Is mechanical insufflation exsufflation (M-IE) useful in children with neuromuscular disease?

Cross Canada Rounds – ProCon debate January 2017
Dr K Keown Respiratory Fellow
BC Children's Hospital

Structure of presentation

- Clinical problem
- Cough physiology
- How M-IE works
- Evaluation of evidence
  - Physiology of M-IE mechanism
  - Use in acute illness
  - Long term use
- Are there alternatives??
- Summary

Introduction: The clinical problem

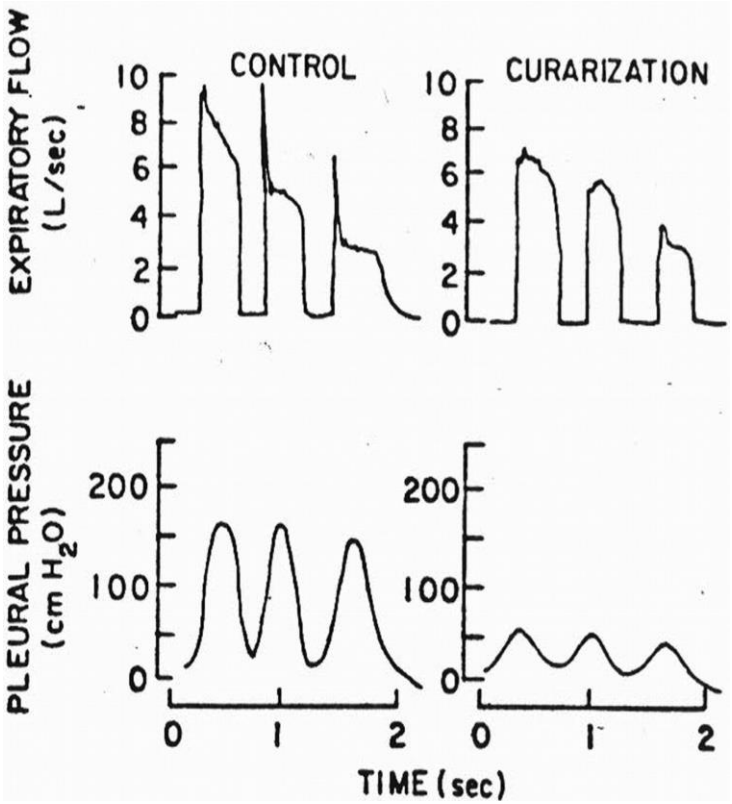
- Respiratory complications are primary cause of morbidity and mortality in NMD
- Progressive weakness
- Weakness causes
  - Chronic hypoventilation
  - Reduced cough effectiveness

Cough in neuro-muscular weakness

Impairment at one or more phase

Result = retention of pulmonary secretions

Impaired secretion clearance compounds issue

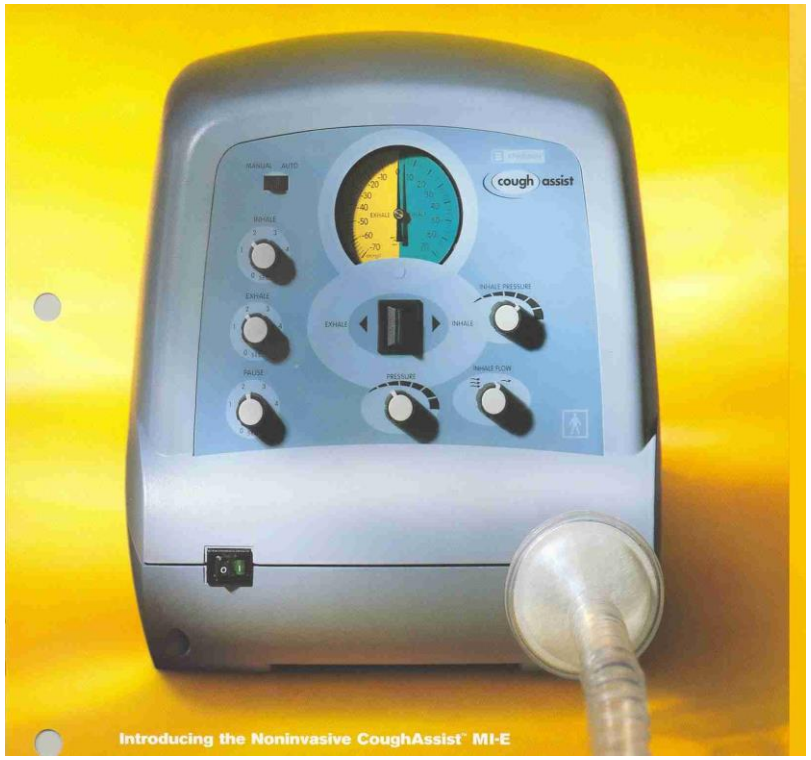


Global Physiology and Pathophysiology of Cough : ACCP Evidence-Based Clinical Practice Guidelines

