### **Neonatal Ventilation:**

### **New Ventilatory Modes and Assessment of Technology**



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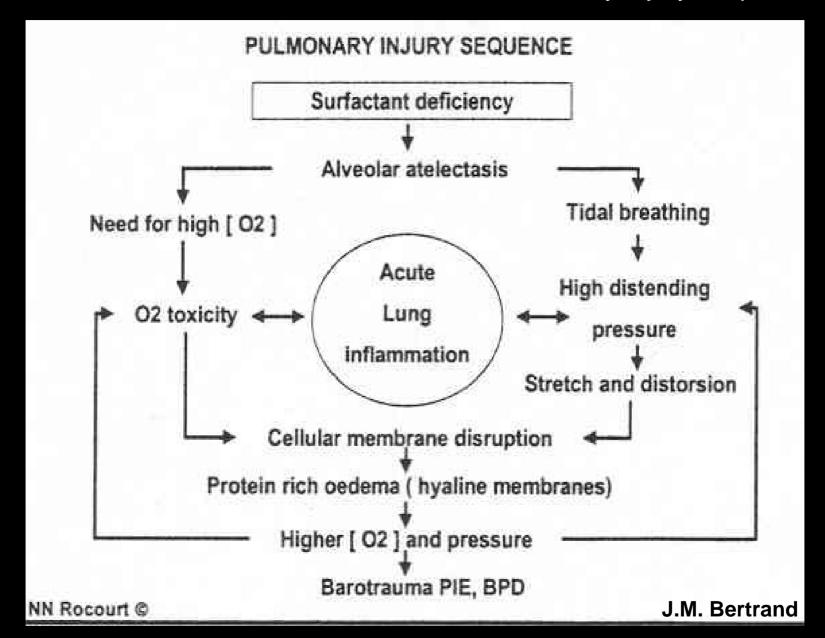
## Technology Assessment:

Health Technology Assessment (HTA) defines the systematic analysis of short and longterm consequences of the application of medical technologies with the aim of supporting decisions in policy-making and practice.

Pereth M, Schwartz FW

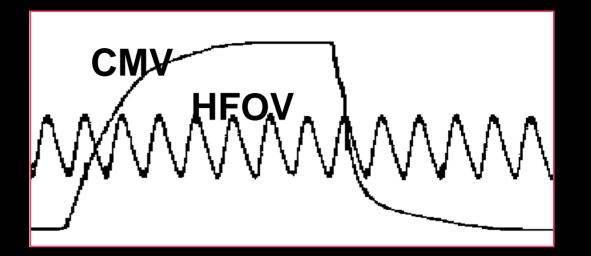
Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz 2001; 44:857-864

### Neonatal Mechanical Ventilation and the Pulmonary Injury Sequence



# **Technology 1:**

**HFOV** 1989 - 2003



Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants (Review)

Henderson-Smart DJ, Bhuta T, Cools F, Offringa M



#### Analysis 01.01. Comparison 01 HFOV vs CV (all trials), Outcome 01 Death by 28-30 days Fewers: He fixed at the new specific to went in the sense of vertical best fixed to be some pull new as devices our important many to Comprise a OLHECVIA CV (Flaids) Cuttomic - C. Daath by 38430 days. Socily H-039 $C\mathcal{F}$ Renth-Buk (Fael) 7.44. Reidle-Rek (Fise.) 9.55 (1 Chrk 1993 7/37 3/26 Tor [ 0.35, 2.99 ] 456 1.661 0.19 | 00 | 389 | Constitution, \$96. C81 110 1860 40.557 101[077, 46] 00/243 47.4 24(144 1.12 [ 0.65, -84] Ogree 1993 1.2 033[00.790] 2/20 39-101-1131 094[04.213] 139 [ 079, 245 ] No. Seenak 2003 8/153 Teta (95% CD) 100.0 1.08 [ 0.001, 1.05 ] into esemblish (HECW), 124 (CV) , excitor to charge many driven and -2.72 d -7.5-309 , P -2006real for owned larke to -0.57 in -0.51

### Analysis 01.02. Comparison 01 HFOV vs CV (all trials), Outcome 02 Mechanical ventilation at 28 - 30 days in survivors

Series: The text ignificancy as the dyster bifor serves as serifical verifician in a state of correctly dysfortion in or sum infants.

Outcome - 02 Mechanical year lation at 28 - 30 days in survivors.

Starty	HKW	CV	Bolative, Mak (Hard)	We ght	Solative Bisk (Fixed)
	r4N	r/h	998 CI	(%)	99% C
Gerstmann 996	9/6/1	205	•	120	0.69   0.3   1.52
I П 989	87,007	85/286	•	79.2	10 [086,14-]
Съзма 993	13/46	9/15		8.8	AL 10,67, 297 [
otal (858 C.)	1/7	190	•	1000	.08 _ 0086, L Gr ]
Diabeter at 09 (ICO), I	06 (CV)				
est ka helesgemi y chisa	pare-1.75 d = 3 p=0	40 P =0.0%			
est for overallefied z=0.60	3 570.5				
			0.1 52 55 1 2 5 10		

### Analysis 01.03. Comparison 01 HFOV vs CV (all trials), Outcome 03 Oxygen at 28-30 days in survivors

Tennillon Tennico

 $verlew. \ \ Feative high tequency and stary earlief on versus conventional vanifolds in translet pulmonary dystinction in meterm monts. Comparisons of HRO visito CV (altrials). \\$ 

Outcome: 03 Oxygenia 28-30 pays 'n vurv'w cs

5 caly	L PCW	CV ⊮N	Berative Risk (Time I) 9396 (TI	Weight (%)	Beatice 3 sk (□ces) 95% C
Moriette 200	5 /1 1	507-10	•	73.3	101 [ 076, 135 ]
Ogeo 1993	17/46	19745	•	8.9	088 [ 055, 146 ]
Ebdo 1999	1.79	197.8	-	6.7	080_090,129]
Thome 998	A4130	807.33	+	36.7	095 (477, 1.16 ]
Van Reempts 2000	-19/123	567.35	+	24.5	096 (07,129]
Total (95% C.)  Stall swette 202 (1 FCV), 21 ext for here organists children.		41 917-008	•	100.0	0.95 1 0.85, 1.09 [
exteriorers effect z=0.75					
			2   22   25   2   5   12		
			Jacob HTDV Laters CV		

