	Z = 1.9	94 (P =	= 0.05)						
Total (95% CI)			1256			638	100.0%	-1.79 [-2.91, -0.66]	•
Heterogeneity: Tau ² =	= 0.00: 0	Chi ² =	3.01. 0	f = 3(P = 0.3	39): 1 ² =	= 0%	- / -	
Test for overall effect					0	, .	0,0		
Test for subgroup dif				· ·	. / D	0 0 0 V I	2 00/		Favours FPD Favours HDPD

Test for subgroup differences: $Chi^2 = 0.05$, df = 2 (P = 0.98), $I^2 = 0\%$

Duration of oxygenotherapy ^{27,32}

		FPD		ŀ	IDPD			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Szyld 2014	13.8	17	208	22.8	25	222	49.2%	-9.00 [-13.02, -4.98]	_
Guinsburg 2018	26.4	34.4	1413	27.7	34.1	480	50.8%	-1.30 [-4.84, 2.24]	
Total (95% CI)			1621			702	100.0%	-5.09 [-12.63, 2.46]	
Heterogeneity: Tau ² Test for overall effect					(P = 0	.005); I	² = 87%	-	-10 -5 0 5 10 Favours FPD Favours HDPD

Mortality in preterm infants^{24,25,28,30,32}

	FPD		HDP			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.10.1 RCTs							
Dawson 2011	2	41	6	39	1.5%	0.28 [0.05, 1.49]	
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	1	11	4	13	0.7%	0.23 [0.02, 2.40]	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015 Subtotal (95% CI)	3	19 71	3	18 70	1.3% 3.5%	0.94 [0.16, 5.39] 0.42 [0.14, 1.24]	
Total events	6		13				
Heterogeneity: Tau ² =	= 0.00; Cł	$ni^2 = 1.$	30, df =	2 (P =	0.52); l ² =	= 0%	
Test for overall effect	:: Z = 1.56	5 (P = 0)	.12)				
3.10.2 RCT with bun	dle						
El-Chimi 2017	0	0	0	0		Not estimable	
Te Pas 2007	2	104	4	103	1.4%		
Subtotal (95% CI)		104		103	1.4%	0.49 [0.09, 2.71]	
Total events	2		4				
Heterogeneity: Not ap							
Test for overall effect	Z = 0.82	2 (P = 0)	.41)				
3.10.3 cohort studie	s						
Guinsburg 2018	456	1456	224	506	95.1%	0.57 [0.47, 0.71]	
Guillsburg 2016	450	1430	224				
5	430	1430	0	0		Not estimable	-
Ng 2015					95.1%	Not estimable 0.57 [0.47, 0.71]	•
Ng 2015 Subtotal (95% CI)		0		0			•
Ng 2015 Subtotal (95% CI) Total events	0 456	0	0	0			•
Ng 2015 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect	0 456 oplicable	0 1456	0 224	0 506			•
Ng 2015 Subtotal (95% CI) Total events Heterogeneity: Not ap	0 456 oplicable	0 1456	0 224	0 506			 ▲
Ng 2015 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect	0 456 oplicable	0 1456 4 (P < 0	0 224	0 506	95.1%	0.57 [0.47, 0.71]	 ▲
Ng 2015 Subtotal (95% CI) Total events Heterogeneity: Not ag Test for overall effect Total (95% CI)	0 456 oplicable :: Z = 5.24 464	0 1456 4 (P < 0 1631	0 224 0.00001) 241	0 506 679	95.1% 100.0%	0.57 [0.47, 0.71] 0.57 [0.46, 0.69]	• •
Ng 2015 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect Total (95% CI) Total events	0 456 oplicable :: Z = 5.24 464 = 0.00; Ch	0 1456 4 (P < 0 1631 ni ² = 1.	0 224 0.00001) 241 62, df =	0 506 679 4 (P = 1	95.1% 100.0%	0.57 [0.47, 0.71] 0.57 [0.46, 0.69]	◆ ↓ 0.01 0.1 1 10 1 Favours FPD Favours HDPD