Chest. 2006;129(1_suppl):48S-53S. doi:10.1378/chest.129.1_suppl.48S

M-IE/Cough assist machine/'Coughalator'

- 1952 - used in poliomyelitis
- Not used for 40 years
- Early 90s - regained popularity
- Delivers pre-set positive pressure during inspiration (insufflation), then abrupt change to negative pressure
- Rapid exsufflation causes increased expiratory flow and secretion clearance



Evidence

Evaluation of evidence for M-IE

1. Physiological mechanism of action: safety/harm
2. Usefulness in acute illness
3. Long term effects

Physiological effects of M-IE

Physiological Effects of Exsufflation with Negative Pressure (E.W.N.P.)
Beck, Scarrone. 1953

- Studied in respect to cardiovascular function, diaphragmatic motion, and intragastric pressure.
- Significant changes in arterial blood pressure during exsufflation
- Marked changes in the electrical axis of the heart

Insufflation – physiological effects

- **High intra-thoracic pressures**
  - abdominal distention, GOR, cardiovascular effects, pneumothorax (Homnick 2007)
  - Two cases of pneumothorax described in adult patients following use of MI-E (Suri 2008)

- **Barotrauma / volutrauma**
  - High TV implicated in ventilator-induced lung injury (Albuali 2007)
  - TV not measured during mechanical insufflation
  - Increased chest wall compliance in NMD = greater risk high inspiratory pressures

Repeated I/E - Physiological effects

- **Atelectatrauma**
  - Ventilator-induced lung injury associated with repeated alveolar collapse and re-expansion (*Saharan 2010*)
  - Lung-protective ventilation strategies : limiting TVs and preventing derecruitment by loss of PEEP or wide swings in pressure (*Saharan 2010*)
- Mechanism of MI-E contradicts these established lung-protective strategies

Forced deflation – physiological effects

- **Airway collapse** – Motoyama, 1986 + Hammer and Newth, 1996
  - demonstrated with flow volume loops that infant airways more collapsible with technique

- **Hypocapnia** - Infant lung function testing*
  - Repeated manoeuvres may result in hypocapnia, affecting vascular and broncho-motor tone
  - High positive pressures may impede venous return to the right heart
  - Invasive nature of technique precludes its use in routine setting

  **Respiratory Mechanics in Infants: Physiologic Evaluation in Health and Disease – Official statement ATS/ERS, June 1992. Am Rev Respir,1993*

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Respiration

ORIGINAL RESEARCH ARTICLE

Laryngeal Response Patterns to Mechanical Insufflation-Exsufflation in Healthy Subjects

ABSTRACT

Andersen T, Sandnes A, Hilland M, Halvorsen T, Fondenes O, Heimdal J-H,

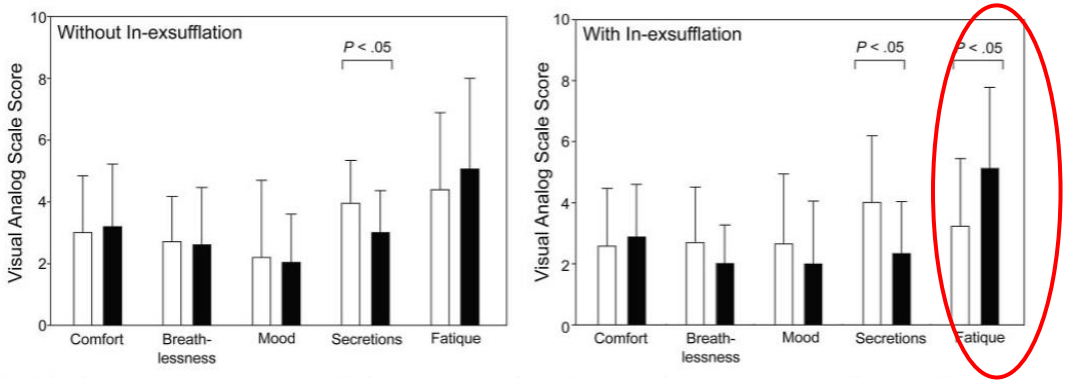
20 volunteers – video recorded flexible transnasal fiber-optic laryngoscopy while performing MI-E

- **Erratic laryngeal movements**
- Greater narrowing of TVFs and hypopharyngeal constriction with higher negative pressures

- *Andersen T et al. Laryngeal response patterns to mechanical insufflation exsufflation in healthy subjects. Am J Phys Med Rehabil 2013*

Evidence: M-IE in acute illness

1. **Chatwin 2009.** MI-E reduces treatment time compared with conventional physiotherapy (30min vs 47, p=0.03)
   - Crossover, 8 patients NMW using NIV



Chatwin M, Simonds AK. The addition of mechanical insufflation/exsufflation shortens airway-clearance sessions in neuromuscular patients with chest infection. Respir Care 2009;54:1473e9.

