

Breathing problems: and how to get on top of them

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MYOTUBULAR FAMILY DAY JULY 12 2014



GET THE BREATHING BASICS RIGHT

- ▶ Identify probability of problems: clinical course, symptoms, investigations
- ▶ Nutrition, vaccination, physiotherapy
- ▶ Sensible use of antibiotics
- ▶ Proactive plan

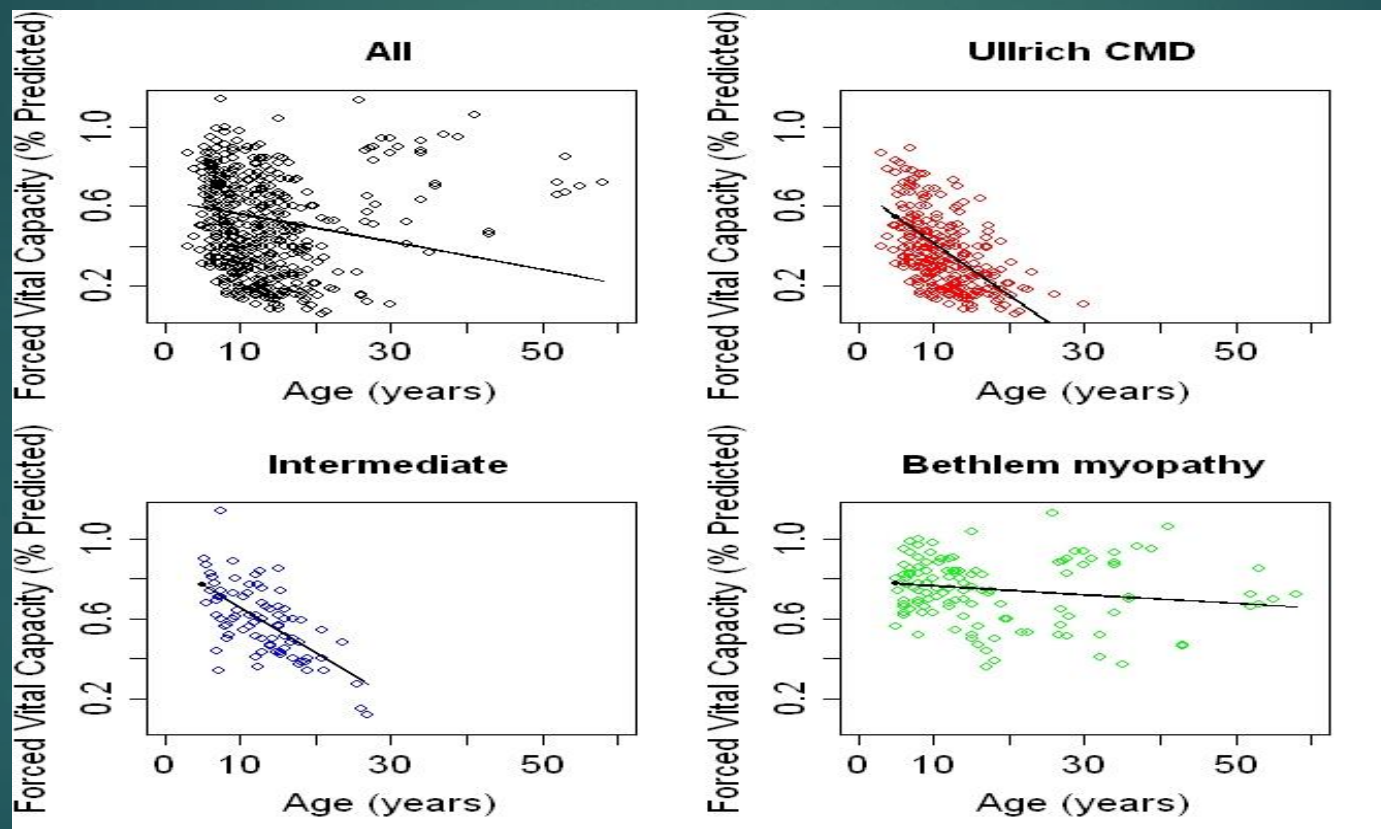
Overview : identification of risk

Condition	Respiratory failure	Secretion clearance difficulty	Recurrent pneumonia	Progression	Disease-specific features
SMA					
Type 1	All by 2 years	Marked	All	Rapid	All require full-time respiratory support
Type 2	~40% in childhood	Early	~25% in first 5 years	Slow	
Type 3	Rare in childhood	Rare in childhood	Rare in childhood	Slow	
SMA with respiratory distress type 1	All by 6 months	Marked	All	Rapid in first year, then slows.	All require full-time respiratory support
DMD/severe childhood onset limb-girdle muscular dystrophy	After loss of ambulation	After loss of ambulation	Late		Cardiomyopathy usually occurs after respiratory problems but may precede them
Facioscapulohumeral muscular dystrophy	When onset <20 years	With infantile onset	With infantile onset	Slow	Severe infantile onset type is frequently associated with sensorineural deafness
Congenital muscular dystrophy					
All types	Any age depending on severity	Any age depending on severity	Any age depending on severity	Slow	
Ullrich	70% in adolescence	Mild	Infrequent		Proximal contractures with marked distal laxity
Rigid spine muscular dystrophy	Early while ambulation preserved	Mild	Infrequent		Hypoventilation may occur in ambulant children with relatively preserved vital capacity
Congenital myopathy					
Central core	Uncommon except in severe recessive type	Uncommon	Uncommon	Slow	Susceptible to malignant hyperthermia
Minicore	Early while ambulation preserved				
Nemaline	Early in severe neonatal form, mild later onset form may develop early while ambulation preserved	In severe form	In severe form	Slow	
Myotubular	85% in severe X-linked form	In severe form	In severe form	Slow	Ophthalmoplegia, rare coagulopathy and liver haemorrhage
Fibre type disproportion	Depends on genotype	Uncommon	Uncommon		
Myotonic dystrophy					
Myotonic dystrophy 1	Common in severe congenital onset, usually improves	Common in severe congenital onset	Common in severe congenital onset	Initial improvement, later slow deterioration	Prominent learning difficulty, somnolence, central hypoventilation
Myotonic dystrophy 2	Uncommon	Uncommon	Uncommon		
Congenital myasthenic syndromes	Often in neonatal period, may occur during inter-current illnesses	Especially during inter-current illnesses	Possible if weakness severe and persistent		Weakness may fluctuate, episodic apnoea in some. Congenital stridor in those with DOK7 mutations
Mitochondrial myopathy	Common	Possible	Possible	Acute deterioration possible	
Charcot—Marie—Tooth	With severe early onset, especially with GDAP1 mutation	With severe early onset	With severe early onset		Stridor, especially with GDAP1 mutation
Pompe	Infantile onset, may be early in later onset while ambulation preserved	Infantile onset	Infantile onset	Infantile rapid, late onset slow	Variable relationship between motor and respiratory progression

PROGRESSION OF NMD

	Congenital Myopathy (CM)	Congenital Muscular Dystrophy (CMD)	Congenital Myasthenic Syndrome (CMS)
Disease Course	Typically static course, with improvement in function and progression later on in life	Early static course with progressive decline	Slowly improving strength, fluctuating weakness (on daily, weekly basis) returning to a baseline
Neonatal Respiratory Distress	Yes (Myotubular myopathy, Nemaline myopathy)	Less likely, except (Walker Warburg Syndrome)	Yes
Key Exam findings	Ptosis, Bulbar Dysfunction	No Ptosis or bulbar Dysfunction	Ptosis, Bulbar Dysfunction (FLUCTUATING)
Cognitive Impairment	NO	Yes , only alpha-dystroglycanopathy subtype	NO
Elevated Serum CK	NO	YES	NO
Muscle biopsy	Myopathic	Dystrophic	
Subtypes (More Common Genes Involved)	<u>Centronuclear</u> (MTM, DNM2, TTN, RYR1, BIN1), <u>Core</u> (RYR1, TTN), <u>Nemaline</u> (Rod) (ACTA1, NEB,) <u>CFTD</u> (TPM3, TPM2, RYR1, SEPN1, ACTA1)	<u>Collagen VI-CMD</u> , <u>LAMA2 CMD</u> (MDC1A), <u>alpha Dystroglycanopathy-CMD</u> (FKRP, FUKUTIN, LARGE, POMT2, POMT1, POMGNT1 GMPPB, ISPD), <u>SEPN1-CMD</u> , <u>LMNA-CMD</u>	<u>Pre- Synaptic</u> (COLQ1,), <u>Post-Synaptic</u> , <u>Fast Channel</u> , <u>Slow Channel</u>
Idiosyncrasies	-Though thought to be static, can have increasing respiratory impairment in later years and those on trach/vent from birth require setting re-evaluation annually	-LMNA, SEPN1- may have profound axial weakness -Collagen VI and SEPN1 –may develop respiratory failure while ambulant	-Treatment with mestinon may improve strength and respiratory function -Intercurrent illness may lead to a sudden profound respiratory crisis, including respiratory arrest