DR intubation in preterm infants^{25,27–30,32}

	Fixed pres	CUTO.	Hand driven pre	C CUICO		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events		Weight	M-H, Random, 95% CI	
3.4.1 RCT	Liono	Total	Liono	Total	reight	in the trained of the training	
Dawson, 2011	26	49	19	50	16.1%	1.84 [0.83, 4.11]	1 +
Szyld, 2014	45	85	76	110	20.2%	0.50 [0.28, 0.91]	
Thakur, 2015	5	19	12	18	8.2%	0.18 [0.04, 0.74]	
Subtotal (95% CI)	-	153		178	44.5%	0.61 [0.19, 1.93]	
Total events	76		107				
Heterogeneity: Tau ² =	0.80; Chi ² =	10.41,	df = 2 (P = 0.006)	; I ² = 81%			
Test for overall effect:	Z=0.84 (P	= 0.40)					
3.4.2 RCT - bundle in	terventions						
EL-Chimi, 2017	3	57	13	55	9.1%	0.18 [0.05, 0.67]	
Te Pas, 2007	18	104	37	103	19.0%	0.37 [0.20, 0.71]	· -•-
Subtotal (95% CI)		161		158	28.1%	0.32 [0.18, 0.58]	▲
Total events	21		50				
Heterogeneity: Tau ² =	0.00; Chi ² =	: 0.96, d	f = 1 (P = 0.33); I ²	= 0%			
Test for overall effect:	Z = 3.80 (P	= 0.000	1)				
3.4.3 Cohort							
Guinsburg, 2018	782	1456	340	506	27.4%		
Subtotal (95% CI)		1456		506	27.4%	0.57 [0.46, 0.70]	•
Total events	782		340				
Heterogeneity: Not ap							
Test for overall effect:	Z= 5.25 (P	< 0.0001)1)				
Total (95% CI)		1770		842	100.0%	0.51 [0.31, 0.82]	▲
Total events	879		497				
Heterogeneity: Tau ² =	0.21; Chi ² =	: 15.51,	df = 5 (P = 0.008)	; I² = 68%			0.01 0.1 1 10 10
Test for overall effect:	Z = 2.78 (P	= 0.005)					FP HDP
Test for subgroup diff	erences: Ch	ni² = 3.19	8, df = 2 (P = 0.20), I ² = 37.3	3%		

MV requirements in preterm infants^{25,27–30,32}.

	FPD)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.7.1 RCT							
Dawson 2011	25	41	24	39	7.9%	0.98 [0.40, 2.40]	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	62	85	85	110	13.8%	0.79 [0.41, 1.52]	
Thakur 2015	6	19	14	18	3.1%	0.13 [0.03, 0.58]	
Subtotal (95% CI)		145		167	24.8%	0.57 [0.23, 1.43]	
Total events	93		123				
Heterogeneity: Tau ² =	= 0.42; Cl	$hi^2 = 5.$	60, df =	2 (P =	0.06); I ² :	= 64%	
Test for overall effect	Z = 1.20	0 (P = 0)).23)				
1.7.2 RCT with bund	le interv	ention					
El-Chimi 2017	17	57	25	55	10.3%	0.51 [0.23, 1.11]	_ _
Te Pas 2007	38	104	52	103	18.0%	0.56 [0.32, 0.98]	
Subtotal (95% CI)		161		158	28.3%	0.55 [0.35, 0.86]	\blacklozenge
Total events	55		77				
Heterogeneity: Tau ² =	= 0.00; Cl	$hi^2 = 0.$	04, df =	1 (P =	0.83); I ² :	= 0%	
Test for overall effect	: Z = 2.63	3 (P = 0).009)				
1.7.3 cohort studies							
Guinsburg 2018	1094	1456	422	506	46.9%	0.60 [0.46, 0.78]	*
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		1456		506	46.9%	0.60 [0.46, 0.78]	\bullet
Total events	1094		422				
Heterogeneity: Not ap	plicable						
Test for overall effect	: Z = 3.79	9 (P = 0	0.0001)				
Total (95% CI)		1762		831	100.0%	0.60 [0.46, 0.78]	•
	1242		622				
Total events							
Total events Heterogeneity: Tau ² =		$hi^2 = 6.$	10, df =	5 (P =	0.30); I ² :	= 18%	
	= 0.02; Cl		,	5 (P =	0.30); l ²	= 18%	0.01 0.1 1 10 1 Favours FPD Favours HDPD