2. **Vianello 2005.** Treatment failure (need for tracheostomy or intubation) lower in the group treated with MI-E vs standard physio (2/11 vs 10/16, p<0.05)
   - Major study design flaws (small study numbers, historical controls, different group numbers, no matching etc etc)
   - No significant difference in other outcomes – duration of stay, NIV, duration of mechanical ventilation

Vianello A, Corrado A, Arcaro G, Gallan F, Ori C, Minuzzo M, Bevilacqua M: Mechanical insufflation–exsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections. Am J Phys Med Rehabil 2005;84:83–88.

Evidence: M-IE in acute illness

3. **Sivasothy 2001.** M-IE improves PCF

- prospective study, 29 subjects (COPD and NMD)
- PCF significantly elevated (greater than M-IE) with MAC

	Normal subjects (n=9)	*COPD (n=8)*	*Neuromuscular weakness*	
			Without scoliosis (n=8)	*With scoliosis (n=4)*
Baseline				
PCEF (l/min)	668 (310–700)	370 (267–483)	104 (43–188)	288 (175–367)
CEV (l)	2.4 (1.31–4.91)	1.02 (0.4–2.51)	0.5 (0.3–0.8)	0.9 (0.50–1.1)
PVT (ms)	35 (30–45)	32 (25–40)	80 (40–220)	44 (40–50)
Manually assisted cough				
PCEF (l/min)	624 (326–700)	226 (120–315)*	185 (93–355)*	193 (185–287)
CEV (l)	2.91 (1.31–5.31)	0.8 (0.20–1.51)	0.7 (0.31–1.07)	0.5 (0.41–1.01)
PVT (ms)	50 (40–85)**	45 (30–60)*	118 (35–360)*	50 (35–55)
Mechanical insufflation				
PCEF (l/min)	676 (494–695)	288 (218–370)	156 (61–247)	231 (148–597)
CEV (l)	2.2 (0.8–5.91)	0.45 (0.2–0.91)*	0.6 (0.3–1.61)	0.7 (0.3–1.3)
PVT (ms)	35 (30–40)	33 (30–40)	85 (20–420)	45 (30–60)
In combination				
PCEF (l/min)	624 (288–695)	245 (218–370)*	248 (110–343)*	362 (218–440)
CEV (l)	2.2 (0.7–5.41)	0.8 (0.3–1.00)	0.6 (0.40–2.19)	0.6 (0.4–1.01)
PVT (ms)	55 (40–100)	40 (35–50)	75 (20–420)	50 (45–120)

Data are expressed as median (range).
*p<0.01.

Sivasothy P, Brown L, Smith I, Shneerson J. Effect of manually assisted cough and mechanical insufflation on cough flow of normal subjects, patients with chronic obstructive pulmonary disease (COPD), and patients with respiratory muscle weakness. Thorax. 2001;56(6):438-444. doi:10.1136/thorax.56.6.438.

4. **Fauroux 2008.** Significant increase in CPF at 40 cm H2O

Physiological measurements of 17 children with NMD pre and post MIE

The MI-E had no significant effect on VC or minute ventilation after each series of six applications

		After MI-E			
Variables	Baseline	15 cm H_2O	30 cm H_2O	40 cm H_2O	p Value†
Breathing pattern					
Vt, L	0.27 ± 0.11	0.27 ± 0.13	0.27 ± 0.16	0.28 ± 0.15	NS
fr, breaths/min	26 ± 11	27 ± 12	26 ± 11	26 ± 10	NS
Ve, L/min	6.3 ± 1.9	5.9 ± 1.5	6.2 ± 2.1	6.3 ± 1.7	NS

Fauroux B, Guillemot N, Aubertin G, et al. Physiologic benefits of mechanical insufflationeexsufflation in children with neuromuscular diseases. Chest 2008;133:161e8.

