INVOLUNTARY BREATH STACKING IN CHILDREN WITH NEUROMUSCULAR DISORDERS

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ABSTRACT

Rationale: Respiratory insufficiency is one of the most common causes of death in patients with neuromuscular disorders (NMD). Due to weakness and cognitive level, children with NMD often cannot perform required maneuvers to recruit lung volume. Data from cooperative adults suggest that breath stacking with a mask and one-way valve can obtain significantly higher lung volumes.

Methods: To study the effectiveness of a breath stacking mask in patients with NMD, we studied 23 children (17 male, 6 female) over 3 years, mean age 11 y (range 3-19 y) and body mass 43.8 kg (range 12-80 kg). Fifteen were cognitively aware and able to communicate verbally. For involuntary breath stacking a one-way valve and pneumotach were attached to a cushioned mask that was held to the face, covering around nose and mouth with a tight seal. Flow signals were acquired to computer (AcqKnowledge BIOPAC Inc.). Tidal volumes (Vt) and minute ventilation (VE) were calculated from the recording for 30 s before and 30 s after 15 s of valve closure during which expiration was prevented. Oxygen saturation (SaO_2) was measured.

Results: The mean Vt before valve closure was 277 ml (range 29-598 ml). The mean increase in volume by stacking was 599 ± 558 ml (range -140 to 2,916 ml). When normalized to body mass, mean increase above normal end inspiratory level was 14.7 ± 14.7 ml/kg (range -2.7 to 52.2 ml/kg). The mean number of stacked breaths was 4.5 ± 3.6 (range 0-17). VE increased on average by 18% after stacking ($p<0.05$, paired t-test). There was no change in SaO_2 after stacking. Four of the 23 children did not stack.

Conclusions: Our findings show that breath stacking with a mask and a one-way valve can achieve breath volumes approximately 3x Vt. The mask was tolerated well, and cooperation of the child was not required.

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LIST OF ABBREVIATIONS

ACBT – active cycle of breathing technique

AD – autogenic drainage

CNS – central nervous system

CRS – clinical respiratory score

DMD – Duchenne muscular dystrophy

f – respiratory frequency (respiratory rate)

HFCWC – high frequency chest wall compression

IBS – involuntary breath stacking

IPV – intrapulmonary percussive ventilation

IS – incentive spirometry

LVR – lung volume recruitment

MIE – mechanical in-exsufflation

NMD – neuromuscular disorder

PEP – positive expiratory pressure

PD & P – postural drainage and pummeling

RR - respiratory rate

V – minute ventilation

Vt – tidal volume

INTRODUCTION

Respiratory insufficiency is one of the most common causes of death in patients with neuromuscular disorders (NMDs), (Gozal, 2000). Mallory summarized his clinical impressions and the related literature on pulmonary complications of neuromuscular disease as follows: breathing with less than normal chest expansion due to weakness leads to contractures at the costo-vertebral joints over time (Mallory, 2004). This leads to reduced compliance of the thorax as well as reduced compliance of the lungs due to areas of atelectasis. Consequently, the workload of the respiratory muscles will increase in many patients (Mallory, 2004). The maximum forced expiratory airflow will also decrease due to involvement of the abdominal muscles, and clearance of airway secretions by coughing will become ineffective, leading to retention of secretions and airway obstruction (Boitano, 2006). Without intervention, patients with NMD will become unable to take breaths deep enough to open areas of atelectasis which puts them at an increased risk for pneumonia (Tzeng & Bach, 2000a). Areas of atelectasis cause an imbalance between alveolar ventilation and pulmonary capillary blood flow. This can lead to reduced oxygenation of the blood (Schwartzstein & Parker, 2006). Ultimately, the elimination of carbon dioxide will also become impaired when patients with NMD develop hypoventilation due to progressive weakness and low tidal volume breathing (Panitch, 2009). These mechanisms result in a progressive loss of respiratory function and ultimately to a need for mechanical ventilation.

In short, the principal problems that need to be addressed in children with NMD are decreased compliance of the lungs and thorax, subsegmental atelectasis of the lungs, and decreased peak cough flow. Interventions aimed at reducing the rate of progression

or reversing these untoward trends will lead to improved health and well being of the patients. The project presented herein assesses the short term effects of one such intervention, i.e., involuntary breath stacking (IBS).

