OSCAR & OSCILLATE

& the Future of High Frequency Oscillatory Ventilation (HFOV)

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What do we know already?

Sud S et al. *BMJ* 2010

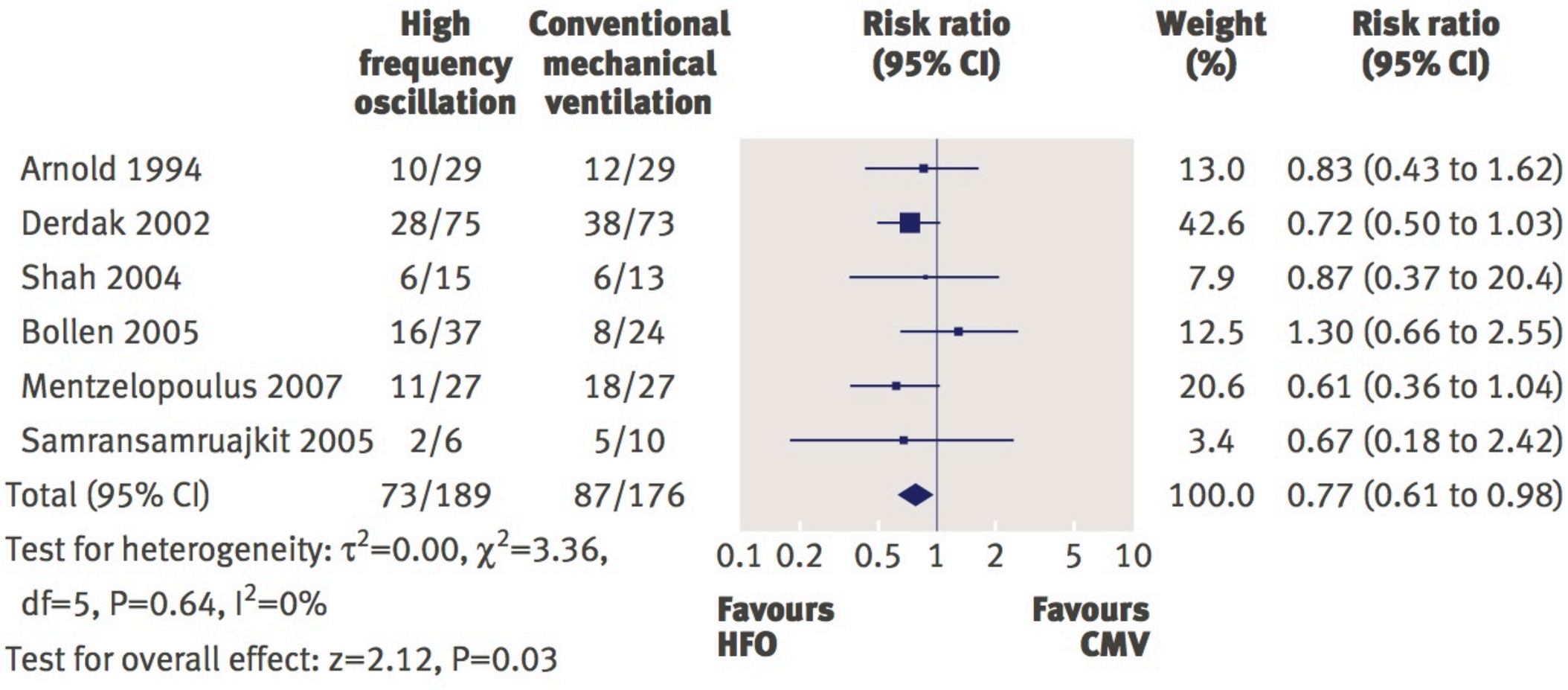


Fig 2 | Hospital or 30 day mortality in patients with acute lung injury/acute respiratory distress syndrome allocated to high frequency oscillation or conventional mechanical ventilation

OSCAR & OSCILLATE

Multi-centre randomised controlled trials of HFOV
verses current ventilation practice in adults with ARDS