Evidence: regular long term use of M-IE

1. Reducing frequency of respiratory illnesses

    - No RCTs showing that MIE is more effective than other forms of physiotherapy in reducing frequency of respiratory illness

2. Improvement in quality of life or survival

    - No long term trials showing that MIE improves survival or quality of life in adults or children with NMD

Reported long term outcomes with regular M-IE

1. Phillips 2015. Fewer admissions and hospitalised days for respiratory infections (p=0.11)

- Series of 6 patients. Retrospective. Comparing pre and post introduction of M-IE status
- Excluding #1 No difference in admission number (14 vs 13)
- No difference in antibiotic use (39 vs 41)

Phillips R D, Edwards E, McNamara D, Reed P (2014) Does use of the Cough Assist Machine reduce respiratory morbidity for children with neuromuscular disease? New Zealand Journal of Physiotherapy 42(2): 126-132.

2. Stehling 2014. M-IE use improves vital capacity (non-sig)

Retrospective data analysis 21 patients (16.1 ± 6.5 years) with NMD using nocturnal NIV.
Unclear if benefit from Insufflation vs exsufflation. Unclear when NIV introduced

	−2 years ($n = 16$)	−1 year ($n = 14$)	Start M-I/E ($n = 21$)	+1 year ($n = 21$)	+2 years ($n = 6$)
VC (L)	0.88 ± 0.45 (0.22–1.62)	0.71 ± 0.38 (0.25–1.49)	0.50 ± 0.24 (0.25–1.12)	0.64 ± 0.28 (0.24–1.40)	0.65 ± 0.29 (0.28–1.15)
VC (% predicted)	29.3 ± 18.8 (4–86)	21.3 ± 12.1 (5–45)	16.7 ± 10.9 (5–54)	22.9 ± 16.8 (7–73)	20.0 ± 11.7 (7–39)
Time (months)	28.4 ± 5.5	13.4 ± 3.1	0	9.4 ± 2.8	25.7 ± 7.4

VC: vital capacity; M-I/E: mechanical insufflator/exsufflator.
[a]Results are presented as mean ± SD (range).

Stehling et al. Mechanical insufflation/exsufflation improves vital capacity in neuromuscular disorders. December 3, 2014

Evaluation of evidence for M-IE

1. Physiology of mechanism ?safety ?potential harm

2. Acute context

3. Long term effects: lung function/quality of life/survival

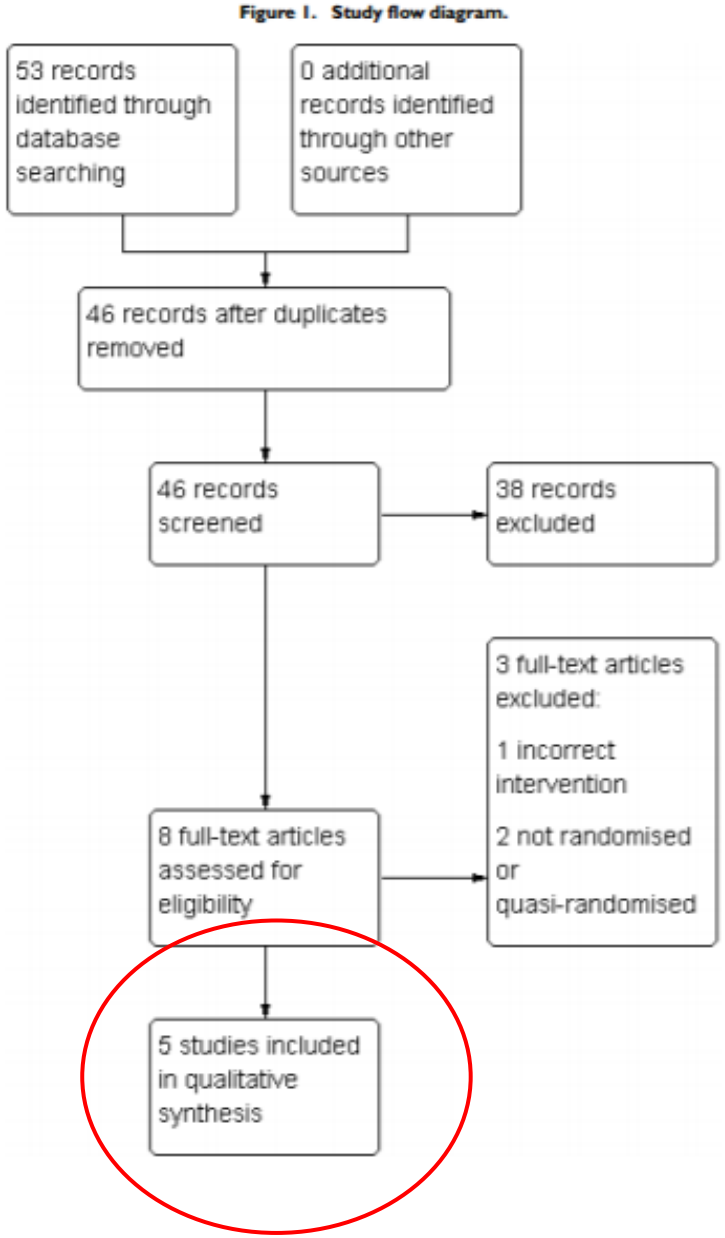
Mechanical insufflation-exsufflation for people with neuromuscular disorders (Review)