### all trials

### Death by 28 – 30 days

RR (96% CI): 1.08 (0.86, 1.35)

### Mech. Ventilation at 28 – 30 days

RR (96% CI): 1.08 (0.86, 1.35)

### Oxygen at 28 – 30 days

RR (96% CI): 0.95 (0.83, 1.09)

### Analysis 01.04. Comparison 01 HFOV vs CV (all trials), Outcome 04 CLD at 28-30 days (O2 + xray) in survivors

Bodeve. Te tardiği fequencyos Istoryaan lafar servis o mentiona sentia on for sure-primonacyolyás atémin lestenin mints. Compartent: 0. IRCV vs CV (aftria)

Outcomes DH CLD at 29 30 days (O2 + xm/) in survivors

Study	IFOV CV B		Perative 3 sk (Fired)	Warght	Resulting Risk (Tisself)	
	m8	Art.	95% CI	(%)	95% €	
Clark 952	0/30	7722	•	0.3	0.45 0.26, 0.79	
Gersmann 996	5/64	75/59	•	30	0.55 [ 0.52 0.94]	
Г 1989	30/267	4 /286	<b>+</b>	72.6	0.99 1 0.83, 1.171	
Ospava 993	4/46	685	<del></del>	3.2	0.65 0.20, 2.16	
Total (95% C.) Total events 159 (H-CV), 1	407 189 (CV)	413	†	00.0	086 [ 074 0 ]	
Test for hoterogeneity this is test for every leftest on 18		002 ° 71.3%				
Table and a second						
			01 02 05 1 2 5 10			
			Layers LLOV Layers CV			

#### Analysis 01.05. Comparison 01 HFOV vs CV (all trials), Outcome 05 Death or CLD at 28-30 days

Review: Best ve high frequency and body vertilation versus conventional vertilation for acute our monary dysfunction in precent mants. Commission, 101, 1979 vs. CV 541 (44):

Study	CV	CY	to at ve Pisk (Fixed)	Victoria	Relative Pisk (-tood)
	1/14	D,A	59% CI	(%)	99% C
Clark 952	7/27	22/28	-	9.8	0.58 0.39, 0.67
Gerstmann 996	5/6/1	27/61	-	10.9	0.50 0.91, 0.09
П 1989	90/377	201/346	•	766	L00 10/88, L141
Ogowa 993	4/40	7/46	•	27	0.57 [ 0, B, LR7 ]
Total (95% C)	474	4.9	•	100.0	090 [080, L0 ]
Intal events 226 (H-CV), .	257 (CV)				

80 807 85 1 2 5 10 Bases HEOV - Besses CV

### all trials

CLD at 28 - 30 days (O2 + xray)

RR (96% CI): 0.86 (0.74, 1.01)

Death or CLD at 28 – 30 days

RR (96% CI): 0.90 (0.80, 1.01)

#### Analysis 01.06. Comparison 01 HFOV vs CV (all trials), Outcome 06 Death by 36-37 weeks or discharge

Review. Electricing high frequency and latent ventilation we sus conventional ventilation for acute pulmonary distinction in proteom infants. Comparison: 0. HPCV vs. CV (all trials)

Outcome - 04 Death by 34-17 weeks or cischarge

Outcome 06 Death by 36	37 weeks or elscharge				
Sh. dy	110%	CV	delatine Bek ( sed)	Wage	Rebrive Risk (Tred)
	r/N	r/N	956.01	(%)	948.0
C a & 1992	8/37	608	•	3.1	10 [ 940, 258 ]
Concludy 2002	73/744	49754	+	7.7	0.86 [ 0.56, U32 ]
Gerstmann 1994	0441	2/81		.2	0.19[00].089]
Johnson 2002	93/498	105/357	•	4/2	0.95   0.75, 1.20
Mortetta 2001	312139	2.8134	+	24	H [000, L/S]
Pareto 1999	7/21	2,78		0.9	095[0.5,613]
Rettwitz Volk 1998	37.6	1750	-	.7	1.36 [ 0.39, 4.75 ]
Thame 1998	7/140	12/144	•	6.7	0.96   0.49, 1.91
Van Keempts 2003	27/147	20(15)	+	89	130 [ 376, 277 ]
Tota (95% C)	238	124	+	000	098 [ 085, 116 ]
Totalevertic 7, 8 (LPOV), 22	21 (CV)				
Test for heterogeneitych sog	эгн-3.17 : II-8 р:- <b>3.</b> 99	P =3.086			
Test for overall effect z=0.20	_1+0.8				
i e			21 02 25 1 2 5 10		

### Analysis 01.08. Comparison 01 HFOV vs CV (all trials), Outcome 08 Death or CLD at 36-37 weeks PMA or discharge

5-si-se-1 + s + lse + ighth-epony so 'labory ser find'or sees as consulform would be not some pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical on 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in banks of the pulmonary dyshical or 'n problem in ban

Grandisons - 0 - LECM vs CV (all trish)

Outcome: 08 Death or CLI	Diat 36-37 weeks FY7	\ on discharge			
Shaly	TIOV CV		Fasta for Kak (Lored)	Weigh	Seledore 1 sk (Lece)
	E/N	r/N	9584 C	30	95% CI
Clark 1992	1/37	678	<b>—</b>	3.0	052 1029, 0.941
Continey 2002	03/944	33/254	•	21.7	081 [067.097]
Geramann 996	064	2661	•	4.8	058_03.094
Johnson 2002	26.400	268/357	•	44.8	0.98 [0.85, 1.08]
Horiette 2001	35/139	37/ DI	•	9.7	0.90 10.70, 241
Naska 1999	301	9/20	•	3	0.48 10:20,51
Set wite Wik 1998	5646	4/50		0.6	36 [ 039, 478 ]
loaner 1958	46/140	457-44	-	7.4	85 [0.4s 48]
Van Reempts 2003	49/147	3W 53	•	6.4	31 [092 36]
otal (99% CI)	238	211	•	50.0	0.92 0.85, 500
otal events 556 (H-OV), 60	0 (CV)				
est for heterogeneity chilisqu	.are=17.39 d=3 p=0.0	0 :-7408			
Test for overall effect z= .91.	p=0.06				