OSCAR

- n = 795 (1006 intended)
- 29 centres
- Expert and non-expert centres
- England, Scotland and Wales
- 2007 – 2012
- 30 Day mortality,
  - days of paralysis, sedation, vasopressors, and antibiotics, duration of treatment in ICU and hospital

OSCILLATE

- n = 548 (1200 intended)
- 39 centres
- Expert and non-expert centres
- Canada, USA, Saudi, Chile and India
- 2007 – 2012
- 60 Day mortality
  - total dose of paralysis and sedation, vasopressors, duration of treatment in ICU and hospital

Inclusion

	OSCAR	OSCILLATE
Respiratory failure	Intubated for less than 7 days since onset of failure	Intubated within 2 weeks of onset of failure
	Expected to need ventilation for more than 2 days	
Hypoxaemia	$P_{aO_2}:F_{iO_2} \geq 200$	
	PEEP ≥ 5 mmHg	
Radiology	Bilateral air space opacification on chest X ray	
Age	≥ 16	16 – 80

Exclusion

OSCAR	OSCILLATE
Evidence of right atrial hypertension	
Suspected vascular pulmonary haemorrhage	
Neuromuscular disorders known to prolong MV	
Lung disease characterised by airway narrowing or air trapping	Severe chronic respiratory disease
Weight < 35 Kg	Weight < 35 Kg or > 1 Kg per cm height
Recent lung surgery	Pre-existing conditions with > 50% 1 year mortality
Participating in other trial	

Control

	OSCAR	OSCILLATE
Stipulation	Usual practice with guidance	Strict protocol
Recruitment	none	40 s of 40 mmHg
Mode	PCV	
Vt	6 – 8 ml/Kg IBW	6 ml/Kg IBW
PEEP	Titrated to F_{iO_2}	
Pplat		< 35 mmHg
Spont breaths		Daily trial
Rescue HFOV	At physicians discretion	Yes with clear indications

Intervention

	OSCAR	OSCILLATE
Recruitment		40 s of 40 mmHg
Ventilator	Novalung R100 (Metran)	Sensor Medics 3100B (CareFusion)
PMaw	5 cmH_2O > Pplat	30 cmH_2O
PaO2	60 – 75 mmHg	55 – 80 mmHg
f	10 Hz then pH ≥ 7.25	7 Hz then pH ≥ 7.2
I:E	1:1	1:2
Bias flow	100 ml	

Exit from HFOV

- 12 hours of:
  - $FiO_2 \leq 0.4$
  - $PaO_2 \geq 60$ mmHg
  - $PMaw \leq 24$ cmH_2O
- Restart HFOV up to 2 days later


OSCAR


OSCILLATE

Randomisation

	OSCAR	OSCILLATE
Allocation	Independent telephone randomisation system	Central web-based randomisation system
Stratification	P_{aO_2}:F_{iO_2} ratio, sex, age, centre	Blocks of 2 or 4 centre
Baseline	Slight advantage to intervention (age)	Slight intervention to control (age and inotropes)

Blinding

- Treatment
  - No blinding
- Analysis
  - Unclear
- Outcomes are objective


OSCAR


OSCILLATE

Results: Follow Up

OSCAR

- 100% on intention to treat
  - 2.5% of control arm received rescue HFOV
  - 2.5% of intervention arm died before HFOV could be commenced
- 97.5% intervention vs 2.5% control received HFOV
  median duration of 3 days (IQR 2 – 5)

OSCILLATE

- 100% on intention to treat
  - 12% of control arm received rescue HFOV
  - 1.5% of intervention arm didn't receive HFOV
- 98% intervention vs 12% control received HFOV
  median duration of 3 days (IQR 2 – 8)