Decline in FVC in collagen VI myopathy (CMD) patients



Foley A Reghan et al
Brain 2013

Genotype-phenotype links - role in guiding care : Congen myasthenia

CMS
Gene
mutatio
ns



Patients were referred at ages from 2 -10 years

O₂/CO₂ sleep study

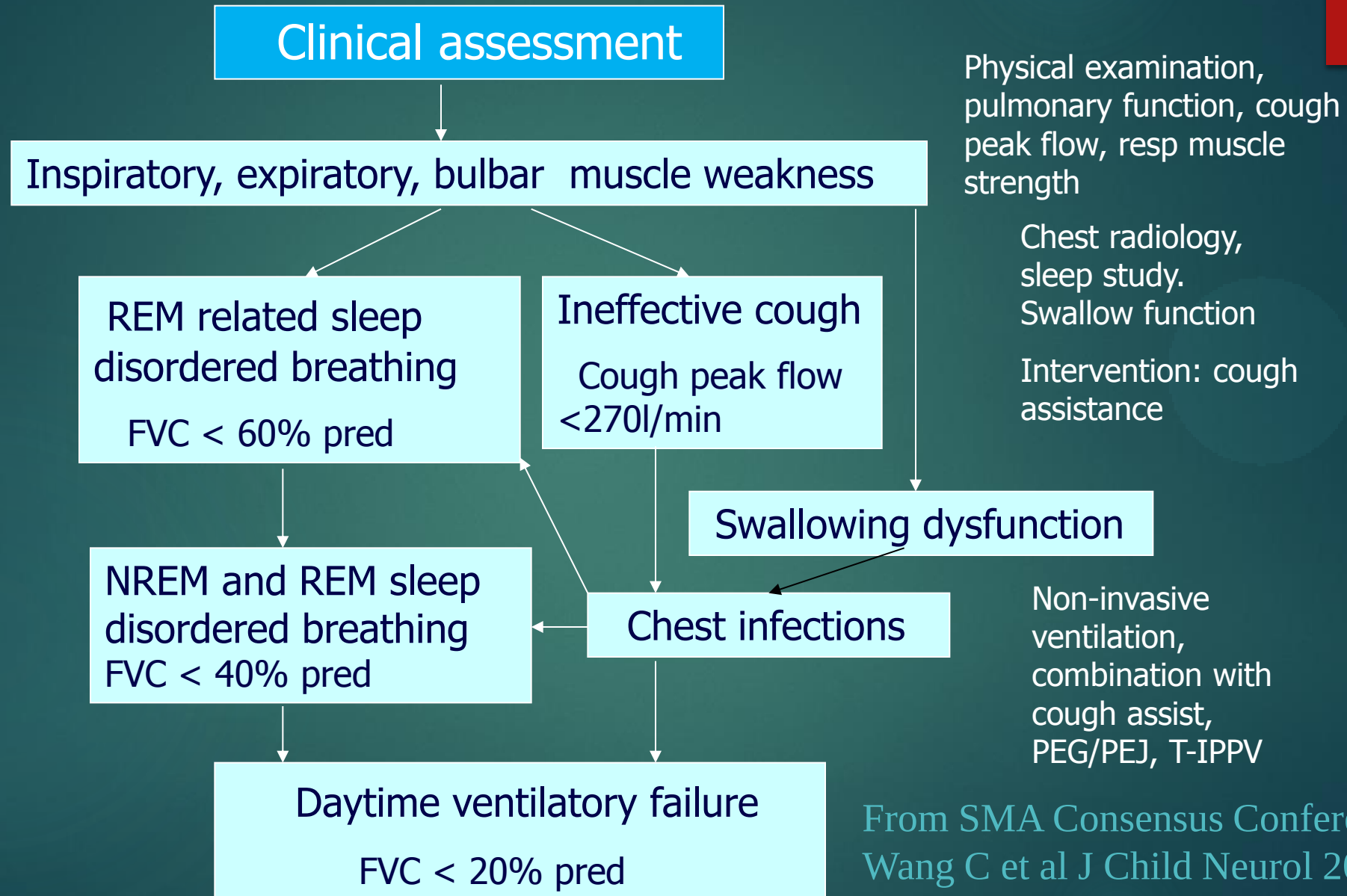
⇒ Mean TcCO₂ 8 ± 1 kPa

⇒ Mean SaO₂ $96 \pm 1\%$

⇒ Nadir SaO₂ $76 \pm 7\%$

All use NIV at night and majority use NIV in the day for rests

Clinical algorithm:

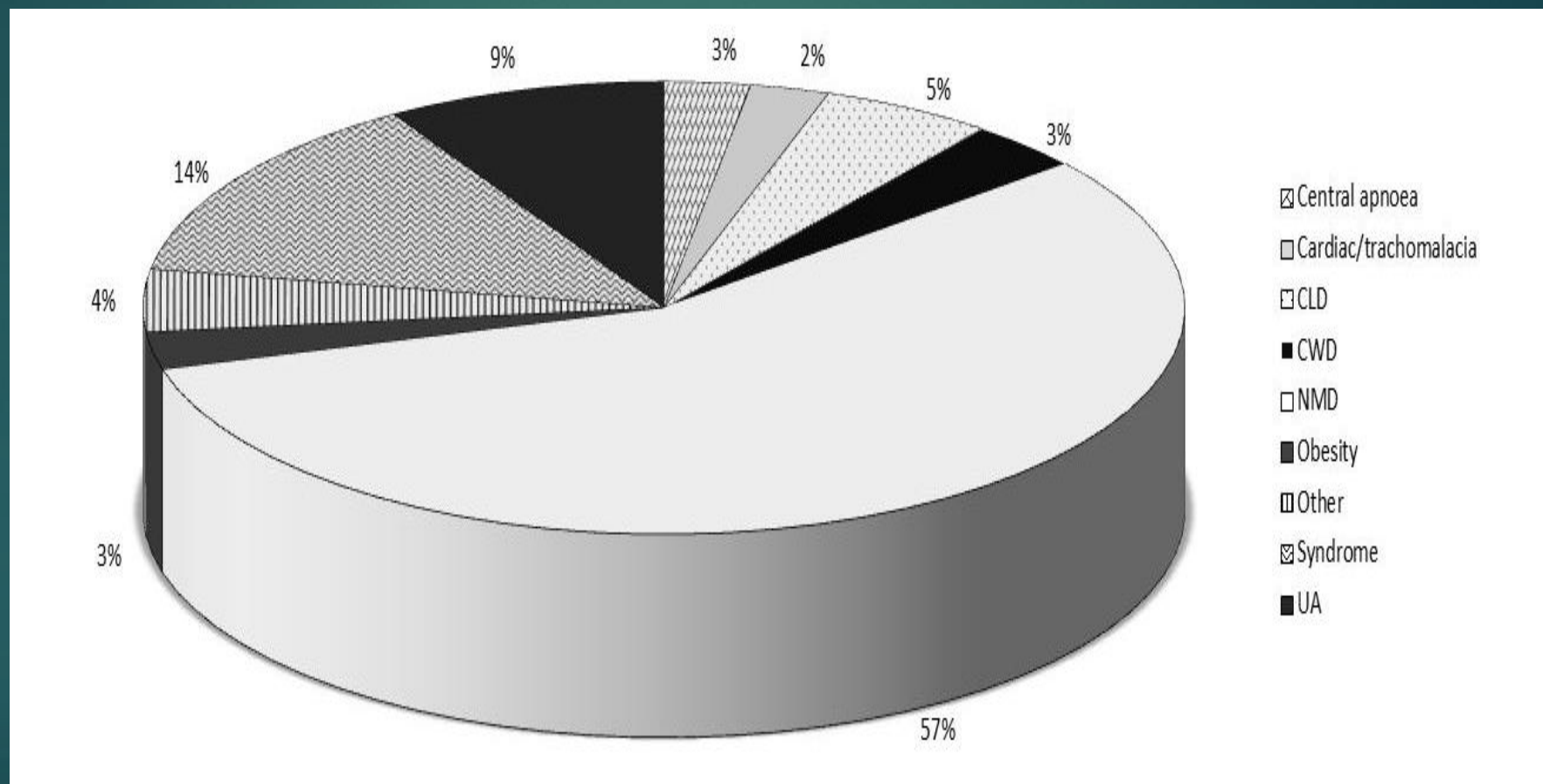


From SMA Consensus Conference
Wang C et al J Child Neurol 2008

Indications for long term respiratory support

- To treat the symptoms of nocturnal hypoventilation.
- To treat the symptoms of daytime hypoventilation.
- To reduce the frequency of hospital admission for chest infections.
- To prevent chest wall deformity in young children with the expectation of improved long-term outcome.
- To prolong life.

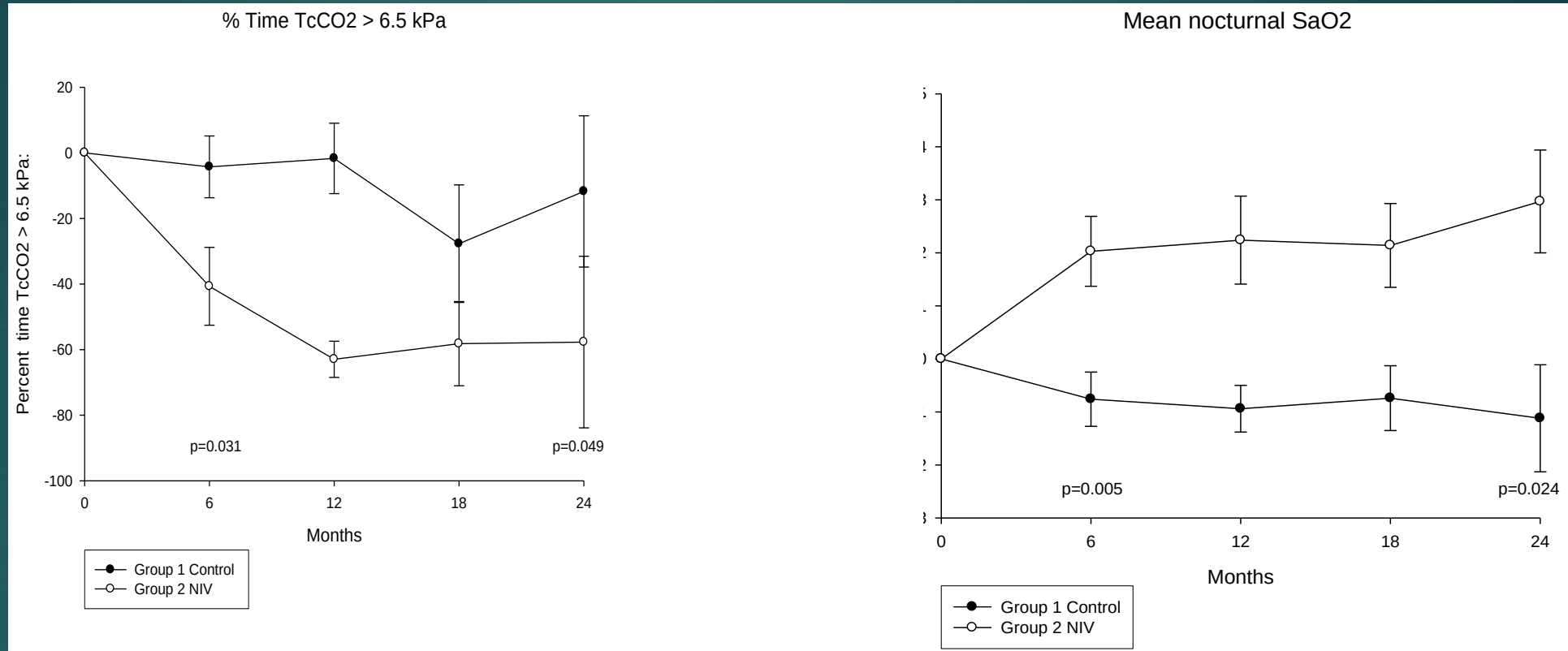
Paediatric NIV : diagnostic categories – Royal Brompton