0.1 0.2 0.5 1 2 5 10 Bases HEOV - Bases CV

### all trials

### **Death by 36-37 weeks or discharge**

RR (96% CI): 0.98 (0.83, 1.16)

### **Death or CLD at 36-370 weeks**

RR (96% CI): 1.08 (0.86, 1.35)

### all trials

# Analysis 01.07. Comparison 01 HFOV vs CV (all trials), Outcome 07 CLD at 36-37 weeks PMA or discharge in survivors

Review: Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants

Comparison: 01 HFOV vs CV (all trials)

Outcome: 07 CLD at 36-37 weeks PMA or discharge in survivors

HFOV n/N	CV n/N	Relative Risk (Fixed) 95% Cl	Weight (%)	Relative Risk (Fixed) 95% CI
3/29	10/22		3.0	0.23 [ 0.07, 0.73 ]
70/201	93/210	-	23.8	0.79 [ 0.62, 1.00 ]
17/64	27/59		7.4	0.58 [ 0.35, 0.95 ]
165/300	163/292	•	43.3	0.99 [ 0.85, 1.14 ]
24/108	30/107		7.9	0.79 [ 0.50, 1.26 ]
3/19	8/18		2.2	0.36 [ 0.11, 1.13 ]
0/41	0/46		0.0	Not estimable
32/126	30/129	-	7.8	1.09 [ 0.71, 1.68 ]
24/122	19/133	-	4.8	1.38 [ 0.79, 2.39 ]
1010	1016	•	100.0	0.88 [ 0.79, 0.99 ]
TV)				
=17.07 df=7 p=0.0	)2 I² =59.0%			
=0.03				
,		01 02 05 1 2 5 10		
=	n/N  3/29  70/201  17/64  165/300  24/108  3/19  0/41  32/126  24/122  1010  EV)  =17.07 df=7 p=0.0	n/N n/N  3/29 10/22  70/201 93/210  17/64 27/59  165/300 163/292  24/108 30/107  3/19 8/18  0/41 0/46  32/126 30/129  24/122 19/133  1010 1016  EV)  =17.07 df=7 p=0.02 l² =59.0%	n/N n/N 95% CI  3/29 10/22  70/201 93/210  17/64 27/59  165/300 163/292  24/108 30/107  3/19 8/18  0/41 0/46  32/126 30/129  24/122 19/133  1010 1016  2V) =17.07 df=7 p=0.02 I² =59.0%	n/N n/N 95% CI (%)  3/29 10/22 3.0  70/201 93/210 - 23.8  17/64 27/59 7.4  165/300 163/292 43.3  24/108 30/107 7.9  3/19 8/18 2.2  0/41 0/46 0.0  32/126 30/129 7.8  24/122 19/133 4.8  1010 1016 1016  2V)  =17.07 df=7 p=0.02 P =59.0%  =0.03

0.1 0.2 0.5 1 2 5 10 Favors HFOV Favors CV

### Analysis 02.07. Comparison 02 HFOV vs CV (with volume recruitment), Outcome 07 CLD at 36-37 weeks PMA or discharge in survivors

Basiew: That is a high five percycle abdroy we tight in versus conventional wants continue use public cocycly five continue sum minute. Comparison: 162,144,59 or CV With your procuping of

Outcome: IO/ CIED at 36-37 weeks PMA and scharge in sun twors.

5 cally	FOV	CV.	Rebaine Risk (Tisser)	V-hight	Selative Risk (Fine.)	
	/*n V/n		9538 C	(20)	9.96 CI	
Clark 1992.	3/25	10/22		3.9	0.23 [ 007, 0.73 ]	
Continey 2002	70:70	952.0	-	99.8	0.79 [ 0.02   0.01 ]	
Gerstmann 1996	17/64	27/36	•	1/	058   035, 035	
Johnson 2002	165/300	163/797	•	47.7	0.99 [ 0.85, 4]	
Moniette 700	24/ 05	30/107	<del></del>	7.9	0.79 [ 0.50   .26 ]	
-lada 1999	3/19	œ e	•	22	0.36] G I, . 3]	
Пости 198	32/ 26	30/179	+	7.8	.09[071.48]	
Van Been de 2003	24/-27	19/133	<del> </del>	4 B	38[079.259]	
Total (95% CI)	909	970	•	1000	088[079.099]	
Total exerts: 358 (LPCV), 38						
Test for incorregencity chilisqu	are=1707/d=75=0	77 × = 74 00%				
lest for overall effect and 17	p=0.03					
			0.1 02 05 1 2 5 10			

### Analysis 02.04. Comparison 02 HFOV vs CV (with volume recruitment), Outcome 04 CLD at 28-30 days (O2 + xray) in survivors

Transfill (F Lawrett)

voverwill decive right frequency outdison yrom bitton versus conventional vertificion for acuse pulmonary distunction in proterm mants. Comparisons 1991 POV vs CV (with volume reconstruct)

Cutcomis: Df CLD at 28 00 date (C2 - xray) in survivors

Study	VO4F P/s	7.2 P/m			Polative Ksk (-med) 95% C
Cark. 952	0/30	7523	•	37.5	0.45   6.26, 0.79
Cersimanii 996	5//4	75/39	-	907	055 [ 037, 034]
Орама 993	1/16	675	•	1.8	065 [ 6.20, 2.16
Total (9995 C) This event a 79 (LPCV), 49 est for hote tigonety chils Text for overall affect weight	guare=0.45 d=-2 p=-0	27 901' =19%	*	102.0	053 [ C36, 0.76 °
			01 02 05 1 2 5 10 From MODE - From CV		

### Analysis 02.05. Comparison 02 HFOV vs CV (with volume recruitment), Outcome 05 Death or CLD at 28-30 days

vovew il stative high frequency as fittory vorte bifor versus conventions verificion for soute ou monary distunction in proterm intents. Comparisons 100 IPCM or CV (with whome participant)

Outcome: 05 Death or CID at 28 30 days

Study	1.307	CV	Bela ve Fisk (Fines)	Véright	Relative Risk (Fixed)	
	γN	n/N	598 CI	(%)	9558 C	
Cark 992	17/37	72.98	-	47.0	0.58 [ 0.35, 0.87]	
Geroomann 996	15/64	27/61	•	463	053 [ 63 , 0.09	
Однан 993	4.46	Tital		1.7	057 [ 0.18, 187 ]	
ota (56% C.)	147	Ja	-	1000	0561 070, 077	
Tital even x 36 (LTOV), 50	6 (CTV)					
est for heterogeneity chils	guarendos dina pind	95 F =00%				
Test for overal effect z=3.5	4 p=0.0004					
			01 to Ca 1 > a 00			