OSCILLATE Cross Over

- Pre planed conditions for rescue therapy including HFOV
  - Refractory hypoxaemia (P_{aO_2} ≤ 60 mmHg with F_{iO_2} of 1.0 with neuromuscular blockade)
  - Refractory barotrauma (persistent pneumothorax or increasing subcutaneous emphysema despite two intercostal catheters on the involved side)
  - Refractory acidosis (pH ≤ 7.05 despite neuromuscular blockade)
- 12% crossed over to HFOV (91% according to protocol)
- Average duration of rescue HFOV was 7 days
- Mortality 71% in the crossed over patients
- Maximum number of patients that might have been saved was 10 (3.5%)

Primary Outcomes

OSCAR

30 Day mortality

Control	HFOV
166 (41.7%)	163 (41.1%)

(P = 0.85)

Stopped early for futility

OSCILLATE

60 Day mortality

Control	HFOV
96 (35%)	129 (47%)

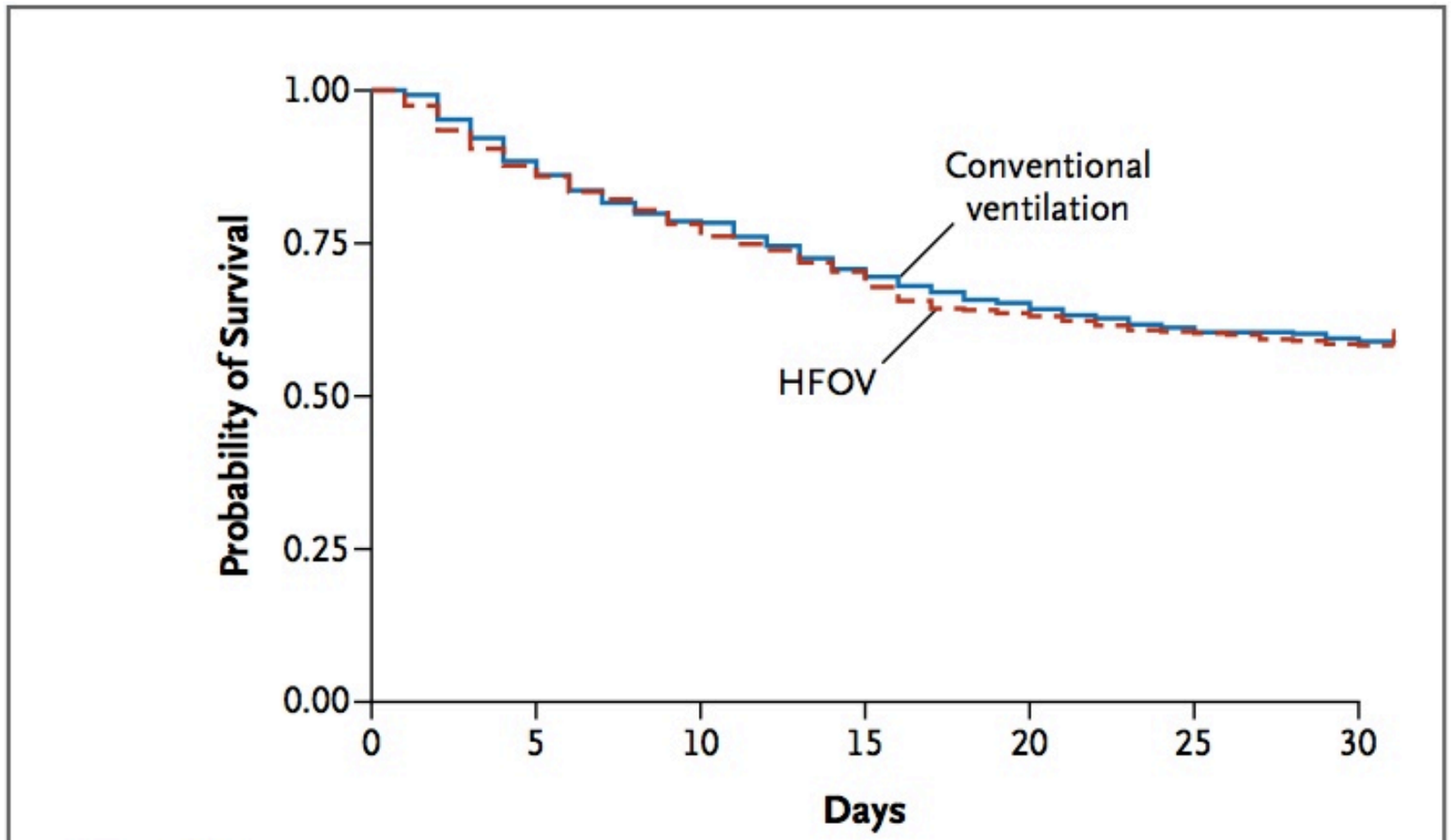
(P = 0.005)