Children initiated on NIV support by age

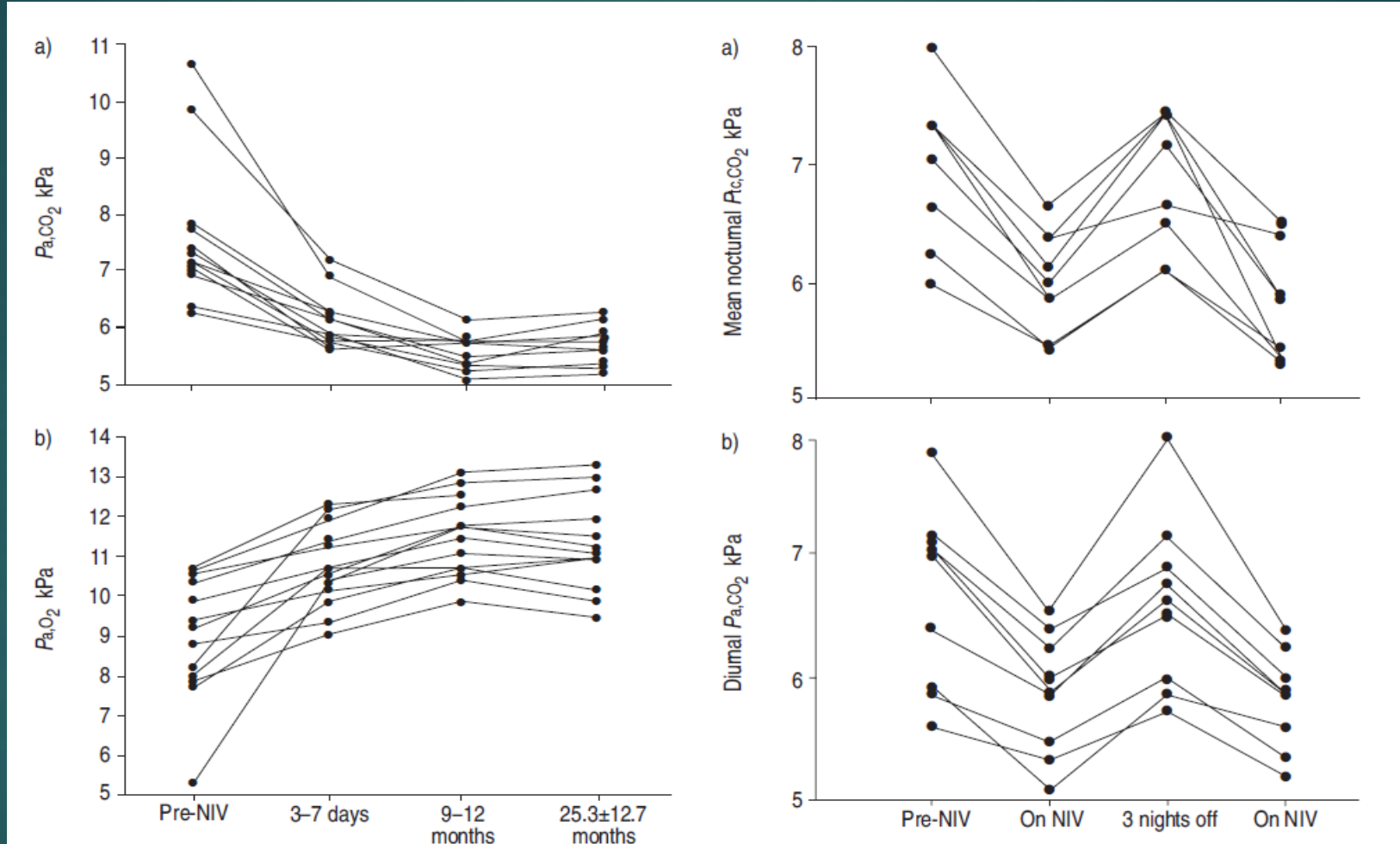
Age (years)	Number
less than 1	61
1 to 3	80
4 to 5	32
6 to 9	51
10 to 17	241

Timing of introduction of NIV: noct hypovent



Significant reduction in time TcCO₂ > 6.5 kPa and mean SaO₂ in NIV group. 70% required ventilation in 1 year, 90% by 2 years. (Ward et al Thorax 2005;60:1019-24)