Respiratory Care of Children with NMD

In the long-term care of patients with NMDs, the efforts of physiotherapists, respiratory therapists and physicians aim at the early recognition of decreasing respiratory muscle strength and on strategies for timely intervention and support. A consensus statement of the American Thoracic Society and a recent Special Report on the respiratory management of patients with Duchenne muscular dystrophy recommend that the respiratory assessment of patients with Duchenne muscular dystrophy should include spirometric measurements of forced vital capacity, forced expiratory volume in one second, maximum mid-expiratory flows, maximum static inspiratory and expiratory pressures, and peak cough flow (Finder et al., 2004; Birnkrant et al., 2010). These guidelines also recommend treatment techniques for airway clearance that include air stacking.

In adults, peak cough flow below 160 l/min or a maximum static expiratory pressure below 60 cmH_2O indicate that airway clearance is likely ineffective and that intervention to recruit lung volume is needed to assist with cough by increasing the volume of expelled air (Tzeng & Bach, 2000b). However, many children with neuromuscular diseases will be unable to perform the breathing maneuvers that are required for spirometry because they lack understanding and may be unwilling to cooperate or are simply too weak. This often leaves only subjective clinical impressions to determine the declining status of these children. Clinical experience also shows that

many children are unable to participate in breathing techniques that are used for lung volume recruitment (LVR) and to reach sufficient peak cough flow levels for efficient cough. Therefore it is important to establish effective techniques to recruit lung volume before the cough maneuver. From a raised volume there is an increase in lung elastic recoil which helps to increase peak cough expiratory flow.

Techniques for Airway Clearance and Lung Volume Recruitment

Various techniques, with and without assistive devices, can be applied to improve the respiratory status of pediatric patients with NMD. For clearance of secretions from the airways, postural drainage and percussion (PD & P) of the chest is a widely used method (McIlwaine, 2007; Reisman et al., 1988). Alternatives to the time-honored but labor-intensive postural drainage and percussion may be equally efficient (Langenderfer, 1998). Percussion at high frequencies is possible with oscillating pressure changes in an inflatable vest that is worn around chest and abdomen. This technique of high frequency chest wall compression (HFCWC) is popular for the treatment of patients with cystic fibrosis who are not limited by weakness and can take deep breaths. In patients with NMD, however, the tendency of high frequency chest wall compression to decrease end-expiratory lung volume (Dosman & Jones, 2005) and the common presence of scoliosis/rib cage distortion in affected patients make it difficult for the vest to fit which limits a wider application of this method. Intrapulmonary percussive ventilation (IPV) is another technique in which rapidly changing airway pressures are used to aid in the removal of secretions. This has been as effective as PD & P or HFCWC in patients with cystic fibrosis (Varekojis et al., 2003) and may also be of use in tracheostomized patients with Duchenne muscular dystrophy (Toussaint, De Win, Steens, & Soudon, 2004).

Autogenic drainage (AD) and active cycle of breathing (ACBT) are examples of breathing techniques that can be taught to patients with sufficient understanding and willingness, as well as physical ability, to cooperate (Lapin, 2002; McIlwaine, 2007). However, respiratory muscle weakness will limit the effectiveness of these breathing techniques. Breathing out against a resistance to keep airway pressure positive throughout expiration is often used in the chest physiotherapy of patients with cystic fibrosis. It is thought that the constant elevated airway pressure while breathing out through a positive expiratory pressure (PEP) mask will allow air to reach behind areas of obstruction through collateral channels (Mahlmeister, Fink, Hoffman, & Fifer, 1991). Although PEP therapy is widely used in patients with Cystic Fibrosis, a recent Cochrane review of 25 studies involving 507 participants found no evidence that this technique performed better than other methods to preserve or improve forced expiratory volume in one second in the short or long term (Elkins, Jones, & Schans, 2004).

Mechanical in-exsufflation (MIE) can be used to support limited cough function. Insufflation of air followed by rapid mechanical exsufflation can improve airway clearance in intubated patients with ineffective cough (Bach et al., 1993). The maneuver can also be performed non-invasively via mouthpiece in cooperative patients who are not intubated. High pressures, i.e. exceeding 40 cmH_2O, may be required to assist cough, in patients with increased airway resistance, e.g. due to scoliosis (Sancho et al., 2004). MIE has been used in the pulmonary management of pediatric patients with neuromuscular disorders, by either a cushioned face-mask or mouthpiece (Miske, Hickey, Kolb, Weiner, & Panitch, 2004). The technique can either assist with clearing secretions by simulating a

cough, or serve as an insufflation of the lung above a reduced vital capacity, to prevent atelectasis and maintain chest wall compliance (Homnick, 2007).