Facors HEGY - Favors CV

### with volume recruitment

### CLD at 36- 37 weeks or discharge

RR (96% CI): 0.88 (0.79, 0.99)

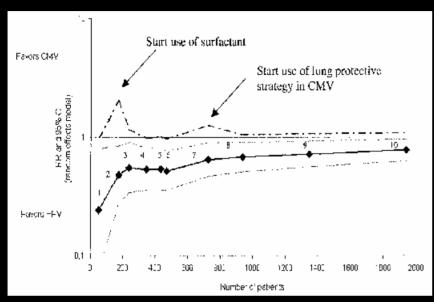
### **CLD at 28 – 30 days**

RR (96% CI): 0.53 (0.36, 0.76)

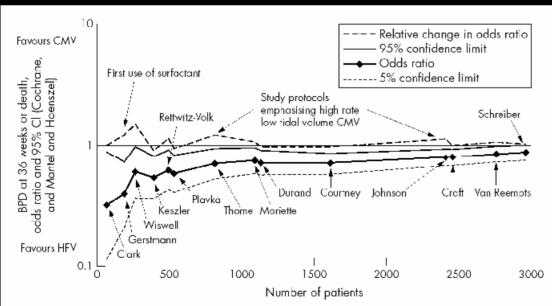
Death or CLD at 28 – 30 days

RR (96% CI): 0.956 (0.40, 0.77)

### **Cumulative Metaanalysis: HFV vs CMV**



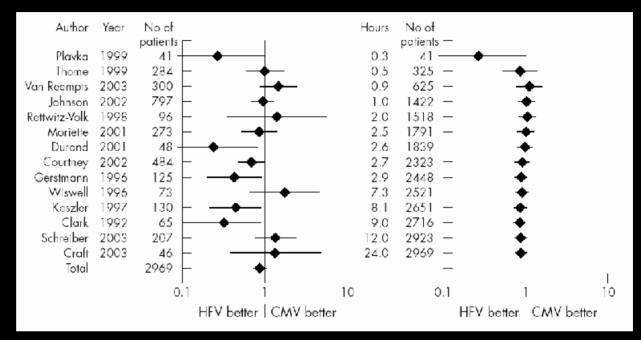
Bollen et al. AJRCCM 2003; 168: 1150-1155



Thome UH Arch Dis Child Fetal Neonatal Ed 2005;90:F466–F473

### **Cumulative Metaanalysis: HFV vs CMV**

Cumulative meta-analysis ordered by time delay to randomisation

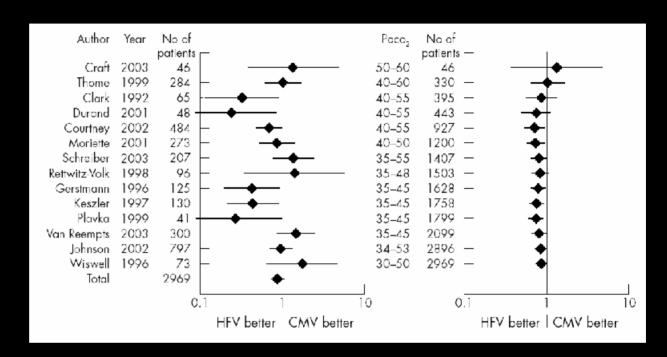


Thome UH Arch Dis Child Fetal Neonatal Ed 2005;90:F466–F473

Covariate: CMV strategy used before randomization!?

### **Cumulative Metaanalysis: HFV vs CMV**

Cumulative meta-analysis ordered by pCO2



# The authors conclusions

- Optimising conventional mechanical ventilation strategy appeared to be as effective as high frequency ventilation in improving pulmonary outcome in preterm infants
- Purchasing costly HFV ventilators appears to be unnecessary for most neonatal intensive care units

Thome UH Arch Dis Child Fetal Neonatal Ed 2005;90:F466–F473

Lung-protective ventilation strategies in neonatology: What do we know—What do we need to know?

Anton H. van Kaam, MD, PhD; Peter C. Rimensberger, MD

Crit Care Med 2007; 35:925-931

A total of 16 RCTs and 4 systematic reviews comparing HFOV with CMV failed to show consistent differences in mortality and bronchopulmonary dysplasia.

A total of 24 RCTs and 3 systematic reviews comparing various CMV modes and settings and 2 RCTs investigating permissive hypercapnia reported no differences in mortality or bronchopulmonary dysplasia.

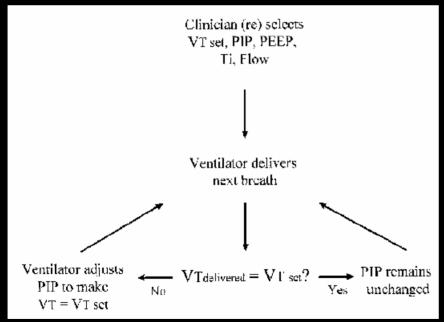
No RCT in newborn infants has substantiated so far that avoiding large tidal volumes and low positive end-expiratory pressure during CMV is lung protective in newborn infants.

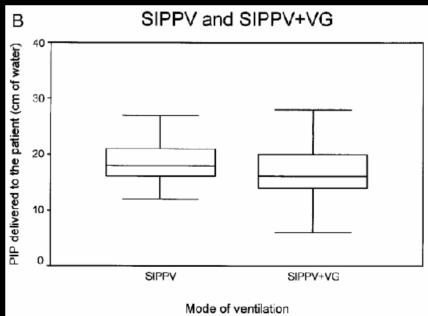
Based on the experimental evidence, HFV should be combined with an optimal recruitment strategy using oxygenation as an indirect marker for lung volume (FiO2 below 30%).