PDA requiring treatment^{28–30,32}

	FPD)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.3.1 RCT							
Dawson 2011	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015 Subtotal (95% CI)	3	40 40	0	50 50	1.2% 1.2%		
Total events	3		0			. , .	
Heterogeneity: Not ap	-		•				
Test for overall effect:		7 (P = 0).14)				
3.3.2 RCT with bund	le interv	entions	5				
El-Chimi 2017	8	57	11	55	10.3%	0.65 [0.24, 1.77]	
Te Pas 2007	21	104	16		18.3%		- + =
Subtotal (95% CI)		161		158	28.6%	1.03 [0.51, 2.10]	•
Total events	29		27				
Heterogeneity: Tau ² =	0.08; Cł	$ni^2 = 1.$	41, df =	1 (P =	0.23); I ² :	= 29%	
Test for overall effect:	Z = 0.08	8 (P = 0).93)				
3.3.3 cohort studies							
Guinsburg 2018	350	1456	121	506	70.2%	1.01 [0.79, 1.28]	🚔
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		1456		506	70.2%	1.01 [0.79, 1.28]	◆
Total events	350		121				
Heterogeneity: Not ap							
Test for overall effect:	Z = 0.06	5 (P = 0)).95)				
Total (95% CI)		1657		714	100.0%	1.05 [0.75, 1.47]	•
Total events	382		148				
Heterogeneity: Tau ² =	,		,	3 (P =	0.31); I ² :	= 16%	
Test for overall effect:							Favours FPD Favours HDPD
Test for subgroup diff	ferences:	Chi ² =	2.13, df	= 2 (P	= 0.34),	$l^2 = 6.2\%$	

IVH^{28-30,32}

	FPC)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.4.1 RCT							
Dawson 2011	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015 Subtotal (95% CI)	2	40 40	0	50 50	3.7% 3.7%	6.56 [0.31, 140.60] 6.56 [0.31, 140.60]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	•	O(P = 0)).23)				
3.4.2 RCT with bund	le interv	entions	5				
El-Chimi 2017	10	57	12	55	25.7%	0.76 [0.30, 1.94]	
Te Pas 2007	7	104	3	103	15.0%	2.41 [0.60, 9.57]	
Subtotal (95% CI)		161		158	40.7%	1.21 [0.40, 3.63]	
Total events	17		15				
Heterogeneity: Tau ² =	= 0.30; Cł	$ni^2 = 1.$	83, df =	1 (P =	0.18); I ² :	= 45%	
Test for overall effect:	z = 0.33	B (P = 0)).74)				
3.4.3 cohort studies							
Guinsburg 2018	145	1218	60	376	55.6%	0.71 [0.51, 0.99]	
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		1218		376	55.6%	0.71 [0.51, 0.99]	◆
Total events	145		60				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 2.04	4 (P = 0).04)				
Total (95% CI)		1419		584	100.0%	0.94 [0.51, 1.73]	•
Total events	164		75				
Heterogeneity: Tau ² =	= 0.14; Cł	1i ² = 4.	74, df =	3 (P =	0.19); I ² :	= 37%	0.01 0.1 1 10 100
Test for overall effect:			,				Favours FPD Favours HDPD
Test for subgroup diff	ferences:	Chi ² =	2.73, df	= 2 (P	= 0.26),	$l^2 = 26.6\%$	

ROP^{28,30}

	FPD)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.6.1 RCT							
Dawson 2011	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015	0	40	1	50	49.8%	0.41 [0.02, 10.27]	_
Subtotal (95% CI)		40		50	49.8%	0.41 [0.02, 10.27]	
Total events	0		1				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.5	5 (P = 0)).59)				
3.6.2 RCT with bund	le interv	entions	5				
El-Chimi 2017	0	0	0	0		Not estimable	
Te Pas 2007	0	104	1	103	50.2%	0.33 [0.01, 8.12]	_
Subtotal (95% CI)		104		103	50.2%	0.33 [0.01, 8.12]	
Total events	0		1				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.68	8 (P = 0).50)				
3.6.3 cohort studies							
Guinsburg 2018	0	0	0	0		Not estimable	
Ng 2015	0	0	0	0		Not estimable	
Subtotal (95% CI)		0		0		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not app	licable					
Total (95% CI)		144		153	100.0%	0.36 [0.04, 3.55]	
Total events	0		2				
Heterogeneity: Tau ² =	0.00; Cl	$ni^2 = 0.$	01. df =	1 (P =	0.92); I ² :	= 0%	
Test for overall effect:					7,1 -		0.01 0.1 1 10 10
Test for subgroup diff				_ 1 /D	- 0.02)	2 00/	Favours FPD Favours HDPD