Loss of lung volume is common under conditions of shallow breathing due to discomfort, weakness and paralysis. Strategies to recover and maintain lung volume are well described in studies of patients undergoing anesthesia or mechanical ventilation support in critical care. Manual hyperinflation is widely used by physiotherapists (McCarren & Chow, 1996) to increase lung compliance and improve oxygenation in stable intubated patients (Patman, Jenkins, & Stiller, 2000). In adults with healthy lungs undergoing anesthesia, computer tomography showed that atelectasis disappeared after a "vital capacity" maneuver of inflating the lungs to a pressure of 40 cmH_2O for approximately 8 seconds (Rothen et al., 1999). Table 1 summarizes the techniques that are available for attempting to improve respiratory status.

Table 1. Comparison of physiotherapy techniques

Technique	Advantages	Disadvantages
PD & P	No patient cooperation required	Used for mucous mobilization, not aimed at LVR Labor and time intensive for caregiver
HFCWC	No patient cooperation required	Used for mucous mobilization, not aimed at LVR Requires equipment and electricity Expensive, limited portability, decreases end-expiratory lung volume
IPV	Can be used in intubated patients	Require patient cooperation Requires equipment and electricity
AD, ACBT	No equipment needed	Requires patient cooperation Affected by muscle weakness
PEP, IS	Portable	Requires patient cooperation Affected by muscle weakness
MIE	Recruits lung volume and assists with cough Can be used with a face mask in uncooperative patients	Requires equipment and electricity Expensive and lacks portability Mouthpiece is difficult with muscle weakness Requires skilled caregivers

PD & P = postural drainage and percussion, HFCWC = high frequency chest wall compression, IPV = intrapulmonary percussive ventilation, AD = autogenic drainage, ACBT = active cycle of breathing technique, PEP = positive expiratory pressure, IS = incentive spirometry, MIE = mechanical in-/exsufflation

Incentive spirometry (IS) is commonly used in patients who can actively breathe in but are at risk for atelectasis from shallow breathing. However, a systematic review of its application to prevent postoperative pulmonary complications did not find evidence of a positive short-term effect (Overend et al., 2001). Conventional IS encourages the

patient to achieve the deepest possible breath in a single attempt (Hilling et al., 1991), and does not block expiration.

In a study of 26 adult patients who could not achieve or sustain maximum deep inspiration due to weakness or pain after surgery, trauma or critical illness, breath stacking with an incentive spirometer and a one-way valve to prevent exhalation after each inspiratory effort added 15 to 20% of volume above spontaneous inspiratory capacity (Baker, Lamb, & Marini, 1990). More importantly, the duration over which higher lung volumes were sustained lengthened significantly from less than 5 seconds with conventional IS to approximately 20 seconds with volume stacking IS.

Maximum insufflation capacity refers to the maximum volume of air that can be insufflated into the lungs and that can be held with a closed glottis. The strength of the oropharyngeal and laryngeal muscles affects the maximum insufflation capacity. A study of 43 adults with NMDs whose vital capacity had decreased below 2 liters found that the regular use of 10 to 15 maximal lung insufflations using volume stacking three times a day significantly increased maximum insufflation capacity and assisted peak cough flow. The peak cough flow was assisted by both a deep insufflation from a ventilator and an abdominal thrust at the moment of glottic opening (Kang & Bach, 2000). These patients were breathing in with assistance from a ventilator and had learned to prevent expiration by closing their glottis before their next inspiratory effort. Those who failed to increase maximum insufflation capacity over time were mostly patients with Amyotrophic Lateral Sclerosis and bulbar paralysis who had difficulty to control their glottis. The patients in that study were using a mouth piece and glottic closure was therefore necessary to maintain insufflation.

The attachment of a one-way valve at the connection of a facemask to a self-inflating bag allows manual hyperinflation by another person, synchronized with a patient's inspiratory effort, and the stacking of volumes by valve closure during exhalation. This technique can be used in non-intubated patients with severe weakness to increase lung volume with two to three compressions of the bag before assisted coughing. The one-way valve substitutes for the function of the glottis and can therefore be also used in patients with bulbar muscle weakness. This breath stacking system is now being used more widely to recruit lung volume (Armstrong, 2009; Boitano, 2006).

Children with NMDs pose a particular challenge to the physiotherapist because they require interventions that do not depend on their cooperation to recruit lung volume. One method that has promise but is understudied is that of involuntary breath stacking (IBS).