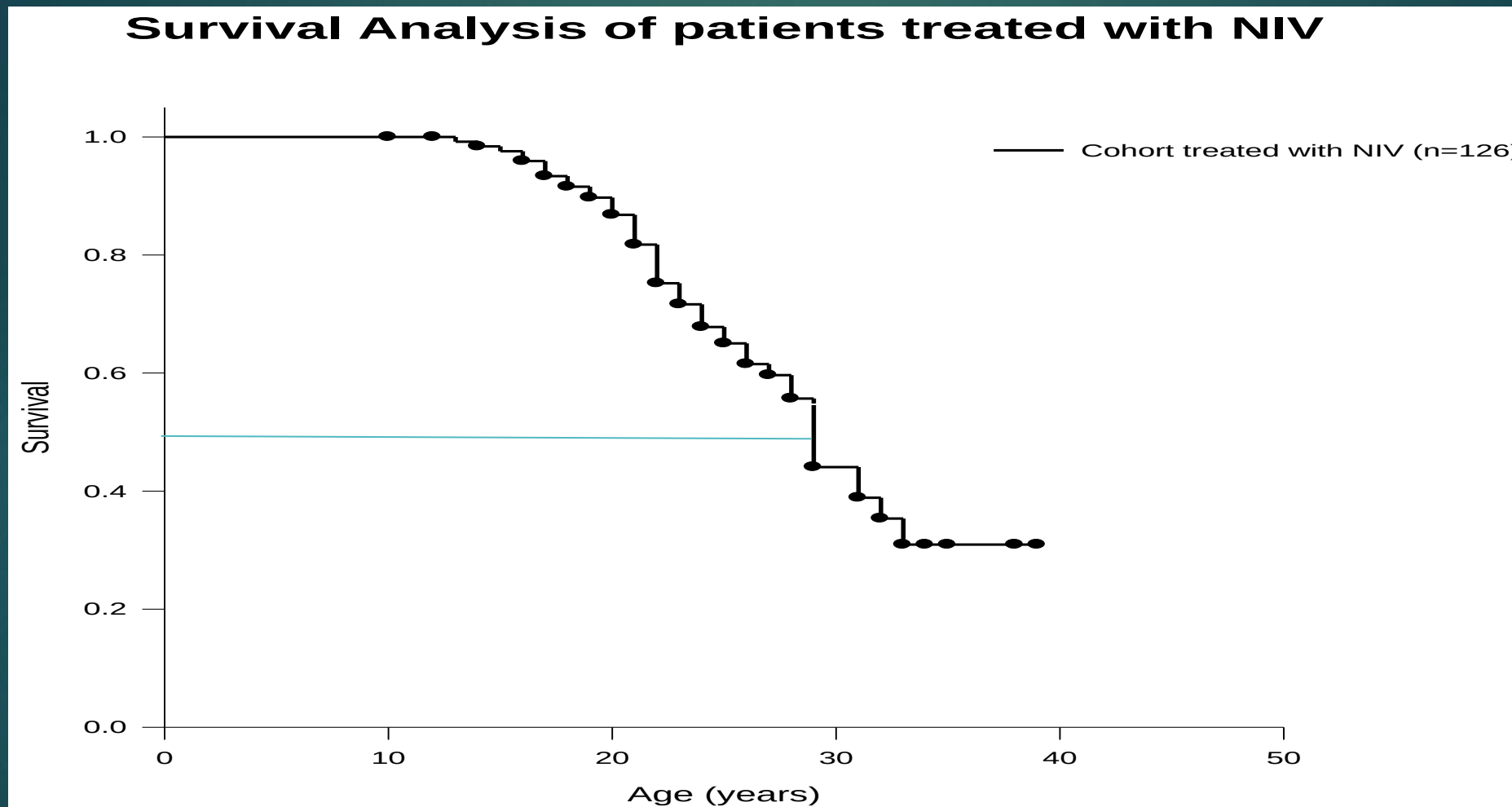
BENEFITS: IMPACT OF NIV ON ABG



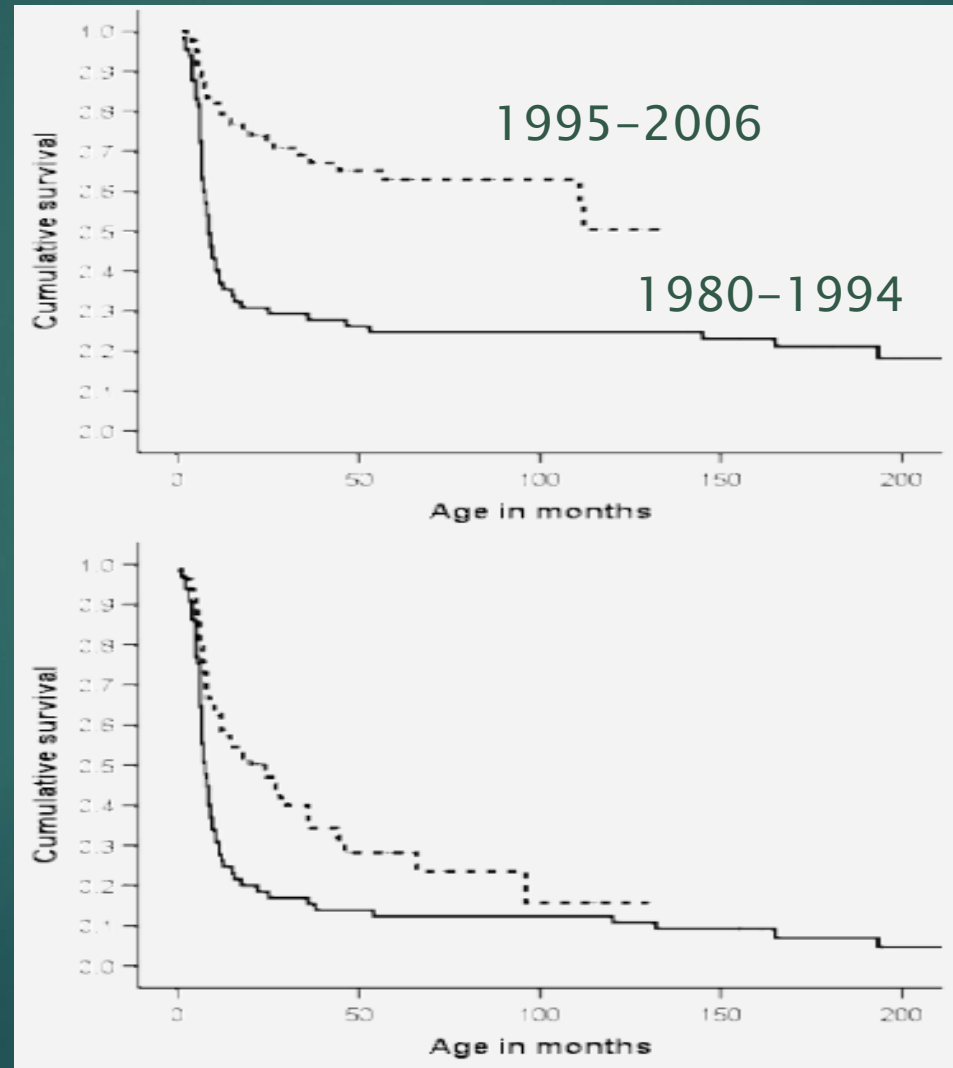
Changes patterns of NIV implementation

- ▶ AIM: To review clinical practice for the initiation of home non-invasive ventilation (NIV) in children with neuromuscular disease (NMD) over 15 yrs 1995-2011
- ▶ Forty-four patients were studied (mean age 12.7yrs, SD 4.8).
- ▶ NIV use increased over the study period (1.4 NIV initiations/yr in 'baseline' group vs. 4.9/yr in 'recent' group, $p < 0.0001$).
- ▶ Patients in the 'baseline' group had more advanced respiratory insufficiency (awake $p\text{CO}_2$ 58.3 vs. 46.3mmHg, ($p = 0.016$)). More patients in the 'baseline' group started NIV at the stage of diurnal hypercapnic respiratory failure (10 of 14 (71%) vs. 8 of 30 (27%), $p = 0.008$), while nocturnal hypoventilation with daytime normocapnia was the most common indication in the 'recent' group (14 of 30 (47%) vs. 2 of 14 (14%), $p = 0.049$).
- ▶ All children in the 'baseline' group had NIV initiated in the intensive care unit. In the 'recent' group, 24 of 30 children (80%) were assessed as clinically stable and had NIV initiated on the respiratory ward without any major adverse events. The average length of hospital admission for NIV establishment was 6.9 days in the 'baseline' group and 3.5 days in the 'recent' group ($p = 0.004$).

Changing outcomes: Duchenne MD Analysis RBH 2009



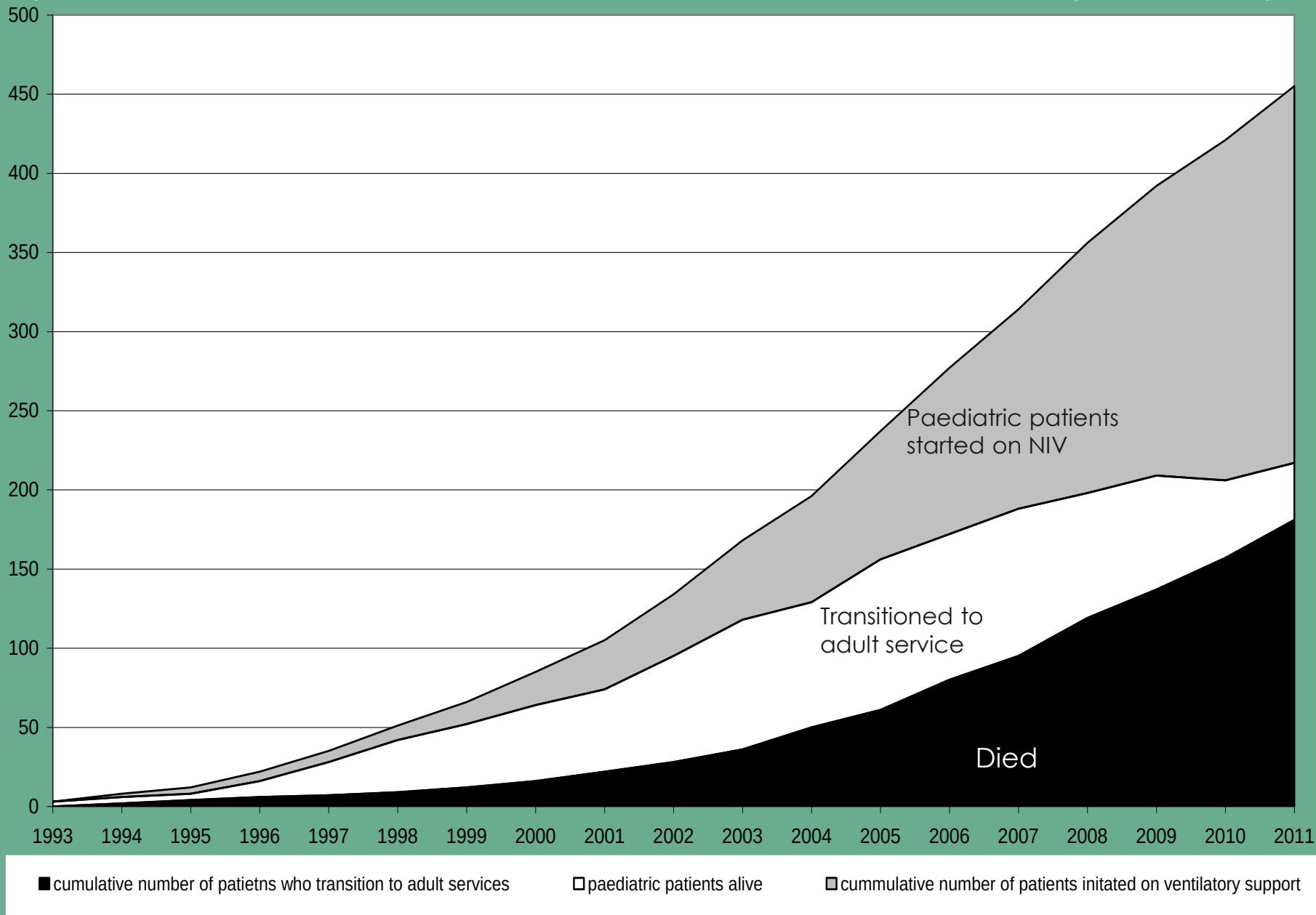
Kaplan-Meier survival SMA I 1995-2006 v.1980-1994



Death or
ventilation
> 24
hrs/day

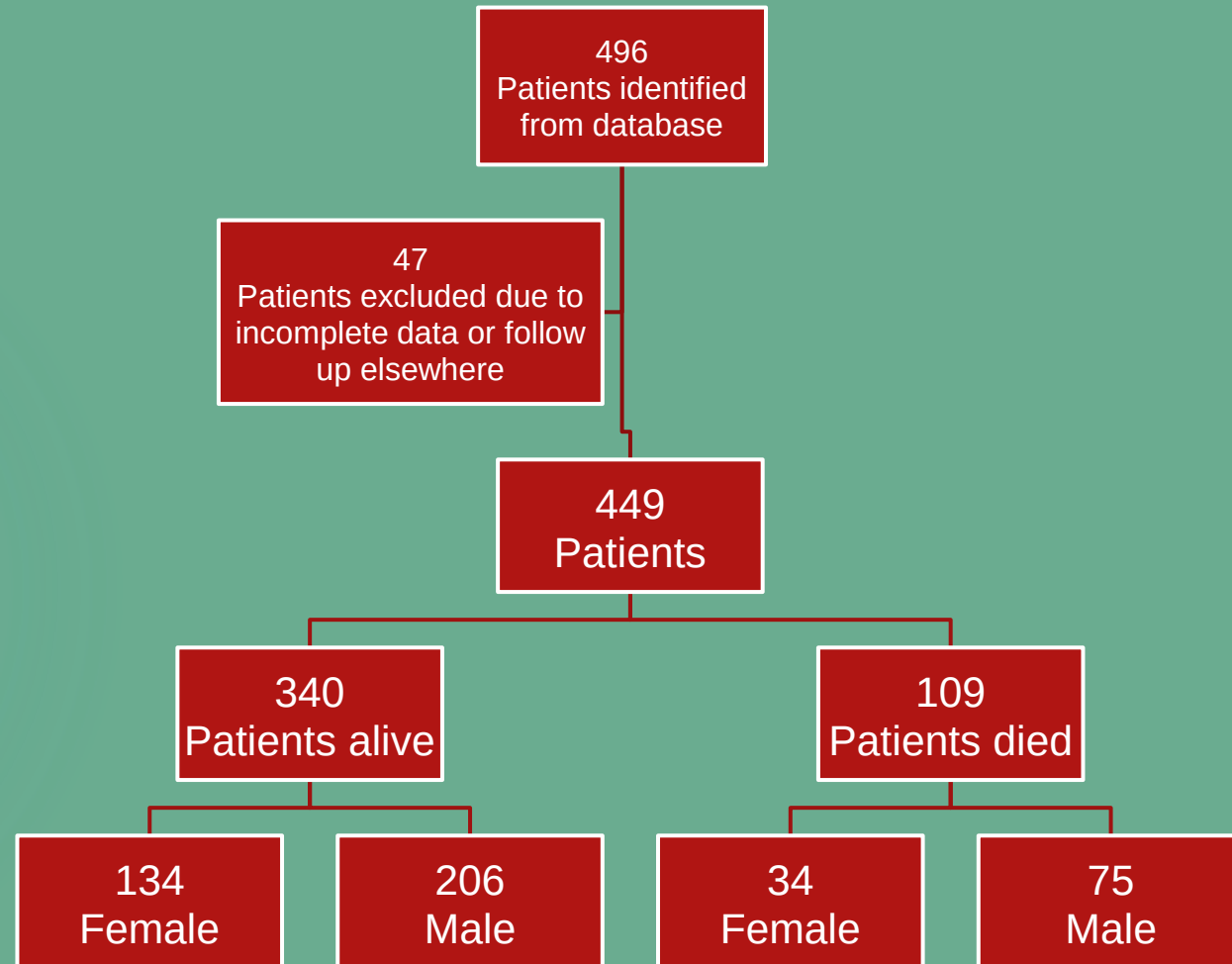
Oskoui M et al
Neurol 2007;
69:1931-36

Growth in paediatric NIV and transition to adult care: Royal Brompton Hospital



N=449

Paediatric patients started on home non-invasive ventilation (RBH)