		Methods			Results		
Some tr Author	ials us	ed a lo	ow lun	ig volu	ume s	trategy	CMV
HIFI et al. (4)	N	_	_	9	9	0.43	0.42
Carlo Clarl Some tri					n the		).50
Gerstmann et al. (9) Keszler et al. (10) Rettwitz et al. (11)	Y Y N	≤0.30 — —	8–9 —	11 11 8	9 10 8	$0.28 \\ 0.50 \\ 0.45$	0.36 $0.65$ $0.42$
Thom Most tr Plavk: Most tr Morie Court lung vo	ials fa	ailed	to ob	tain o	optim	al	$0.25$ $ 0.68^{d}$
Johns Craft that wa			he stu	udy p	roto	ol!	0.33 0.38 c 0.50
Vento et al. (19)	Y	$\leq 0.25$		13	11	$0.29^{e}$	0.67

# Technology 2 Volume Targeted Ventilation: 2001 - 2007

Concept: deliver the set Vt at the lowest airway pressure possible





# Technology 2 Volume Targeted Ventilation: 2001 - 2007

	SIMV	SIMV + VG	P Value	SIPPV	SIPPV + VG	P Value
PIP, mean (standard error) cm of water	17.1 (3.4)	15.0 (7.5)	<.001	18.7 (8.3)	17.1 (9.3)	<.001
Mean airway pressure, mean (standard error) cm of water	6.9 (2.8)	6.5 (3.1)	.005	9.8 (4.6)	9.6 (4.5)	.008
Expired tidal volume, mean (standard error) mL/kg	5.0 (5.6)	4.9 (5.2)	.59	4.8 (3.4)	4.8 (3.2)	.62
Expired minute volume, mean (standard error) mL/min/kg	291 (2.1)	289 (2.1)	.89	331.6 (2.0)	334.5 (2.2)	.72
Fractional inspired oxygen, mean (standard error)	0.31 (0.3)	0.31 (0.3)	.38	40.4 (0.4)	41.0 (0.4)	.56
Transcutaneous partial pressure of carbon dioxide, mean (standard error) kPa	5.9 (2.2)	6.0 (2.2)	.47	6.4 (2.8)	6.4 (2.9)	.86
Transcutaneous partial pressure of oxygen, mean (standard error) kPa	8.6 (8.8)	8.4 (8.7)	.40	7.7 (4.4)	7.6 (4.0)	.30

Cheema IU *Pediatrics* 2001;107:1323–1328

	PSV + VG (n = 30)	PSV (n = 23)
Birth weight (g)	$1,125 \pm 370$	$1,197 \pm 333$
GA (weeks)	$28.5 \pm 2$	$29.4 \pm 1.6$
Antenatal steroids	26 (86%)	20 (86%)
Age at study (hours)	$3\pm 2$	$3\pm 2$

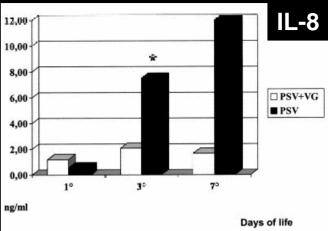
 $<sup>{}^{1}</sup>P = \text{ns. SD}$ , standard deviation.

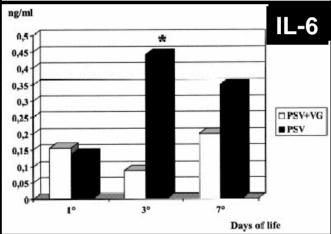
### TABLE 3—Outcome<sup>1</sup>

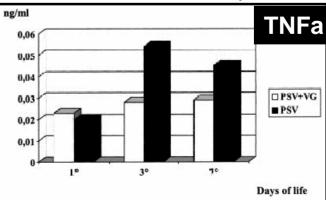
	PSV + VG group (n = 30)	PSV group (n = 23)
Length of ventilation (days; mean ± standard deviation)	8.8 ± 3	12.3±3
Surfactant (doses; median)	1	1
$BPD(n)^2$	3 (10%)	4 (17%)
CLD (n) <sup>3</sup>	3 (10%)	4 (17%)
Deaths (n)	5 (16%)	6 (26%)
IVH (≥3) (n)	1 (3%)	2 (8%)
PLV (n)	1 (3%)	2 (8%)
$ROP (\geq 2) (n)$	2 (6%)	1 (4%)
PIE (n)	2 (6%)	2 (8%)
PDA closure (n)	22 (73%)	20 (86%)
PNX (n)	0 (0%)	3 (13%)

<sup>&</sup>lt;sup>1</sup>ROP, retinopathy of the premature; PIE, pulmonary interstitial emphysema; PNX, pneumothorax; PDA, patency of ductus arteriosus; BPD, bronchopulmonary dysplasia. P = ns.

### Lista G Pediatr Pulmonol. 2004; 37:510-514







<sup>&</sup>lt;sup>2</sup>O<sub>2</sub> dependency at 28 days.

<sup>&</sup>lt;sup>3</sup>O<sub>2</sub> dependency at 36 weeks.

### Volume targeted ventilation: A Self Weaning Mode

### Methods:

PSV group: The weaning strategy consisted of reducing the pressure support level progressively over time, so that the work of breathing was shifted from ventilator to the patient.

PSV-VG group: Weaning was a moreautomatic process once appropriate levels of Vt had been established.

Similar blood gas goals (e.g., pH>7.25; pO2, 50–75 mmHg; pCO2, 40–65 mmHg) were achieved during weaning from mechanical ventilation in both groups.

### Infants at less than 30 weeks of gestation with RDS

	HFOV $(n = 13)$	PSV + VG (n = 12)	P
Mechanical ventilation at 7 days	3/13 (23)	2/12 (17)	1.000
O <sub>2</sub> -therapy duration (days)	$20.3 \pm 14.6$	$22.0 \pm 15.9$	0.783
NCPAP duration (days)	$6.9 \pm 4.2$	$5.2\pm2.4$	0.232
Mechanical ventilation duration (days)	$4.1 \pm 1.1$	$4.5\pm2.2$	0.566
Second dose of surfactant	12/13 (92)	12/12 (100)	1.000
Patent ductus arteriosus	11/13 (85)	9/12 (75)	0.644
Pneumothorax	0/13	1/12 (8)	0.480
Bronchopulmonary dysplasia	4/13 (31)	3/12 (25)	1.000
Intraventricular hemorrhage	2/13 (15)	2/12 (17)	1.000
Periventricular leucomalacia	1/13 (8)	1/12 (8)	1.000
Retinopathy of prematurity	2/13 (21)	3/12 (25)	0.644
Necrotizing enterocolitis	0/13	0/12	1.000
Length of stay in intensive care	$26.4 \pm 11.8$	$27.3 \pm 12.4$	0.854
Length of stay in hospital	$66.2 \pm 19.9$	$62.8 \pm 24.2$	0.704
Mortality	2/13 (15)	2/12 (17)	1.000

<sup>&</sup>lt;sup>1</sup>Mean  $\pm$  SD or rate (%).