IBS was tested in 30 healthy adults and in 20 ambulatory adult patients with neuromuscular, restrictive and obstructive respiratory disorders (Marini, Rodriguez, & Lamb, 1986). The IBS procedure utilized a mouthpiece, a one-way valve and a calibrated turbine respirometer to measure the inspiratory and expiratory volumes. The final volume was usually reached after 10 to 12 efforts, i.e. after 20 to 30 seconds of blocked expiration. This volume was established at the balance point between the subject's inspiratory effort and the recoil of chest wall and lungs. The peak values of stacked vital capacity were significantly higher than conventional vital capacity. While IBS was used in that study to develop an alternative method for the estimation of vital capacity, the results also provide some guidance with regard to the target duration that could be employed for breath stacking as a lung volume recruitment tool in pediatric

patients. This study was performed in cooperative, ambulatory adult subjects who could use a mouthpiece.

A more recent study compared the inspiratory volume during breath stacking with a face-mask and a one-way valve to standard incentive spirometry in patients who had undergone abdominal surgery (Dias, Plácido, Ferreira, Guimarães, & Menezes, 2008). There was a significantly higher inspiratory volume during the breath stacking compared to the incentive spirometry, both in the pre-operative and in the post-operative periods. This is the only study to date using a face mask and a one-way valve for lung volume recruitment. Again, the subjects were cooperative adults. The use of a mask instead of a mouthpiece is preferable in pediatric patients because it does not require their cooperation and ability to close their lips tightly.

Putative Benefits of IBS

To understand the mechanisms by which breath stacking can be of benefit to patients with NMD one has to consider collateral ventilation and pulmonary interdependence as factors that determine the effectiveness of breath stacking techniques (Fink, 2002). Collateral ventilation refers to ventilation that bypasses obstructed airways through collateral channels, i.e. between alveoli (pores of Kohn), between bronchioles and alveoli (communications of Lambert) and between bronchioli (pathways of Martin), (Delaunois, 1989). Interdependence describes the effect of uneven distribution of pressures, volumes and shapes of neighboring lung regions when there is inhomogeneous ventilation. Interdependence can enhance collateral ventilation by increasing the pressure difference between a non-expanding region and the neighboring expanding lung.

Collateral ventilation does not play a significant role in healthy humans but can become important when airways are obstructed by disease (Delaunois, 1989). Early in life, collateral ventilation is minimal (Cetti, Moore, & Geddes, 2006; Terry, Menkes, & Traystman, 1987), and it is not clear when this mechanism becomes important during childhood to provide alternative pathways for airflow into obstructed areas of the lung. Besides age, the lung volume and the volume history of the lung, i.e. the characteristics of preceding breaths, are factors that affect the magnitude of collateral ventilation (Kikuchi, Hildebrandt, Sekizawa, Sasaki, & Takishima, 1992). Increasing the lung volume can decrease the resistance of airflow through collateral pathways (Menkes & Traystman, 1977). This is not of much importance in healthy young adults who also decrease the resistance of the regular pathways with increasing lung volume while the resistance through collateral pathways remains relatively much higher (Terry, Traystman, & Newball, 1978). However, if the resistance to airflow through regular pathways is greatly increased, e.g. if airways are plugged by mucus and regions of atelectasis develop, collateral ventilation may provide the needed air to open the obstructed areas.

Patients with weakness or pain often breathe shallowly and are therefore at risk for insufficient clearance of secretions from their airways, closure of lung units and poor uptake of oxygen. Strategies to recover lung volume by deep inspiration require understanding and participation by the patient that cannot be expected from many children with neuromuscular conditions. Involuntary breath stacking with a one-way valve blocking expiration through a facemask is currently used in the treatment of patients with neurological and NMDs at the Winnipeg Children's Hospital and several other pediatric centers in North America. However, there are no studies in children to

date that would prove the efficacy of IBS. If IBS can achieve a meaningful increase of lung volume in pediatric patients with NMDs, future studies can then clarify potential clinical benefits in the long term.

In patients who are otherwise prone to retain secretions or to develop atelectasis, effective lung volume recruitment can counteract these mechanisms and thereby increase oxygenation. Low oxygen level, documented by pulse oximetry, is a common reason for extended length of stay for children at the Children's Hospital. Ineffective airway clearance increases the risk for lower respiratory tract infection and can therefore lead to more frequent admissions to hospital.