Morrow B, Zampoli M, van Aswegen H, Argent A

THE COCHRANE COLLABORATION®

Cochrane review 2013

- To determine the efficacy and safety of MI-E in people with NMDs
- All studies were short-term (<2days)
- None reporting mortality, morbidity, quality of life, serious adverse events or any of the other prespecified outcome



Morrow B, Zampoli M, van Aswegen H, Argent A. Mechanical insufflation-exsufflation for people with neuromuscular disorders. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD010044. DOI: 10.1002/14651858.CD010044.pub2.

Cochrane review - Authors' conclusions

1. *Existing studies do not clearly show that MI-E improves cough expiratory flow more than other cough augmentation techniques.*
2. *Important short and long-term outcomes not addressed*
3. ***There is insufficient evidence for or against the use of MIE in NMD***
4. *RCTs are needed to test the safety and efficacy of MI-E.*

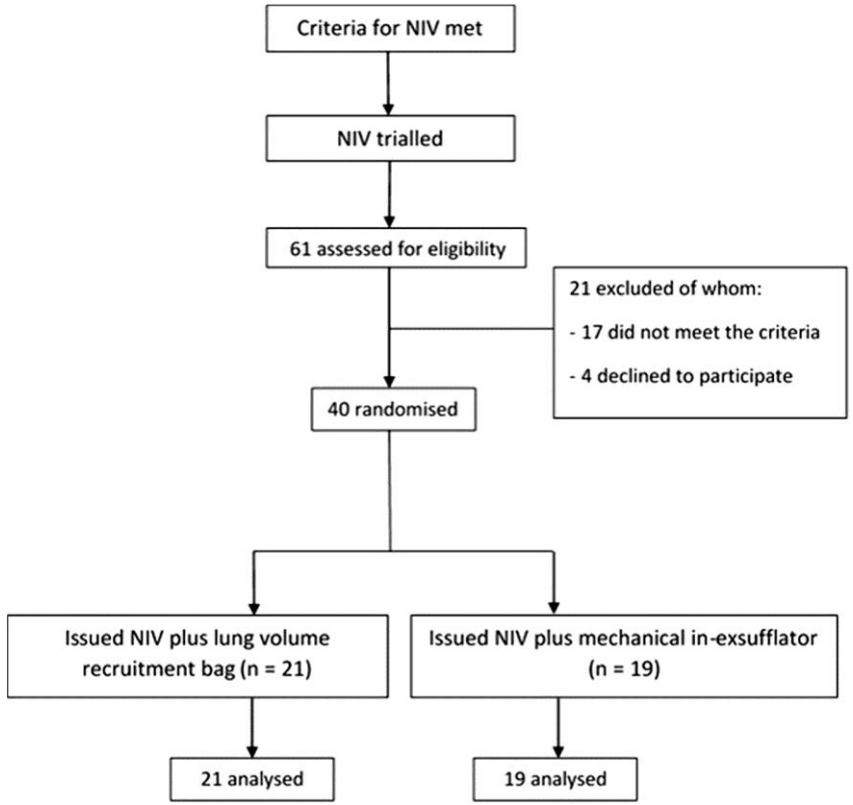
Are there evidence based alternatives to M-IE?

ORIGINAL ARTICLE

A preliminary randomized trial of the mechanical insufflator-exsufflator versus breath-stacking technique in patients with amyotrophic lateral sclerosis

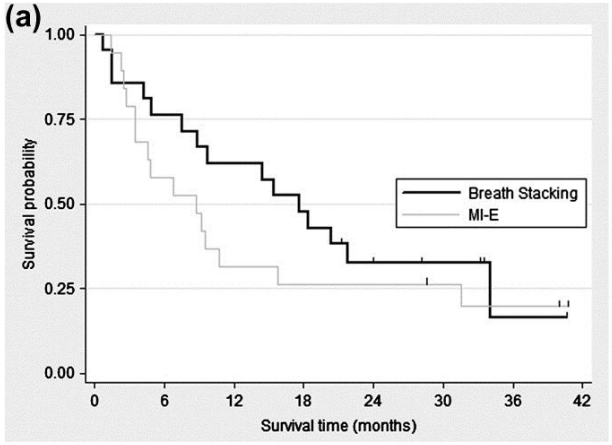
Muhammad K. Rafiq, Michael Bradburn, Alison R. Proctor, Catherine G. Billings, Stephen Bianchi, Christopher J. McDermott & ...show all