Outcome: Bottom line

- ▶ 40% Paediatric NIV pts have transitioned to adult care
- ▶ 24% have died
- ▶ 9% were able to discontinue ventilatory support

Other roles: Planned surgical procedures – Scoliosis

Planning for surgical procedures

- ▶ Surgery in children with NMW should take place in units with experienced paediatric surgeons, anaesthetists and physiotherapists, and where there are facilities for paediatric intensive care and NIV. [D]
- ▶ Extubation protocols for high-risk children (those with vital capacity <60% predicted and/or ineffective cough and/or already use NIV for hypoventilation) should include effective airway clearance techniques and immediate use of non-invasive ventilation following extubation. [√]
- ▶ Children with NMW who require surgery (including scoliosis surgery) should be assessed by a multidisciplinary team prior to any intervention. [√]

Scoliosis

- ▶ The effect of wearing a spinal brace on respiratory function should be assessed and weighed against the limited evidence of benefit in terms of affecting final scoliosis severity. [D]
- ▶ The primary consideration when planning surgery for children with scoliosis associated with NMW should be comfort and quality of life. [√]

Impact of intermittent NIV on chest wall growth

Baseline

6 months

12 months

18 months

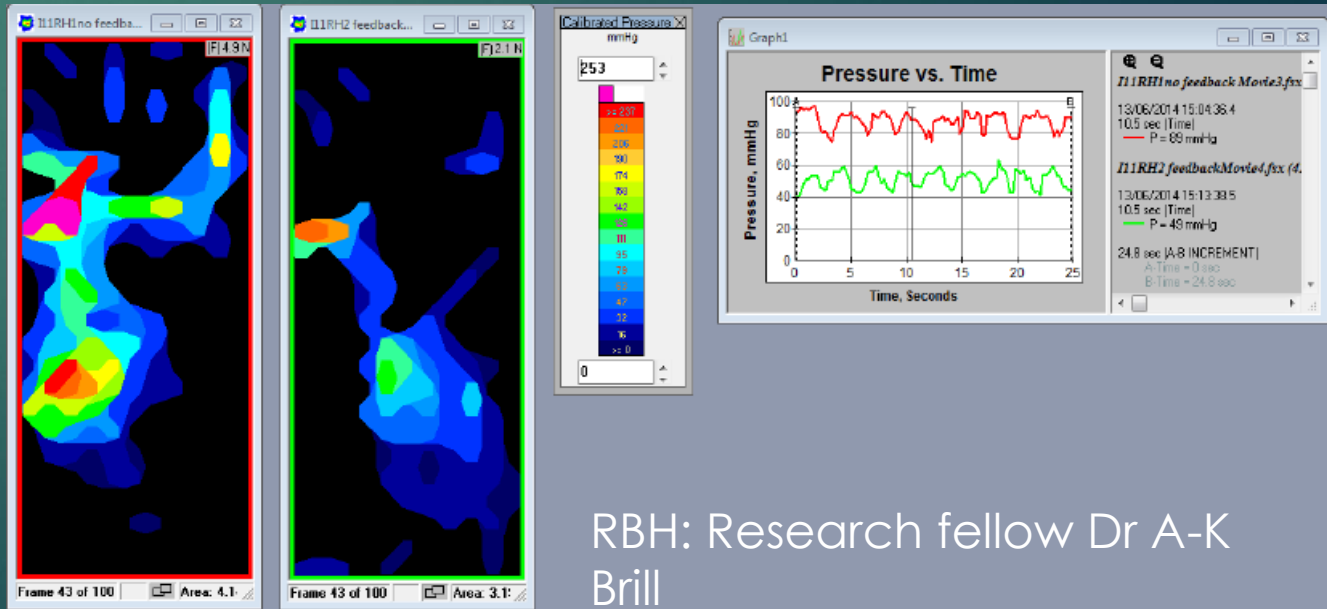
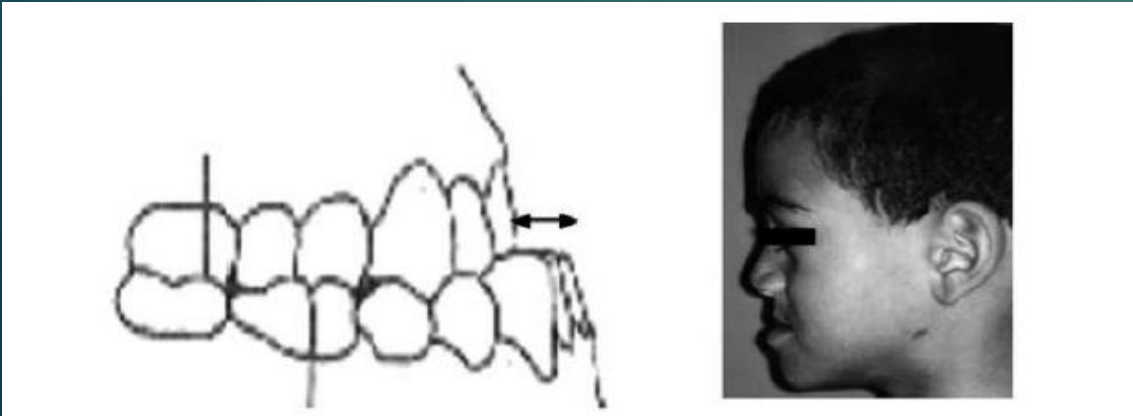
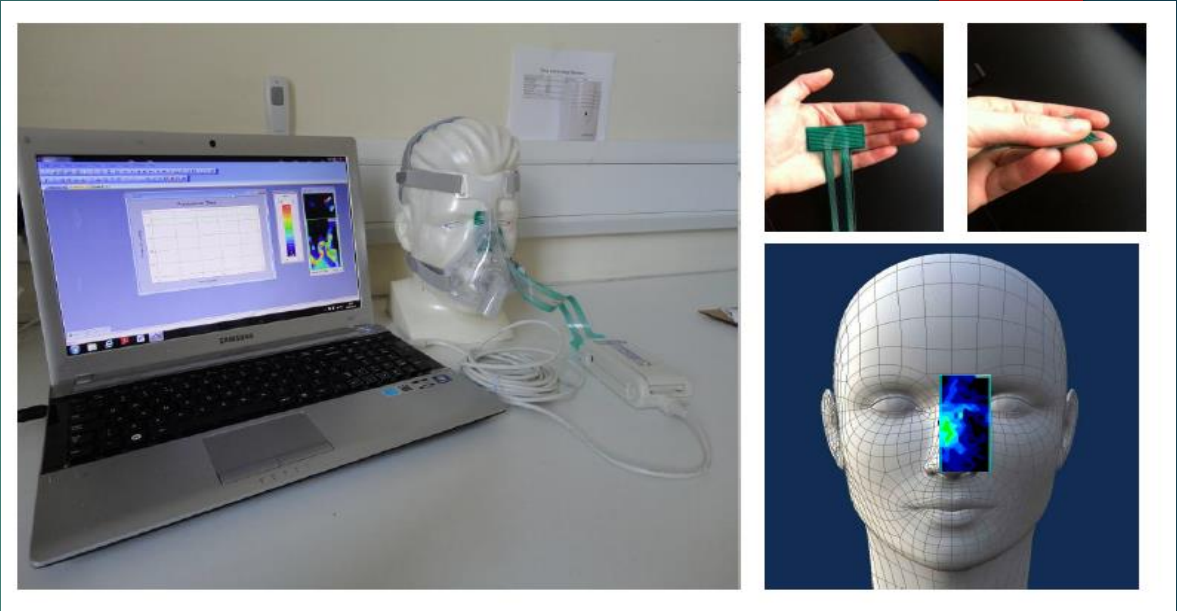
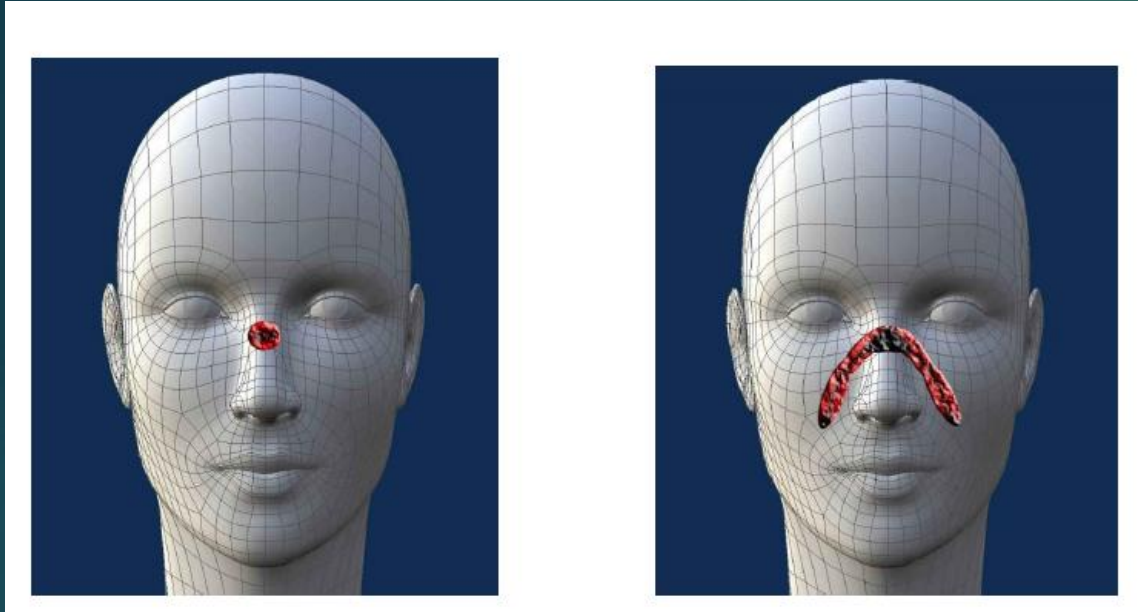


Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I

Patient	Resuscitation status: for intubation and ventilation?	Total number of intubations	Referred for management to facilitate discharge	Non protocol-led extubation success	Protocol-led extubation success	Admissions managed with non-invasive aids	Home mechanical insufflation/exsufflation?	NIPPV use at discharge after initiation	NIPPV use at present or before death
A	Y	3	Y	0	2	2	Y	Nocturnally	Nocturnally
B	Y	1	Y	0	1	0	N	Nocturnally	24 h a day
C	N	0	Y	NA	NA	0	N	18 h a day	24 h a day
D	Y	2	N	0	Not attempted	0	N	Acclimatisation to NIPPV	Nocturnally
E	Y	0	Y	NA	NA	2	Y	18 h per day	16 h per day
F	Y	0	N	NA	NA	2	Y	Acclimatisation to NIPPV	Nocturnally
G	Y	2	Y	1	1	2	Y	Nocturnally	Nocturnally
H	N	0	N	NA	NA	0	N	Nocturnally	23 h per day
I	Y	2	N	1	1	0	Y	Nocturnally	16 h per day
J	Y	2	N	1	1	2	N	When unwell with a respiratory tract infection	Nocturnally
K	N	0	N	NA	NA	1	Y	18 h a day	20 h per day
L	Y	1	N	0	1	1	N	Acclimatising to NIPPV	Nocturnally
M	Y	4	Y	0	2	1	Y	Nocturnally	Nocturnally

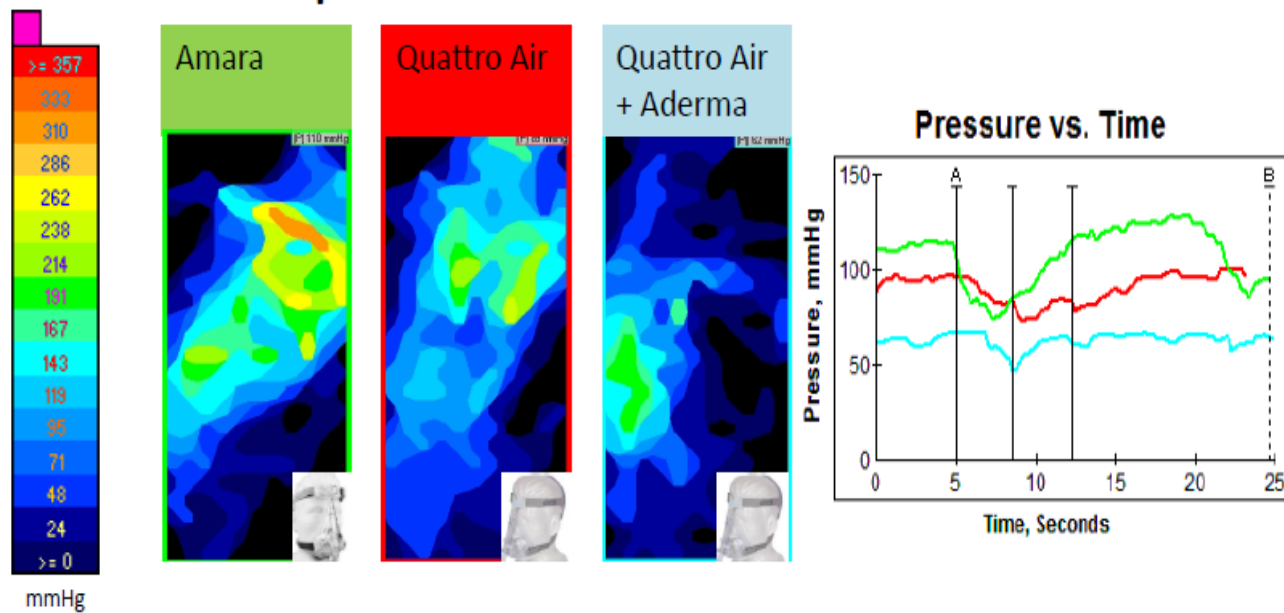
N, no; NA, not applicable; NIPPV, non-invasive positive pressure ventilation; Y, yes.

Current Research: Improving mask comfort and design



RBH: Research fellow Dr A-K Brill

Comparison of different masks



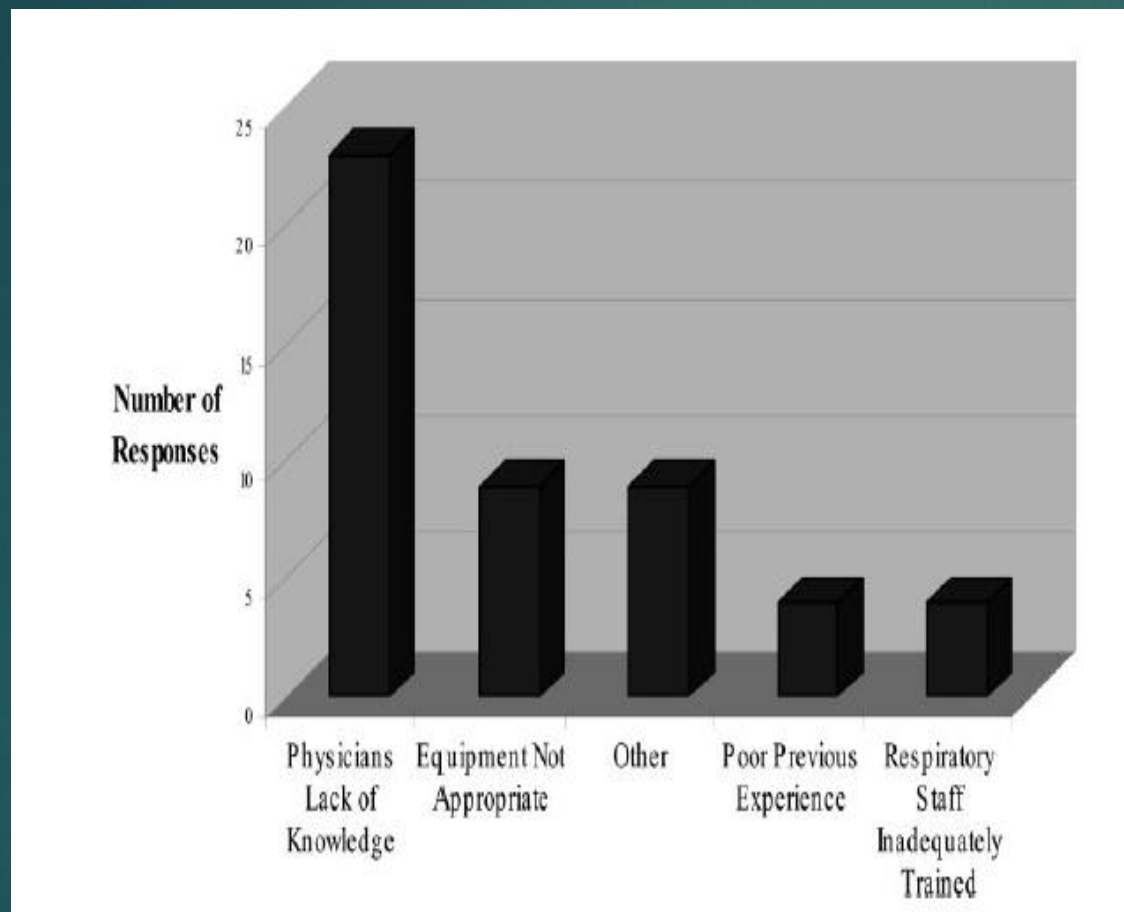
	Amara		Quattro Air		Quattro Air + Aderma	
Contact Pressure	114	mmHg	96	mmHg	62	mmHg
Ventilator setting	20/5	cm H2O	20/5	cm H2O	20/5	cm H2O
Air leak	3	l/min	5	l/min	4	l/min

Pilot case study

Improving mask fitting skills

	No visual feedback (NFB)	With visual feedback (FB)	Significance
Air leak (L/min)	2.1 ± 2.8	1.5 ± 1.9	ns
Contact pressure nasal bridge (mmHg)	62.6 ± 11.1	57.3 ± 10	p = 0.013
Comfort on VAS (0-100)	48.1 ± 15	42.2 ± 8.3	p = 0.036

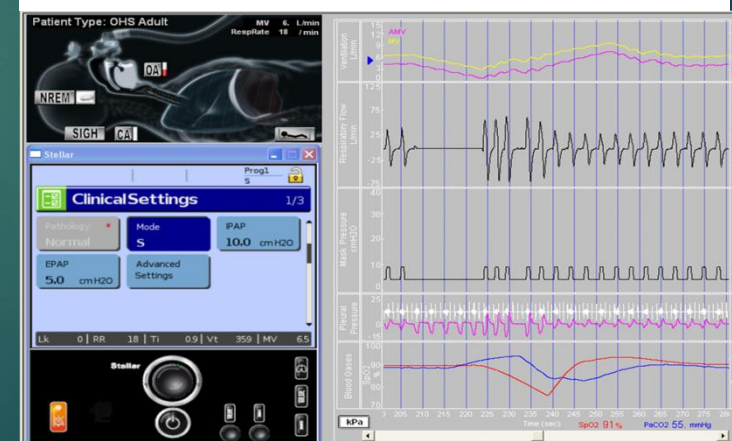
Implementation of NIV in clinical practice