Weaning Criteria: FiO2 0.40

MAP 6 cmH2O,

pO2 50 mmHg and pCO2 50 <65 mmHg

Lista G et al. Pediatr Pulmonol 2006; 41:357–363



Length of mechanical ventilation as an outcome parameter

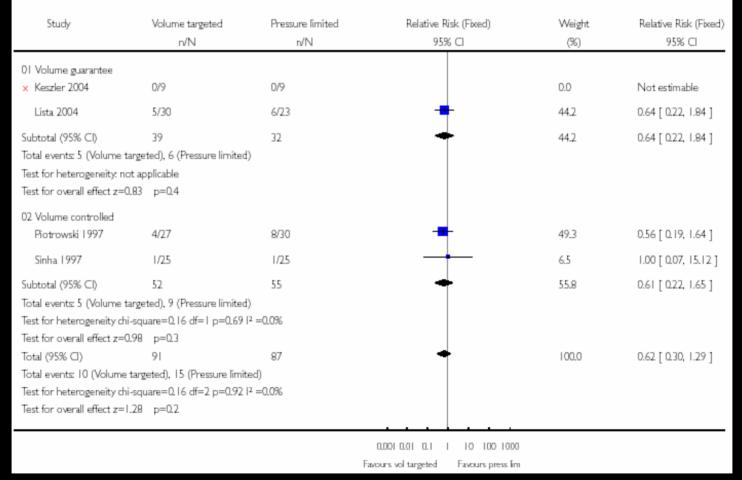
### Outcome VTV: Death in Hospital

### Analysis 01.01. Comparison 01 Volume-targeted vs pressure limited ventilation, Outcome 01 Death in hospital

Review: Volume-targeted versus pressure-limited ventilation in the neonate

Comparison: 01 Volume-targeted vs pressure limited ventilation

Outcome: 01 Death in hospital



The Cochrane Library 2007,

### Outcome VTV: Duration of mechanical ventilation

# Analysis 01.04. Comparison 01 Volume-targeted vs pressure limited ventilation, Outcome 04 Duration of intermittent positive pressure ventilation (days)

Review: Volume-targeted versus pressure-limited ventilation in the neonate

Comparison: 01 Volume-targeted vs pressure limited ventilation

Outcome: 04 Duration of intermittent positive pressure ventilation (days)

Study	Volu	ıme targeted	Pre	ssure limited	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	N	Mean(SD)	95% □	(%)	95% □
01 Volume guarantee							
Lista 2004	30	8.80 (3.00)	23	12.30 (3.00)	-	69.0	-3.50 [ -5.13, -1.87 ]
Subtotal (95% CI)	30		23		-	69.0	-3.50 [ -5.13, -1.87 ]
Test for heterogeneity	y: not ap	plicable					
Test for overall effect	z=4.21	p=0.00003					
02 Volume controlled	ł						
Sinha 1997	25	5.10 (2.72)	25	6.75 (5.58)		31.0	-1.65 [ -4.08, 0.78 ]
Subtotal (95% CI)	25		25		-	31.0	-1.65 [ -4.08, 0.78 ]
Test for heterogeneity	y: not ap	plicable					
Test for overall effect	z=1.33	p=0.2					
Total (95% CI)	55		48		-	100.0	-2.93 [ -4.28, -1.57 ]
Test for heterogeneity	y chi-squ	iare= 1.53 df= 1 p	=0.22  2	=34.8%			
Test for overall effect	z=4.24	p=0.00002					
					-100 -5.0 0 5.0 10.0		
				Fase	ours vol targeted Favours press ltd		

The Cochrane Library 2007, Issue 1

### Outcome VTV: Severe IVH (grade 3 – 4)

## Analysis 01.11. Comparison 01 Volume-targeted vs pressure limited ventilation, Outcome 11 Severe IVH (grade 3 or 4)

Review: Volume-targeted versus pressure-limited ventilation in the neonate

Comparison: 01 Volume-targeted vs pressure limited ventilation

Outcome: Severe VH (grade 3 on 4)

Study	Volume targeted r/N	Pressure limited		iisk (Fixed) % C	Weight (%)	Rolative Risk (Exed) 95% CI
OT Volume guarantee						
Lista 2007	1/30	2/23	<b>←</b>		17.8	0.38 [ 0.04, 3.97 ]
Subto.al (95% € )	30	23			17.8	0.38 [ 0.04, 3.97 ]
Totallevents: I (Volume targe	ced), 2 (Pressure limited)					
Test for heterogeneity; not ap	p icable					
Test for overall effect z=0.80	p=0.4					
02 Volume controlled						
⊇ourowski 1997	3/27	11/30	4		82.2	0.30 [ 0.09, 0.97 ]
Subtotal (95% Cl)	27	30			82.2	0.30 [ 0.09, 0.97 ]
Total events: 3 (Volume targe	ced), 11 (Pressure limited)					
Test for heterogeneity; not ap	ep icable					
Test for overall effect z=2.01	p=0.04					
Tota (95% C)	5/	.53			0.001	0.32 [ 0. , 0.90 ]
Total events: 4 (Volume targe	ced), 13 (Pressure limited)					
lest for heterogeneity chi squ	.are=0.03 d== p=0.86 ± =0	0.0%				
Test for overall effect z=2. 6	p=0.03					
			0. 0.2 0.5	1 2 5 10		
			Favours voll argetes:	Favours press firm		

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# Performance of neonatal ventilators in volume targeted ventilation mode

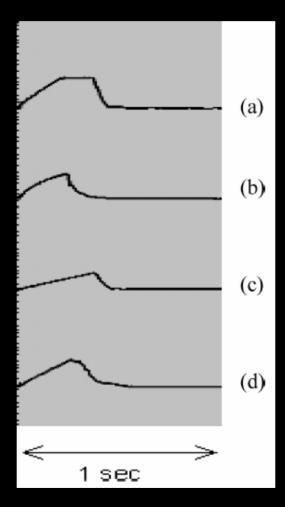
# Airway Pressure Waveforms:

Ti of 0.35 sec

Peak inflating pressure of 25 cm H2O

PEEP of 5 cm H2O.