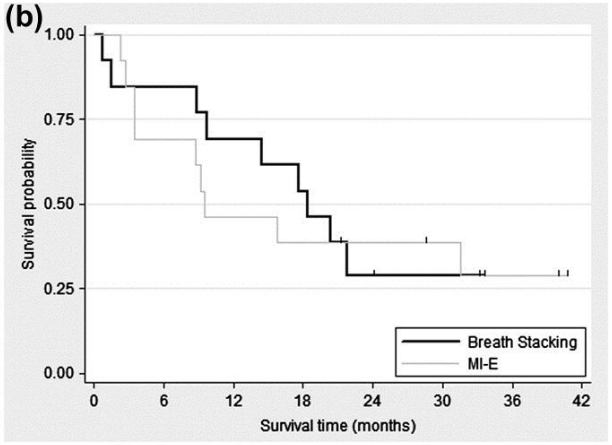
Pages 448-455 | Received 20 Feb 2015, Accepted 12 Apr 2015, Published online: 03 Jul 2015

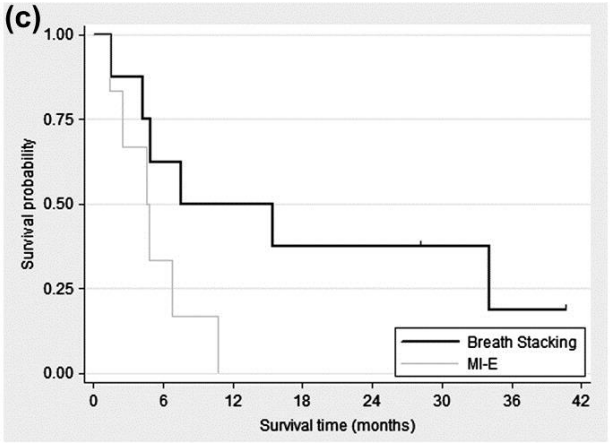


- Forty eligible ALS patients
- Randomized to (twice daily)
  1. breath-stacking using a lung volume recruitment bag (*n* = 21) or
  2. MI-E (*n* = 19)
- followed up at three-monthly intervals for at least 12 months or until death

Rafiq 2015. Improved survival Breathstacking vs M-IE







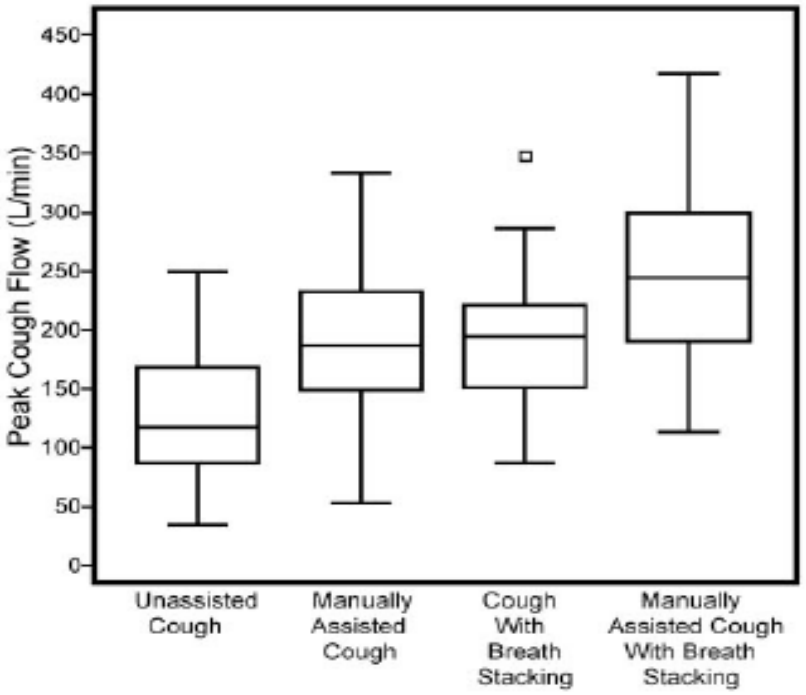
Kaplan-Meier survival curves.
(a) Overall study.
(b) Patients with moderately impaired bulbar function.
(c) Patients with severely impaired bulbar function.

Survival days severe bulbar impairment: 229 vs 138 (p=0.07)
Improved QOL (SQUALI >75% 280d vs 205d)

Muhammad K. Rafiq, Michael Bradburn, Alison R. Proctor, Catherine G. Billings, Stephen Bianchi, Christopher J. McDermott & Pamela J. Shaw (2015) A preliminary randomized trial of the mechanical insufflator-exsufflator versus breath-stacking technique in patients with amyotrophic lateral sclerosis, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 16:7-8, 448-455, DOI: 10.3109/21678421.2015.1051992

Breathstacking – does the evidence stack up?