Scientific evidence is needed to establish the efficacy of IBS and the potential role in the care path of children with muscle weakness, neurological disorders and other conditions that reduce lung inflation. This information is important to decide on best strategies for physiotherapy to recruit and preserve lung volume in patients with insufficient spontaneous lung expansion. The relatively simple and inexpensive equipment for IBS could then be offered with confidence to caregivers not only in the institutional setting but also for use in the community. Furthermore, the results from the proposed study may translate to technological modifications of stacking masks that could indicate to the user when target volumes and pressures are reached during treatment. The first step, however, is to show the efficacy of IBS, as well as to examine any short term consequence on respiratory status and parameters and oxygenation.

PURPOSE

The present study aimed to evaluate if involuntary breath stacking is efficacious in increasing breath volume in children with NMD. Further, this study was to determine the immediate effect of the IBS procedure on the respiratory status.

OBJECTIVES

- To determine the effect of IBS on breath volumes
- To determine the effect of IBS on respiration (frequency, tidal volume, and minute ventilation)
- To determine the effect of IBS on oxygen saturation
- To determine the effect of IBS on clinical respiratory status

HYPOTHESIS

Involuntary breath stacking in children with neuromuscular disorders will result in a significant increase in breath volume with no untoward effects on respiration, oxygen saturations and clinical respiratory status.

METHODOLOGY

Subjects

Children over one year of age with NMD who were admitted to Winnipeg Children's Hospital and required chest physiotherapy for airway clearance or who attended the Muscular Dystrophy Clinic at Rehabilitation Centre for Children or Children's Hospital Physiotherapy for out-patient follow-up were studied. The study ran from March, 2006 to October, 2009. The University of Manitoba Research Ethics Board approved this project. Written informed consent was obtained from caregivers, and assent was obtained if the patient was 16 years or older. Subjects with facial injuries, severe craniofacial deformations, nasogastric tubes, tracheotomies, need for oxygen or the inability to tolerate a facemask were excluded from the study.

Sample Size

Since the study population included patients with a range of disease severities and because there were no published data on the effect of IBS with the proposed technique in other populations, the calculation of an appropriate sample size posed a challenge. A normal tidal volume in healthy subjects is 5 to 7 ml/kg (Tobin, Chadha, & Jenouri, 1983) and because a spontaneous sigh reaches at least 3 times this volume (Perez-Padilla, West, & Kryger, 1983), we decided to define a successfully stacked volume to be 15 ml/kg, or two average tidal volumes stacked above tidal volume (Vt). After we had started to collect measurements in our population, Dias et al. reported on involuntary breath stacking with a facemask and one-way valve in adults (Dias et al., 2008). From their graphic presentation of data we calculated a maximum stacked volume in their patients of

24 (4.5) ml/kg [(mean (S.D.)]. With this information we could estimate that a sample of 10 patients reaching our goal with a variance of 10 ml/kg would provide statistically relevant findings with a power of 0.8 and type I error probability of <0.05.

Assuming a baseline oxygen saturation of 95 (3%) [(mean (S.D.)] in the study population and setting a goal of at least 2% increase to an average of 97% after volume stacking, this finding in 15 subjects would have a statistical power of 82.6% with a confidence level of 95% (one sample, one way test). Similarly, if one assumes 0 ± 3 points change in 15 subjects undergoing control intervention, a 3 point decrease on average in the sum of changes noted in the clinical assessment (see below) after stacking intervention would have a statistical power of 98.7% (82.6% for a 2 point decrease). The proposed sample size of 20 subjects should therefore have been sufficient to detect clinically significant changes after IBS.

Experimental Design

The study had a randomized cross over design. Inpatient subjects were randomized by blocked order randomization to two streams, either receiving the intervention or the sham in the morning and the reverse in the afternoon of the same day (sham IBS to IBS or ISB to sham IBS). Subjects were assessed at the Children's Hospital pre- and post-intervention, and post-physiotherapy treatment, using a clinical respiratory assessment tool and oximetry. The post-physiotherapy assessment data were not analyzed for this thesis. Patients seen as out-patients at the Rehabilitation Centre for Children or at the Children's Hospital Physiotherapy Department received both the stacking interventions and the sham but did not receive routine chest physiotherapy. They were randomized to have the stacking intervention or the sham first. Both stacking and sham

were done in one session for outpatients. For both inpatient and outpatients, the physiotherapist who undertook the clinical respiratory status assessment (Table 2) and provided the routine physiotherapy treatment left the room during the intervention/sham to avoid bias in her observations. Another physiotherapist performed the intervention (sham IBS or real IBS).

For inpatients, the experiments were done near the end of admission on the wards of the Winnipeg Children's Hospital to minimize the effect of spontaneous changes that could occur during the acute phase of illness.