Volume guarantee level 10 mL



Draeger Babylog 8000 (Draeger Medical, Germany),

SLE 5000 infant ventilator (SLE systems, UK),

Stephanie paediatric ventilator (F. Stephan Biomedical, Germany)

V.I.P. Bird Gold (Viasys Healthcare, USA)

# Performance of neonatal ventilators in volume targeted ventilation mode

### **Settings:**

Inflation time of 0.35 sec

Peak inflating pressure of 25 cm H2O

PEEP of 5 cm H2O

Volume guarantee level 10 mL

### Lung model:

Crs = 0.4 mL/cm H2O

Rrs = 70 cm/H2O/L/sec

"similar to the compliance and resistance of babies with the respiratory distress syndrome"

### **Results: Measured volume delivery**

All ventilators delivered a lower Vt than preset

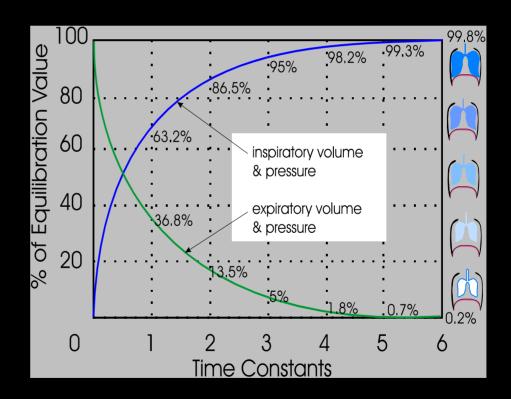
Atul Sharma et al Acta Pædiatrica 2007; 96: 176–180

### Time constant: $T = Crs \times Rrs$

Resulting time constant:

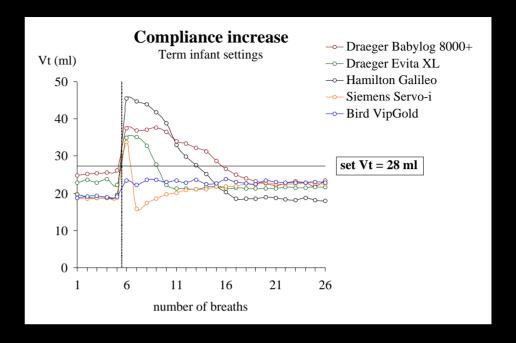
T = 0.4 mL/cm H2O X 70 cm/H2O/L/sec = **0.28 sec** 

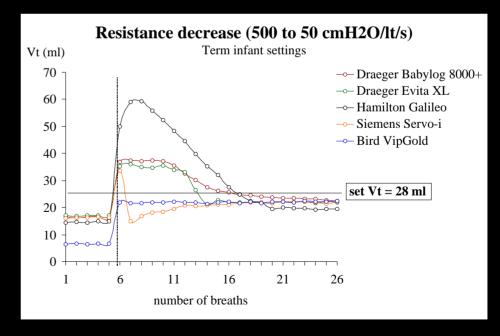
Will pressure equilibrium be reached in the lungs?



 $3 \times T = 3 \times (0.4 \text{ mL/cm H2O} \times 70 \text{ cm/H2O/L/sec}) = 0.84 \text{ sec}$ 

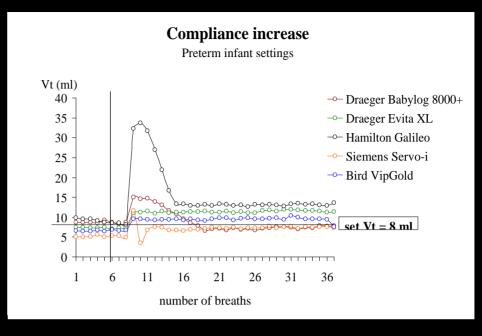
## Is VTV safe?

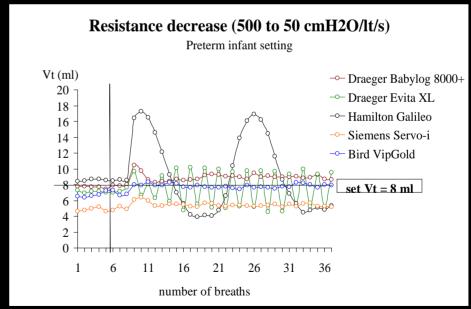




Jaecklin T et al. ICM 2007

## Is VTV safe?



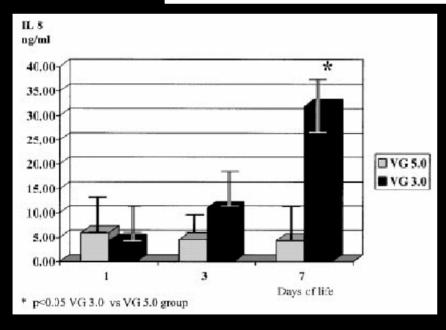


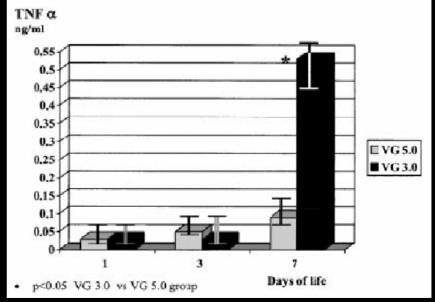
Jaecklin T et al. ICM 2007

### **Effects of Ventilation With Different Tidal Volumes**

### 3 ml/kg versus 5 ml/kg

_	VG 5.0 (n = 15)	VG 3.0 (n = 15)
Birth weight (g)	$1,150 \pm 360$	$1,085 \pm 290$
Gestational age (weeks)	$27 \pm 1.2$	$27 \pm 1.6$
a/APO <sub>2</sub>	$0.15 \pm 0.05$	$0.15 \pm 0.04$
Antenatal steroids, complete course (two cycles), n (%)	12 (80%)	12 (80%)
$\overline{{}^{1}P} = \text{ns.}$		