Maheshwari V et al Chest 2006;129:1226-33



STUDYSHOTS.co.uk

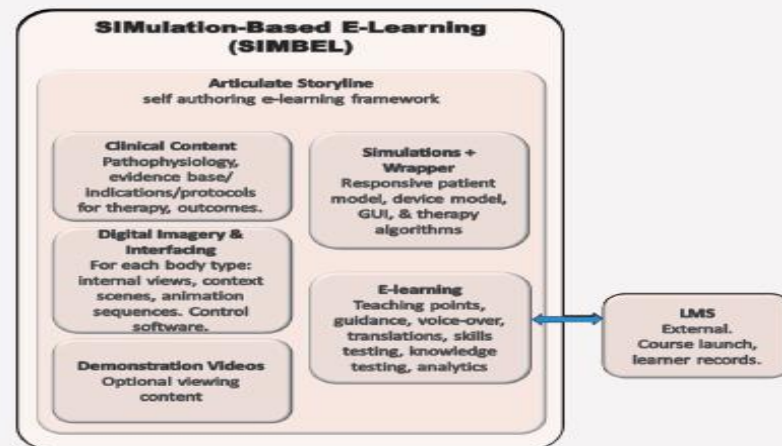
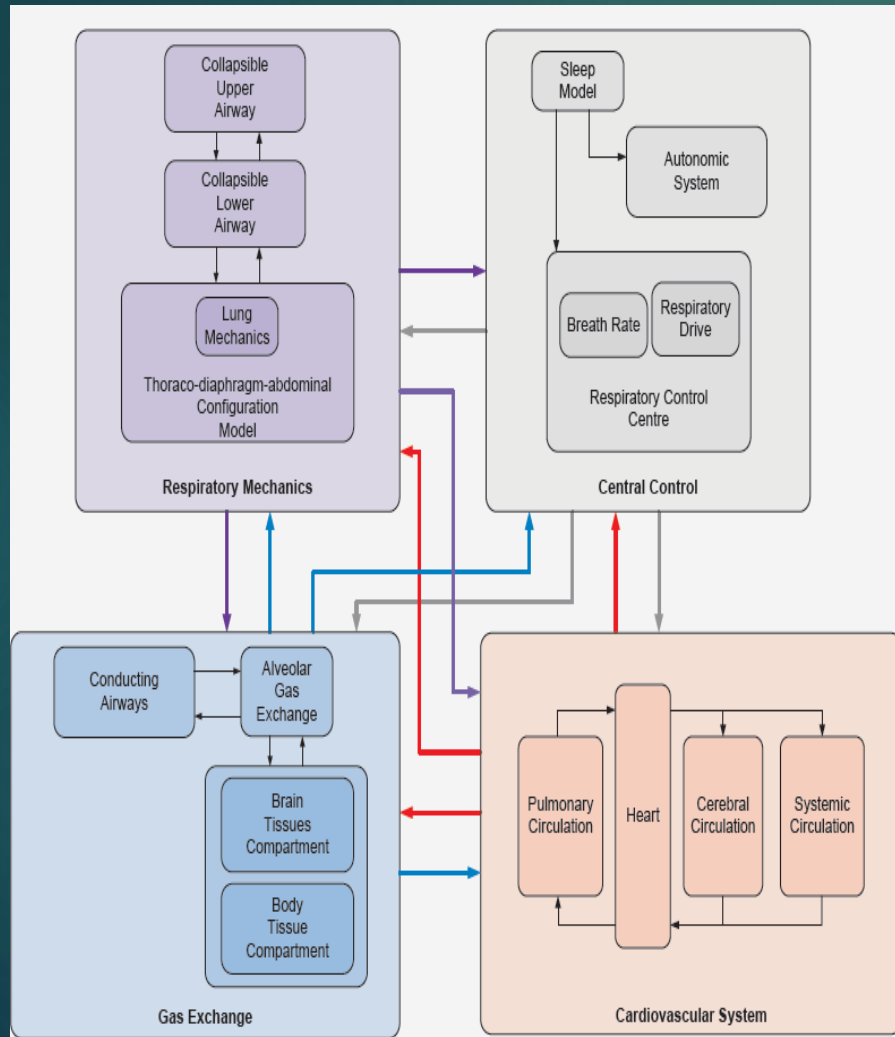


Research fellow A Hare

>

NIV Simulator

Access at ERS website : e learning resources
<http://www.ers-education.org/e-learning/simulators.aspx>

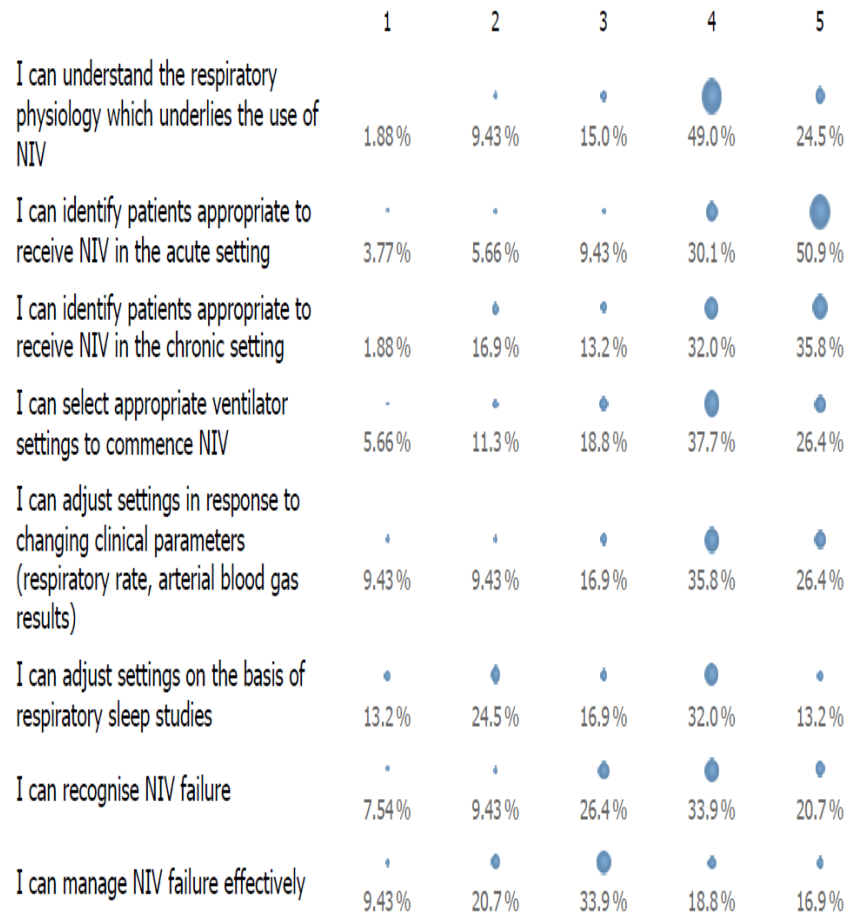


Hare A &
Simonds A
American
Thoracic
Society 2014

NIV Simulator evaluation

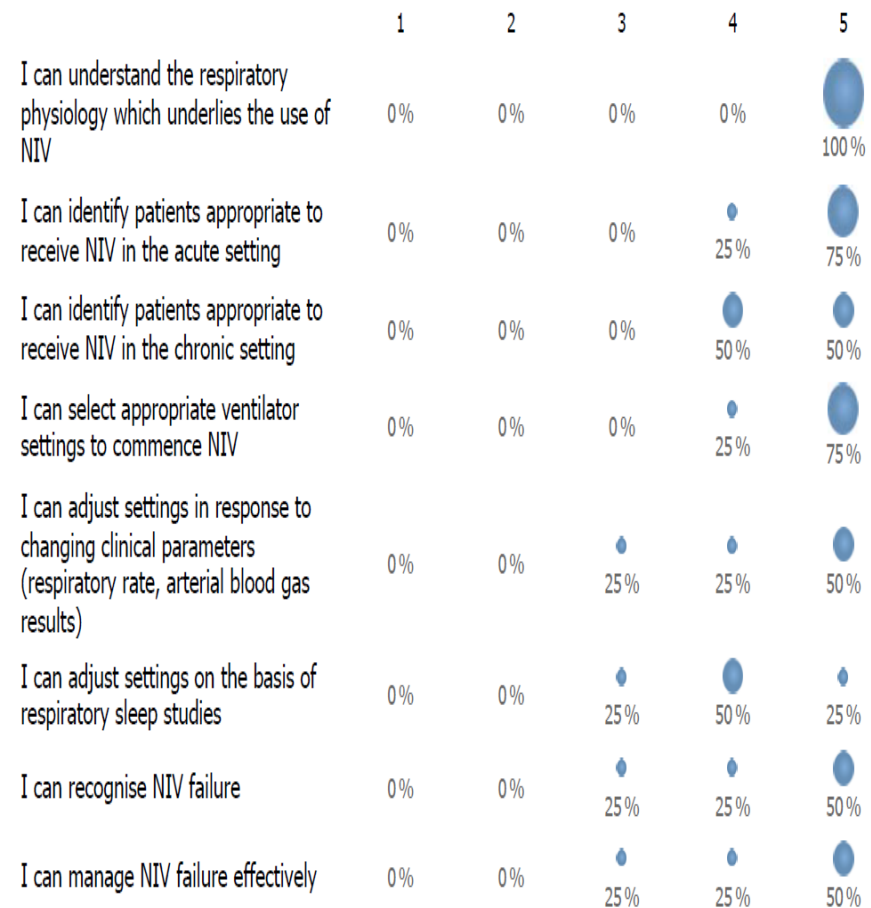
Pre Sim use

The list below represents different skills in non-invasive ventilation (NIV). Using a scale of 1-5, where 1 is not at all confident, and 5 is highly confident, rate how confident you are that you can perform these tasks as of now.



Post Sim use

The list below represents different skills in non-invasive ventilation (NIV). Using a scale of 1-5, where 1 is not at all confident, and 5 is highly confident, rate how confident you are that you can perform these tasks as of now.