Relative risk of death in the HFOV cohort
1.33 (CI 1.09 – 1.64)

Stopped early for risk of harm

Results

OSCAR



No. at Risk

Conventional ventilation	397	351	312	281	259	243	236
HFOV	398	349	311	280	253	241	233

Figure 3. Kaplan–Meier Survival Estimates during the First 30 Study Days.

Results

OSCILLATE

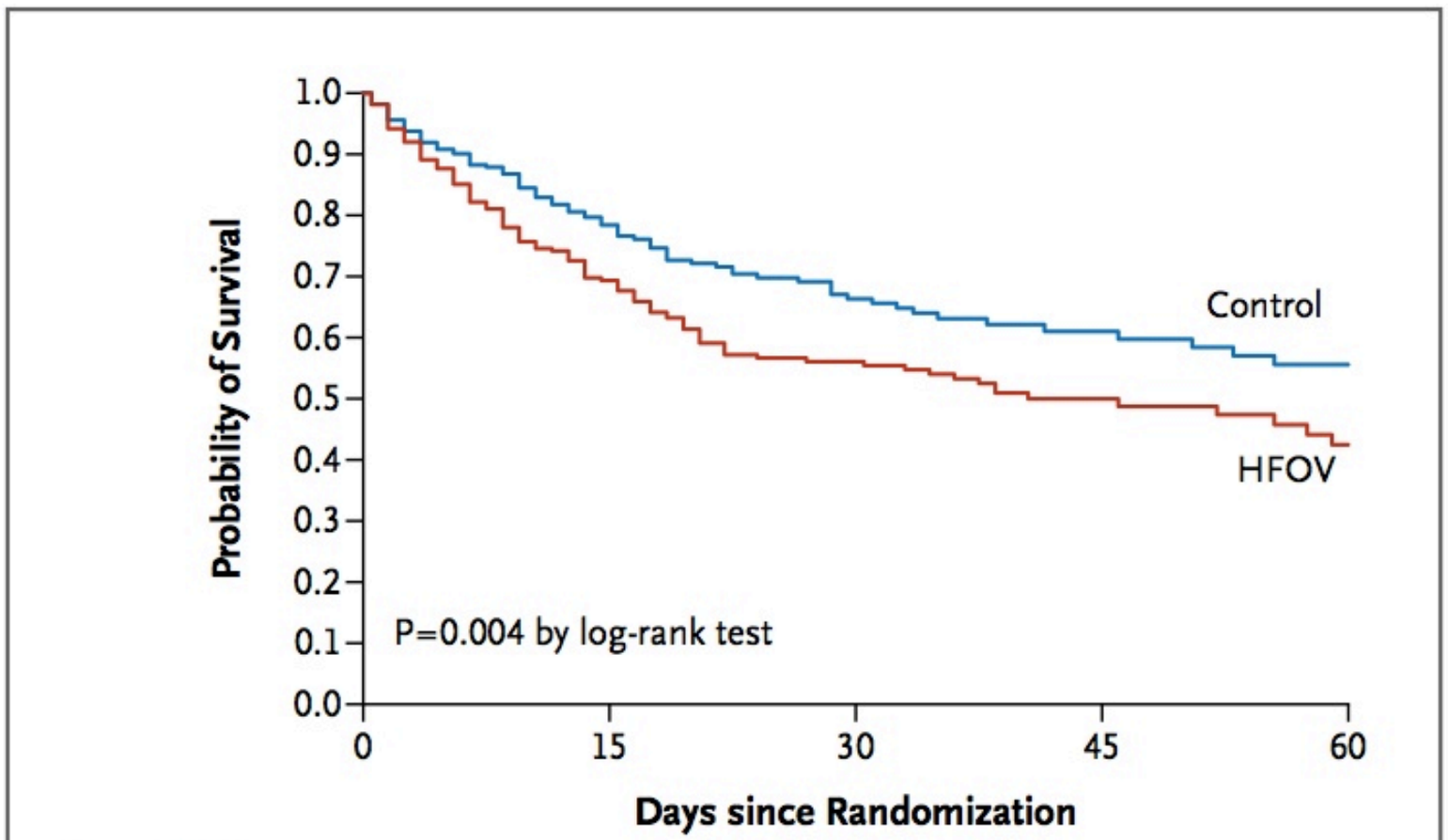
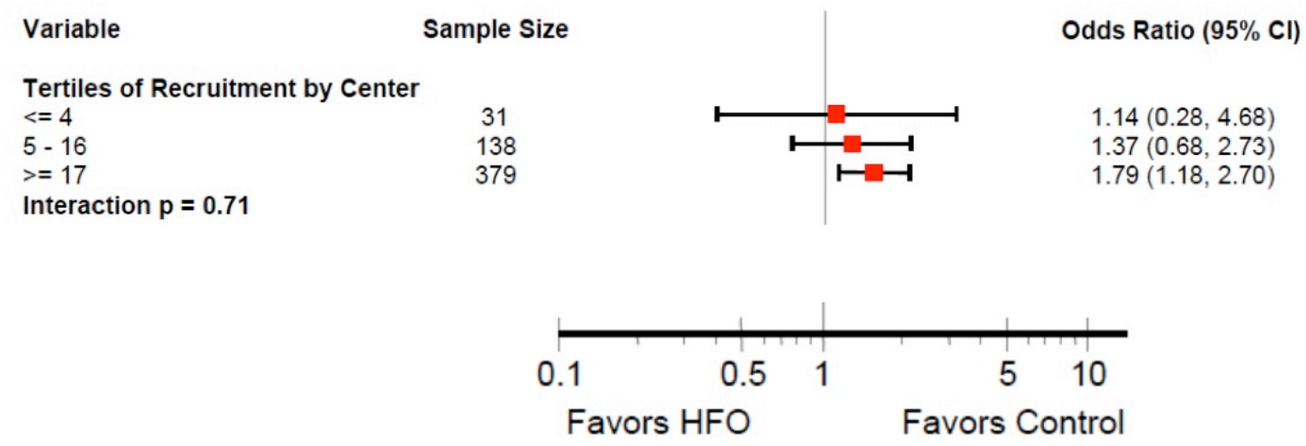


Figure 2. Probability of Survival from the Day of Randomization to Day 60 in the HFOV and Control Groups.

Multivariate Analysis on 60 Day Mortality

OSCILLATE

- No significant association with
  - Baseline hypoxia
  - Respiratory compliance
  - BMI
  - Vasopressors
  - Treatment centre experience



Secondary Outcomes

Intervention vs Control

	OSCAR	OSCILLATE
Sedation	9.4 vs 8.5 days	Midazolam: 199 mg vs 144 mg (P<0.001) Fentanyl: 2980 µg vs 2400 µg (P=0.06)
NMJ blockade	2.5 vs 2.0 days	98% vs 63% (P<0.001)
Vasopressors	2.9 days vs 2.8 days	91% vs 84% (P=0.01)
Antibiotics	12.8 vs 12.4 days	
Refractory hypoxia		7% vs 14% (P=0.007)

The Future for HFOV

Dubious