Involuntary breath stacking

A cushioned facemask of appropriate size to cover nose and mouth was connected via a directional valve to a research pneumotachograph system (Hans Rudolph, Inc. Kansas City, MO, USA) that measured airflow and pressure (Figure 1). The pneumotach was accurate within ± 2 % over a with flow range of 0 – 160 liters/minute. The dead space in the mask was measured by filling the mask with water and putting the face of a research assistant inside to displace the volume water that would be pushed out when the mask was sealed on the face. The remaining water in the mask was measured using a graduated cylinder. The dead space was nominally 158 ml.

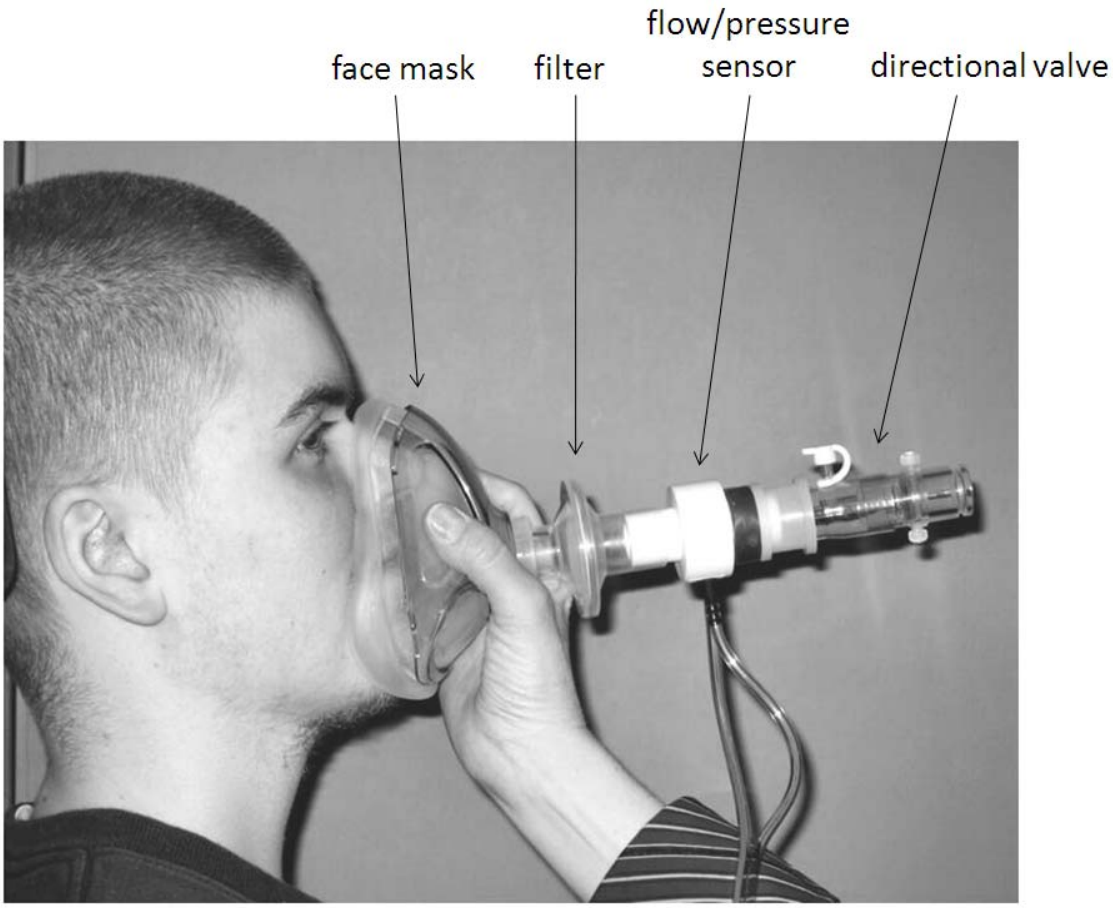

Figure 1 Experimental set up.
The assembly shows the cushioned face mask covering nose and mouth, the antibacterial filter, the pneumotachograph and the directional valve (the valve is off/open during the sham recordings).

Breath stacking was applied over 15 seconds. Length of time rather than number of breaths was chosen to minimize the effect of different breathing patterns between the participants based upon age or respiratory status. In healthy older children and adolescents this would include between 3 to 5 breaths in 15 seconds since the respiratory rate (*f)* at rest is between 12-15 breaths per minute in that age group. The average Vt is 5-7 ml/kg, and therefore one would expect a stacked volume during the 15 second occlusion of 15 to 20 ml/kg.