'Intelligent' ventilation

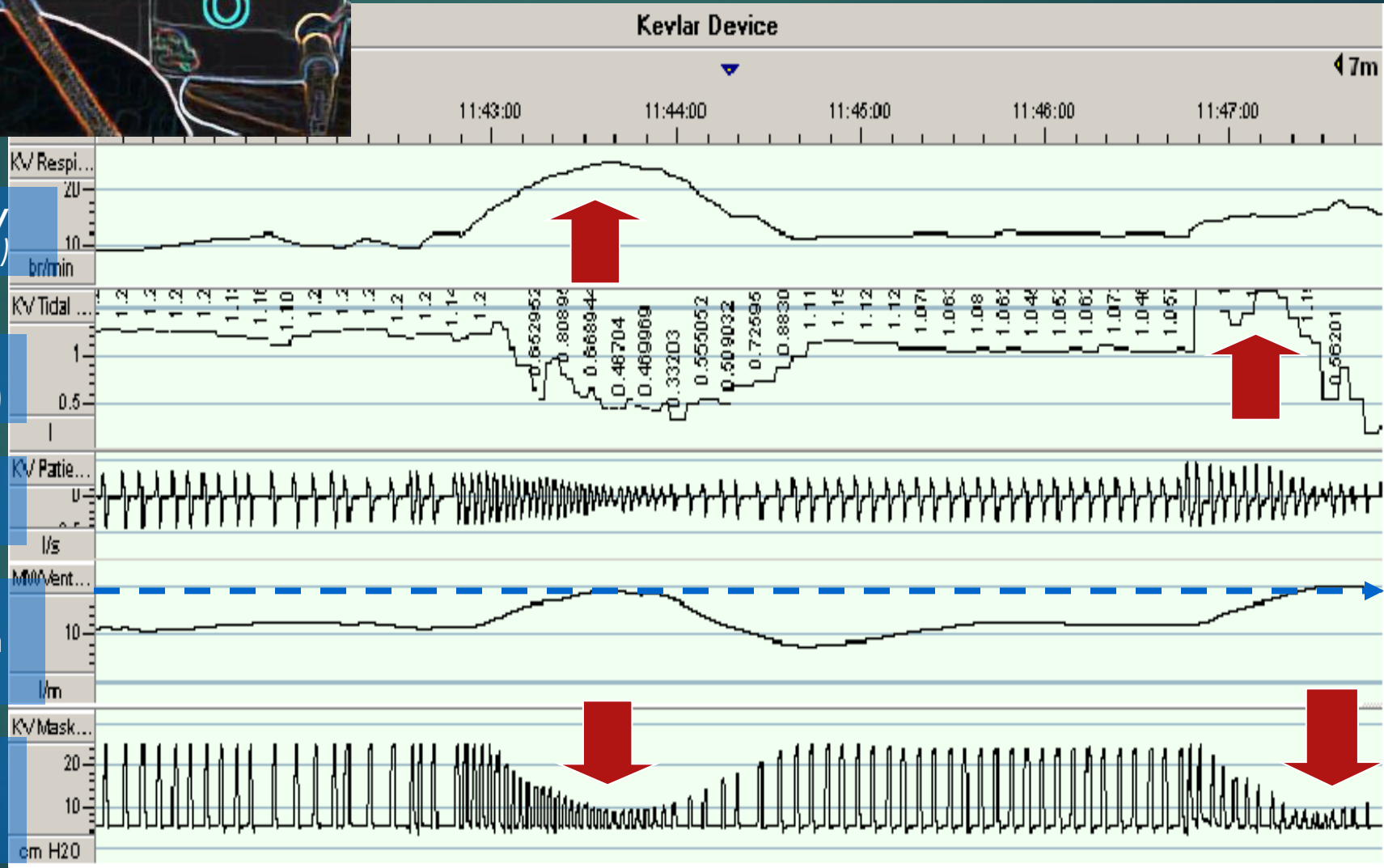
**Respiratory
Rate (bpm)**

**Tidal
Volume (L)**

**Flow
(L/sec)**

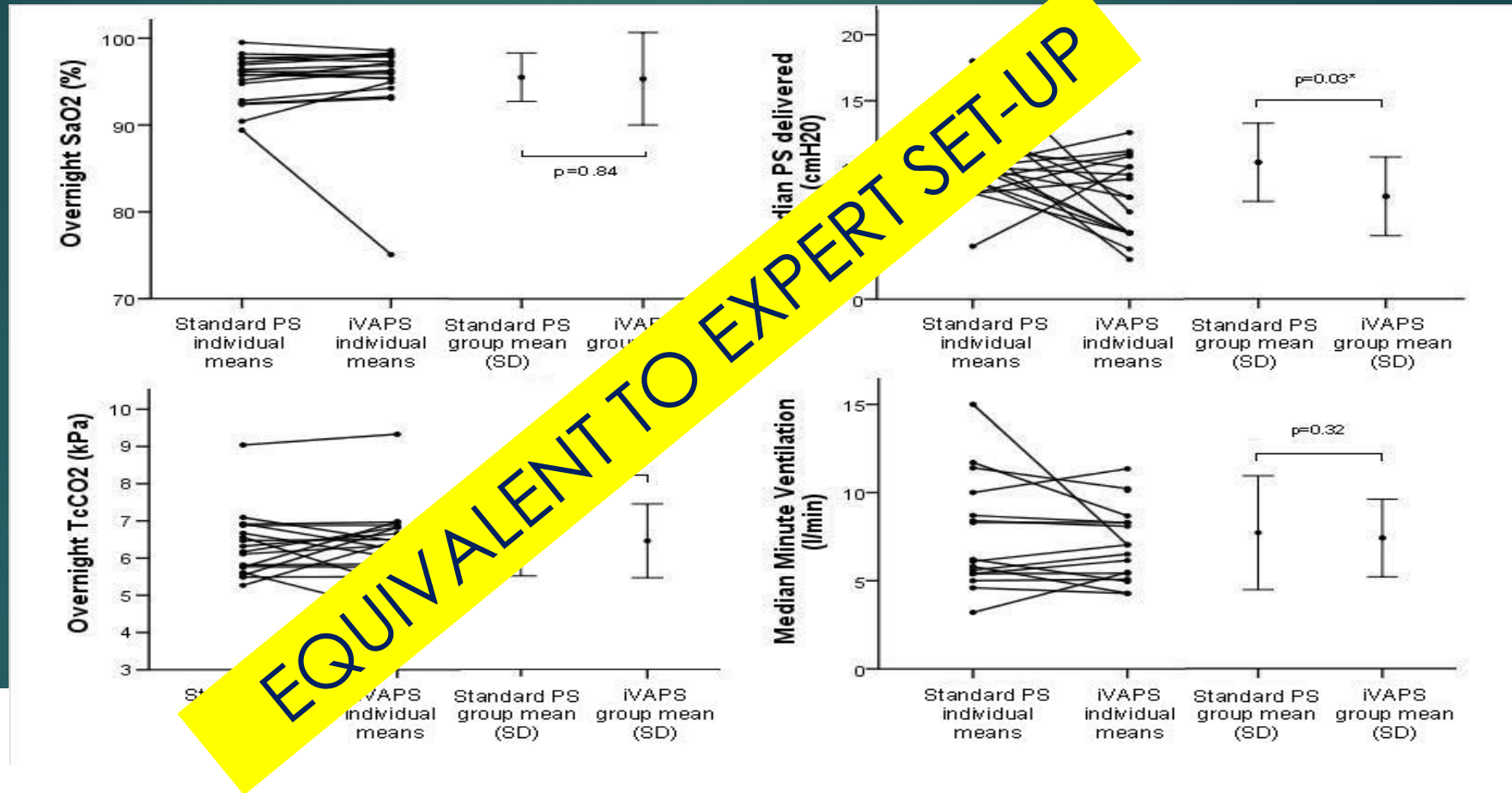
**Minute
Ventilation
(L/min)**

**Mask
Pressure
(cmH₂O)**



Research fellow J Kelly

'Intelligent' ventilation (iVAPS) in stable NIV users



Adherence (naive users Month 1)

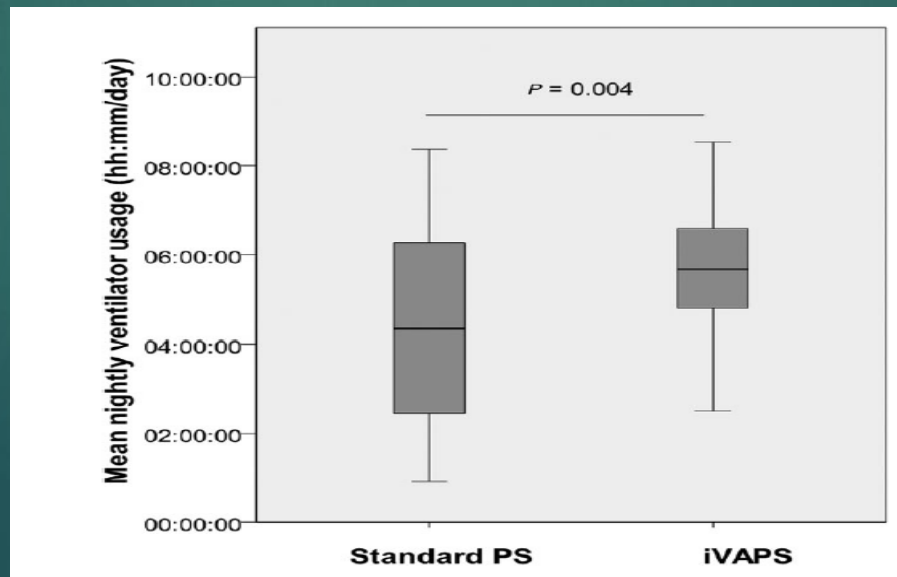
Mean Ventilator Usage Time (hh:mm/day)

Intelligent vent

5:38 (01:46) hrs

Standard PSV

4:38 (02:18) hrs $p=0.002^*$



Kelly et al
Respirology
2014

Guidelines and standard of care

GUIDELINE FOR RESPIRATORY MANAGEMENT OF CHILDREN WITH NEUROMUSCULAR WEAKNESS

J Hull, R Aniapravan, E Chan, M Chatwin, J Forton, J
Gallagher, N Gibson, J Gordon, I Hughes, R McCulloch,
R Ross Russell, A Simonds.



British Thoracic Society guideline for respiratory management of children with neuromuscular weakness

Jeremy Hull,¹ Roona Aniapravan,² Elaine Chan,³ Michelle Chatwin,⁴ Julian Forton,⁵
Jayne Gallagher,¹ Neil Gibson,⁶ Jill Gordon,⁷ Imelda Hughes,³ Renee McCulloch,⁸
Robert Ross Russell,² Anita Simonds⁴

BTS guidelines

Thorax 2012;67:i1-i40

Quality Standards 2014

Each Quality Standard includes the following:

- A quality statement which describes a key marker of high-quality, cost-effective care for this condition.
- Quality measures which aim to improve the structure, process and outcomes of health care.

Summary
Quality Statements for the respiratory management of children with neuromuscular weakness
Respiratory assessment of children with NMW to take place at each planned medical clinic visit.
Children with NMW who have an unplanned hospital admission for a respiratory illness to be assessed by a specialist respiratory physiotherapist and where clinically appropriate, the child and their carers are shown how to carry out effective airway clearance, and provided with the necessary equipment for this purpose.
Children with NMW who have an ineffective cough or a history of recurrent respiratory exacerbations to have an individualised written management plan to deal with respiratory exacerbations.
Children with NMW to have access to inpatient services which include specialist respiratory physiotherapy and expertise in the use of non-invasive ventilation.
Assessment for sleep-disordered breathing to take place no less than annually for all children with NMW who have symptoms of obstructive sleep apnoea or hypoventilation, children with clinically apparent diaphragmatic weakness and children with rigid spine syndromes.

www.brit-thoracic.org.uk/document-library/clinical-information/children-with-nmw/quality-standards-for-the-respiratory-management-of-children-with-nmw/

Thank you Any questions?



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