NEC^{29,30,32}

s Total ions 7 57 0 104 161 7 ni ^z = 0.28, c (P = 0.58)	8 1 1 1f= 1 (P = 0.59); I	55 103 158	Weight 10.3% 1.2% 11.4%	M-H, Random, 95% Cl 0.82 [0.28, 2.45] 0.33 [0.01, 8.12] 0.75 [0.27, 2.10]	M-H, R	andom, 95% C	-	
7 57 0 104 161 7 ni ² = 0.28, c	1 9 if = 1 (P = 0.59); I	103 158	1.2%	0.33 [0.01, 8.12]		•	_	
0 104 161 7 ni ² = 0.28, c	1 9 if = 1 (P = 0.59); I	103 158	1.2%	0.33 [0.01, 8.12]		•	_	
161 7 hi ² = 0.28, d	9 If = 1 (P = 0.59); I	158				•	-	
7 ni² = 0.28, c	9 lf = 1 (P = 0.59); I		11.4%	0.75 [0.27, 2.10]				
, ni² = 0.28, c	if = 1 (P = 0.59); I	I² = 0%						
		l² = 0%						
(P = 0.58)								
		506	88.6%	0.90 [0.62, 1.31]		- -		
1456		506	88.6%	0.90 [0.62, 1.31]		•		
0	42							
(P = 0.59)								
1617		664	100.0%	0.88 [0.62, 1.25]		•		
7	51							
		I² = 0%			I I I I I I I I I I I I I I I I I I I			
					0.01 0.1	1	10	100
		 4) I² = 0% 				FP HDP		
1	1456 0 9 (P = 0.59) 1617 7 hi ² = 0.40, c 9 (P = 0.49)	1456 0 42 4 (P = 0.59) 1617 7 51 $hi^2 = 0.40, df = 2 (P = 0.82);$ 9 (P = 0.49)	1456 506 0 42 4 (P = 0.59) 1617 664 7 51 51 hi ² = 0.40, df = 2 (P = 0.82); I ² = 0% 9 (P = 0.49)	1456 506 88.6% 0 42 4 (P = 0.59) 1617 664 100.0% 7 51 hi ² = 0.40, df = 2 (P = 0.82); i ² = 0%	1456 506 88.6% 0.90 [0.62, 1.31] 0 42 4 (P = 0.59) 1617 664 100.0% 0.88 [0.62, 1.25] 7 51 51 1617 664 100.0% 0.88 [0.62, 1.25] $\rho = 0.40$, df = 2 (P = 0.82); P = 0% 9 (P = 0.49) 9 (P = 0.49) 10 (P = 0.40) 10 (P = 0.40)	1456 506 88.6% 0.90 [0.62, 1.31] 0 42 4 (P = 0.59) 1617 664 100.0% 0.88 [0.62, 1.25] 7 51 51 $1000 (0.62, 1.25)$ hi ² = 0.40, df = 2 (P = 0.82); l ² = 0% 0.01 0.1	1456 506 88.6% 0.90 [0.62, 1.31] 0 42 4 (P = 0.59) 1617 664 100.0% 0.88 [0.62, 1.25] 7 51 hi ² = 0.40, df = 2 (P = 0.82); i ² = 0% 0 (P = 0.49) FP HDP	1456 506 88.6% 0.90 [0.62, 1.31] 0 42 4 (P = 0.59) 1617 664 100.0% 0.88 [0.62, 1.25] 7 51 10 10 hi ² = 0.40, df = 2 (P = 0.82); i ² = 0% 0.01 0.1 1 0 (P = 0.49) FP HDP 10

cPVL^{28,30,32}

	FPC)	HDP	D		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.5.1 RCT							
Dawson 2011	0	0	0	0		Not estimable	
Kookna 2019	0	0	0	0		Not estimable	
Menakaya 2014	0	0	0	0		Not estimable	
Szyld 2014	0	0	0	0		Not estimable	
Thakur 2015 Subtotal (95% CI)	0	40 40	0	50 50		Not estimable Not estimable	
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not app	licable					
3.5.2 RCT with bund	le interv	entions	5				
El-Chimi 2017	0	0	0	0		Not estimable	
Te Pas 2007	2	104	5	103	4.8%	0.38 [0.07, 2.03]	
Subtotal (95% CI)		104		103	4.8%	0.38 [0.07, 2.03]	
Total events	2		5				
Heterogeneity: Not ap							
Test for overall effect:	Z = 1.13	3 (P = 0)).26)				
3.5.3 cohort studies							
Guinsburg 2018	95	1209	46	373	95.2%	0.61 [0.42, 0.88]	
Ng 2015	0	0	0	0		Not estimable	-
Subtotal (95% CI)		1209		373	95.2%	0.61 [0.42, 0.88]	\bullet
Total events	95		46				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 2.63	B(P = 0)).009)				
Total (95% CI)		1353		526	100.0%	0.59 [0.41, 0.85]	•
Total events	97		51				
Heterogeneity: Tau ² =	0.00; Cł	$ni^2 = 0.$	28, df =	1 (P =	0.60); I ² :	= 0%	0.01 0.1 1 10 100
Test for overall effect:	Z = 2.82	1 (P = 0)).005)				Favours FPD Favours HDPD
Test for subgroup diff	Foroncos	$Chi^2 =$	0.27 df	-1(P)	- 0.60)	$^{2} - 0\%$	

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