- **Toussaint 2009.** Breath stacking, MAC and breathstacking+MAC all significantly improved Peak cough flow
  - Cough augmentation techniques in 179 clinically stable patients with NMD
  - breath-stacking plus MAC greatest effect PCF ($P < .001$)



Toussaint, Michel, et al. "Limits of effective cough-augmentation techniques in patients with neuromuscular disease." *Respiratory Care*, Mar. 2009, p. 359

Breathstacking – does the evidence stack up?

- **Improves atelectasis and maintains compliance** ($p = 0.03$)

  Noah Lechtzin, David Shade, Lora Clawson, Charles M. Wiener, Supramaximal Inflation Improves Lung Compliance in Subjects With Amyotrophic Lateral Sclerosis, Chest, Volume 129, Issue 5, May 2006, Pages 1322-1329, ISSN 0012-3692, http://dx.doi.org/10.1378/chest.129.5.1322

- **Increased Vt + minute ventilation** ($P < 0.05$)

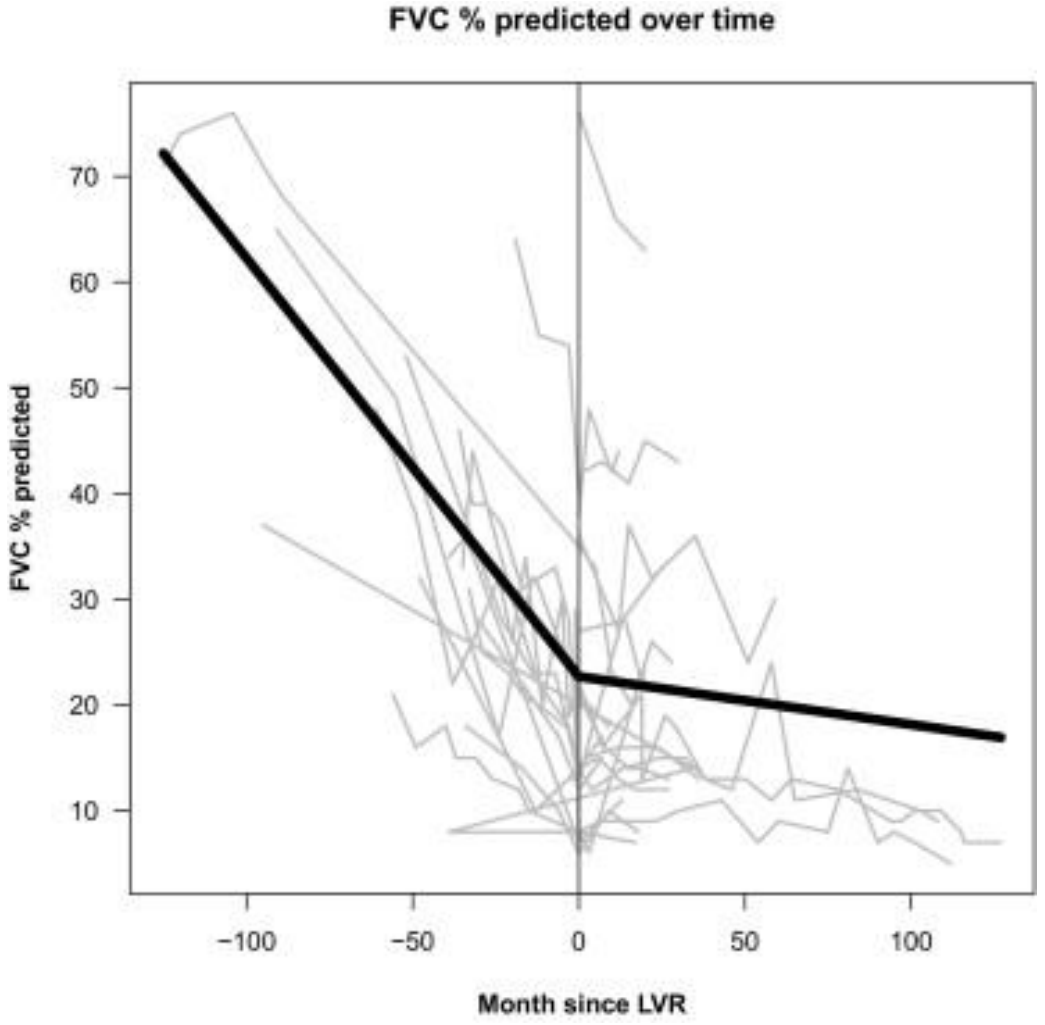
  Breath Stacking in Children With Neuromuscular Disorders. Jenkins Pediatric Pulmonology 49:544–553 (2014)