Three stacking interventions were applied to each subject, resulting in a total of six interventions [three Sham (valve open) and three real IBS (valve closed)]. For the sham intervention the valve was not put into the circuit. For the real intervention the valve was in for 15 seconds. The sham trial was important to rule out the possible effects of the placement of a mask on the child's face and of the effect of dead space ventilation during the one minute of recording time. Prior to each series of interventions, the mask was applied to the subject and 30 seconds of flow and pressure data were recorded. After each intervention, a period of 30 seconds was recorded with mask in place and valve open. Flow and pressure signals were converted using an analog to digital converter (BIOPAC Systems, Inc., Santa Barbara, CA, USA) and a portable computer at the bedside. Pressure inside the mask was measured as a single pressure from the proximal port on the pneumotach. Breath volumes (l) were calculated by integration from the flow curve which was obtained from the differential pressure drop across the pneumotach resistance. The analysis of the recordings obtained with the mask held against the face for the 30 seconds pre and post intervention/sham included the calculation of the average tidal volume, the respiratory rate (breaths per minute), and the calculation of minute ventilation. The average of the three trials was used for analysis.

The stacked volume, or IBS volume (ml) was defined as the maximum volume achieved during the closed valve intervention (15 seconds) minus the average tidal volume (Vt) before the intervention (Figure 2, Equation 1). The IBS volume (ml/kg) was also expressed relative to body mass. The number of stacked breaths was counted using the number of volume increases excluding the first breath after valve closure.

Equation 1. IBS Volume = Max Volume – average Vt (pre IBS)

We set the clinically meaningful threshold for the volume stacked to be twice the average tidal volume above end inspiratory level. This threshold was based upon the volume normally associated with a spontaneous sigh which has been defined as breaths twice normal volume (Thach & Taeusch, 1976; B. Thach, 2001) or a tidal volume at least twice as large as the mean tidal volume during regular breathing (Perez-Padilla et al., 1983). The IBS ratio was used to determine a clinically meaningful IBS volume (Equation 2).