Lista G et al. Pediatr Pulmonol 2006; 41:357–363

### **Effects of Ventilation With Different Tidal Volumes**

### 3 ml/kg versus 5 ml/kg

TABLE 3—Ou	itcomes of I	Neonates	in Two	Groups'	

	VG 5.0 group (n = 15)	VG 3.0 group (n = 15)
Length of ventilation	$9.2 \pm 4$	16.8 ± 4*
(days; mean $\pm$ SD)		
Surfactant	$2\pm1$	$2\pm1$
(number of doses; median)		
BPD (n)	2 (13%)	3 (20%)
Deaths (n)	1 (6.6%)	1 (6.6%)
IVH $(>/=3)$ (n)	1 (6.6%)	1 (6.6%)
PLV (n)	1 (6.6%)	1 (6.6%)
ROP (>/=2) (n)	0	0
PIE (n)	1 (6%)	1 (6%)
PNX (n)	0	0
PDA closure (n)	11 (73.3%)	10 (66.6%)
Postnatal steroid therapy	2/15 (13%)	3/15 (20%)

<sup>&</sup>lt;sup>1</sup>In terms of incidence of bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), pulmonary interstitial emphysema (PIE), pneumothorax (PNX), and patency of ductus arteriosus (PDA). \*P = 0.05.

Lista G et al. Pediatr Pulmonol 2006; 41:357–363

# **Technologie 3:**

Maintenance of spotaneous breathing efforts:

Pressure Support BiPAP APRV

2005 - .....

	HFOV $(n=13)$	PSV + VG (n = 12)	P
Mechanical ventilation at 7 days	3/13 (23)	2/12 (17)	1.000
O <sub>2</sub> -therapy duration (days)	$20.3 \pm 14.6$	$22.0 \pm 15.9$	0.783
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Pneumothorax	0/13	1/12 (8)	0.480
Bronchopulmonary dysplasia	4/13 (31)	3/12 (25)	1.000
Intraventricular hemorrhage	2/13 (15)	2/12 (17)	1.000
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Retinopathy of prematurity	2/13 (21)	3/12 (25)	0.644
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Length of stay in hospital	$66.2 \pm 19.9$	$62.8 \pm 24.2$	0.704
Mortality	2/13 (15)	2/12 (17)	1.000
las con con			

 $^{1}$ Mean  $\pm$  SD or rate (%).

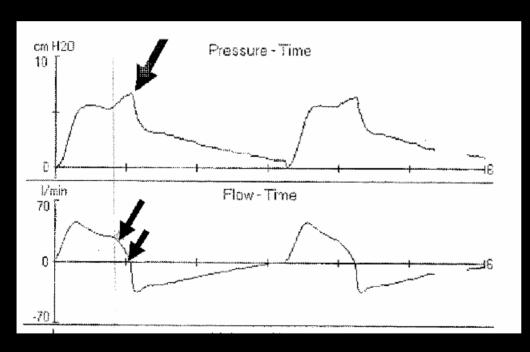
Dani C Pediatr Pulmonol 2006; 41:242-249

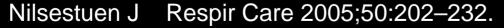
HFOV: The high-volume startegy was used ????
PSV + VG: Vt 5 ml/kg, PEEP of 3 cmH2O

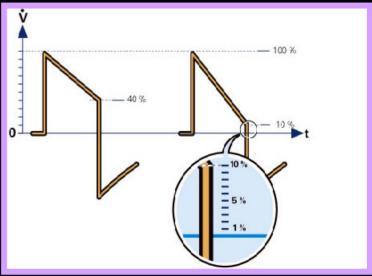
Ventilatory Goal: pH >7.20, pCO2 <65 mmHg, and pO2 >50 mmHg.

# Pressure-Support and flow termination criteria

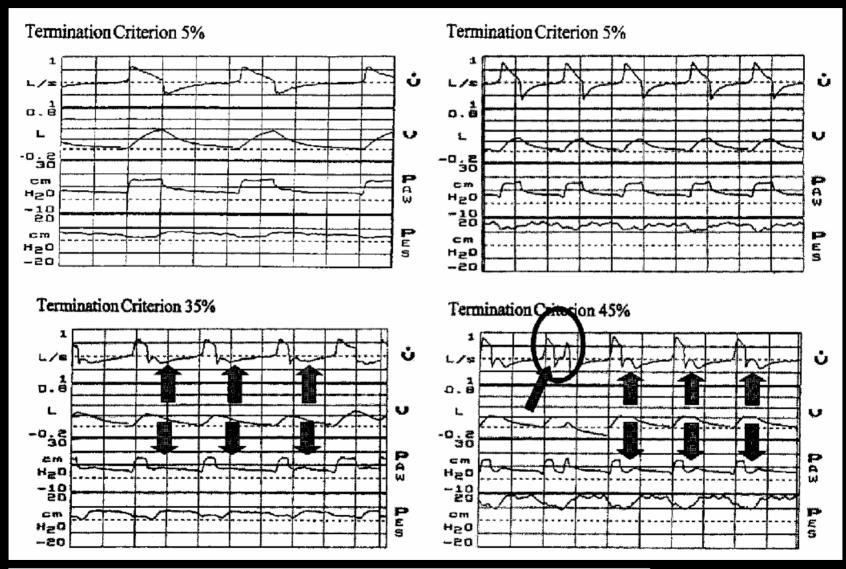
The non synchronized patient during Pressure-Support (inappropriate end-inspiratory flow termination criteria)







## Pressure-Support and flow termination criteria



Increase in RR, reduction in VT, increase in WOB

Nilsestuen J Respir Care 2005 Health technology assessment is only useful when the policy environment is mature enough to handle its results

van Beusekom I, Kahan J.

Annu Meet Int Soc Technol Assess Health Care Int Soc Technol Assess Health Care Meet. 2002; 18: abstract no. 323.

Lung-protective ventilation strategies in neonatology: What do we know—What do we need to know?

Anton H. van Kaam, MD, PhD; Peter C. Rimensberger, MD

Crit Care Med 2007; 35:925-931

Have the study questions be addressed adequately?

Most of the RCTs show weaknesses in the design, which may explain the inconsistent effect of high-frequency ventilation on bronchopulmonary dysplasia.

RCTs on CMV only focused on comparing various modes and settings, leaving the important question whether reducing tidal volume or increasing positive end-expiratory pressure is also lung protective in newborn infants unanswered.