- **Significant increase in peak cough flows** ($p < 0.05$) ($P < 0.001$)

  Maximum Insufflation Capacity Seong-Woong Kang; and John R. Bach, CHEST 2000; 118:61– 65*

  Bach JR, Bianchi C, Vidigal-Lopes M, Turi S, Felisari G: Lung inflation by glossopharyngeal breathing and "air stacking" in Duchenne muscular dystrophy. Am J Phys Med Rehabil 2007;86:295–300

Lung Volume Recruitment Slows Pulmonary Function Decline in DMD



- Retrospective cohort study of FVC trajectory in adults with DMD pre & post LVR
- 22pts, FVC, 21.8±16.9 % pred
- 86% using NIV

<u>FVC Rate of decline:</u>

Pre-LVR = **- 4.7 %** predicted/yr

Post LVR = **- 0.5 %** predicted/yr

($p < 0.001$)

Douglas A. McKim, Sherri L. Katz, Nicholas Barrowman, Andy Ni, Carole LeBlanc, Lung Volume Recruitment Slows Pulmonary Function Decline in Duchenne Muscular Dystrophy, Archives of Physical Medicine and Rehabilitation, Volume 93, Issue 7, July 2012, Pages 1117-1122, ISSN 0003-9993, http://dx.doi.org/10.1016/j.apmr.2012.02.024.

Devices for LVR/Breathstacking

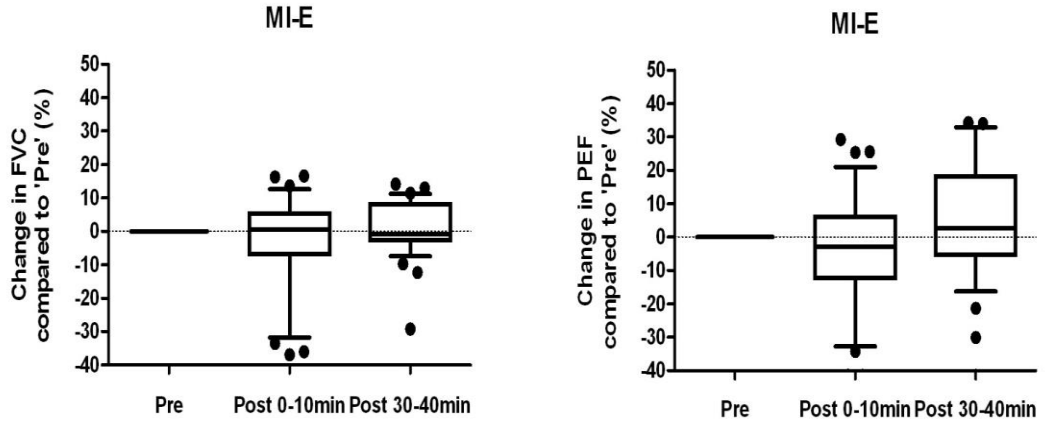
Self-inflating AMBU-bag with one-way valve	**Inexsufflator (M-IE)**
Direct feedback given to provider → comfortable volume delivered May need abdominal thrust to generate cough	Mechanically provides positive pressure breaths (at unknown volumes) followed by rapid negative pressure which generates a cough
Readily available	Not covered by all provincial insurance plans (support in Ont., Que., BC)
Inexpensive ($30-70)	Expensive (~ $4500-6000)
Portable	Cumbersome, less portable

Seear et al (not yet published)

- Crossover of 3 physio techniques in 40 stable NMD
  - intra-pulmonary percussive ventilation (IPV)
  - mechanical insufflation-exsufflation (MI-E)
  - BiPAP-assisted maximal inspiration (BAMI)

- **M-IE produced no significant improvements in FVC or PEF and some children got worse**

- M-IE was treatment least preferred technique



Type of treatment	Which treatment did you like best?	Which treatment worked best?
BAMI	16 (42.1%)	7 (18.4%)
IPV	10 (26.3%)	15 (39.5%)
MI-E	9 (23.7%)	9 (23.7%)
None	3 (7.9%)	7 (18.4%)

Summary

- >60 years old – no long term studies assessing safety or long term effects
- Non-physiological mechanism of action and potential lung damage – no studies directly assessing physiological effects of M-IE (in adults or children)
- No convincing evidence of superiority over other cough augmentation techniques
- **Cheaper, evidence based, effective treatments have been demonstrated to reduce morbidity, slow decline in FVC and improve outcomes in NMD**


EAST
WEST