Equation 2. IBS Ratio = IBS Volume / (average Vt) * 100

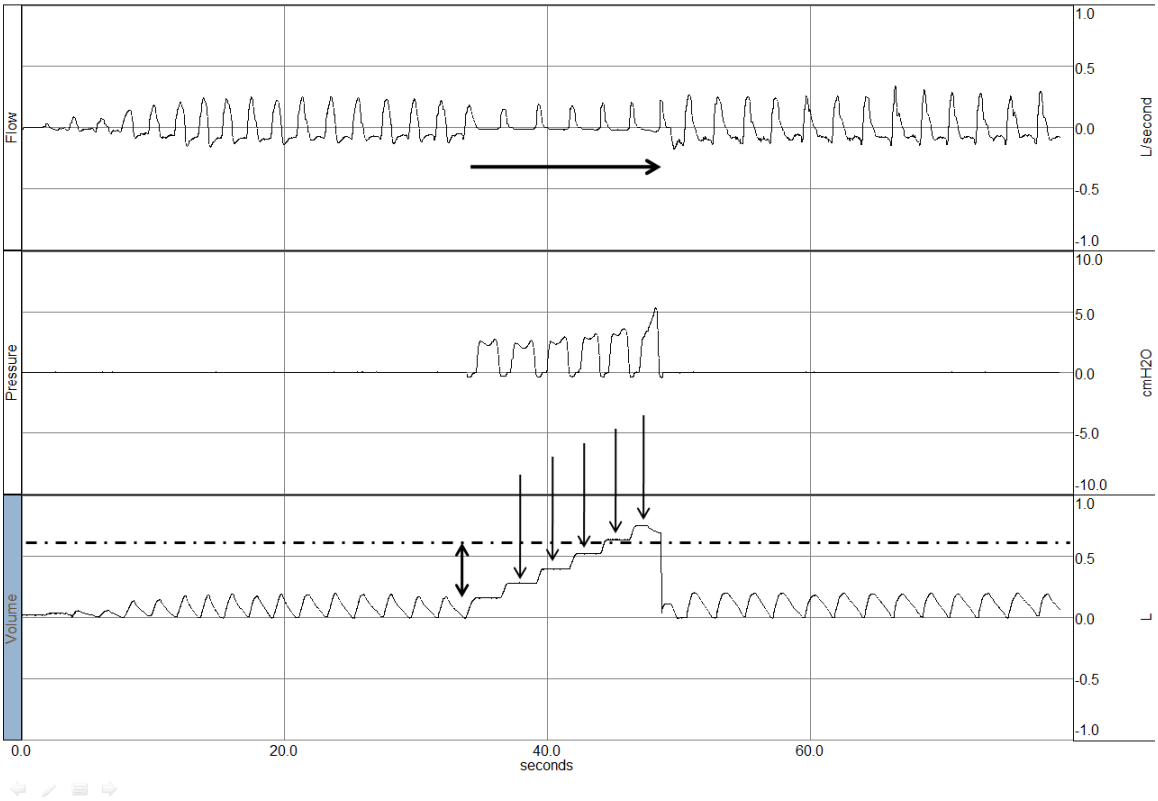

Figure 2 Illustration of IBS-derived parameters.
IBS volume (vertical arrow) between average tidal volume and max volume. Down arrows point to individual breaths during valve closure. Dotted line represents twice average tidal volume. The horizontal arrow indicates breath stacking time.

Point measurements of oxygen saturation were assessed using a pulse oximeter (Datex-Ohmeda, Inc., Mississauga, ON, Canada) for 30 seconds before the application of the facemask, after the recordings with the facemask and after the subsequent physiotherapy. The same pulse oximeter was used on all patients. The sites for the application of the oximetry sensor were different between subjects, based on convenience and most stable reading, but remained unchanged within individuals.

In three subjects we continuously monitored oxygen saturation using a Nonin Digital Pulse Oximeter (Nonin Medical, Inc., Plymouth, Minnesota, USA) through the entire breath stacking procedure. From the continuous saturation monitoring, point saturations were taken at the start of the recording, at 15 seconds into the recording, at the beginning of the intervention, at the end of the intervention, at 15 seconds post intervention and at 30 seconds post intervention. Continuous oximetry was used to insure the validity of 15 second point oximeter assessments.

Clinical Respiratory Score (CRS)

The clinical respiratory score was based on routine assessments by physiotherapy that are carried out on all respiratory patients. The CRS included a zero anchored, 3 point scale looking at seven parameters (max score of 14): respiratory effort, cough effort, cough clearance, breath sound intensity, crackles on auscultation, wheezes and upper airways sounds (Table 2). The term upper airway sounds refers to the often audible sound of secretions pooling in the back of the throat or upper airways. This is a common problem due to either an ineffective or infrequent cough. On auscultation the upper airway sounds are widely transmitted throughout the lung fields. Cough effort was excluded during the analysis, as it became apparent that the scoring system for this

category was suspect due to an inability to differentiate between weak or not observed categories. Without this component, the maximal CRS score was 6 X 2 = 12.

Table 2. Clinical respiratory assessment

	0	1	2	score
respiratory effort	normal	mildly increased	moderately increased	
cough clearance	expectorates	swallows	needs suction	
breath sound intensity	normal	slightly decreased	greatly decreased	
crackles on auscultation	none	few	many	
wheezes	none	few	many	
upper airways sounds	none	few	many	
sum of score				

Statistical Analysis

To evaluate the primary hypothesis of IBS efficacy, the stacked volume during IBS was compared to the sham using a paired t-test. The short term effects of IBS on the average tidal volume, breaths per minute, minute ventilation, and oxygen saturation were done by comparing changes before and after intervention with paired t-test. Alpha at 0.05 was considered statistically significant. The clinical respiratory score was compared pre and post sham and stacking intervention using the Wilcoxon test for paired data. The independent t-test was used to compare IBS volume to cognitive status, gender, etc. Furthermore, the IBS in inpatients was compared with that in outpatients by independent t-test.

Pearson correlation analysis was used to assess the relation between IBS volume normalized to body mass correlated and age. One way ANOVA was used to compare the

change in IBS volume between diagnostic groups. PASW Statistics Grad Pack18.0 for windows (SPSS, Inc., Chicago, IL, USA) was used for data analysis.

RESULTS

Twenty four patients participated in the study. One patient's data was excluded due to a face mask leak. Twenty three children, 15 inpatients and 8 outpatients, were included in the final analysis. Seventeen were male and 6 were female.

The age ranged from 3-19 years [mean 11, SD (5.1)], with body mass ranging from 12 – 80 kg [mean 43.8, SD (20.9)]. Eight were diagnosed with Duchenne muscular dystrophy, 5 with other myopathies and 10 with central nervous system disorders. Fifteen were assessed as cognitively aware and able to communicate verbally, and 8 were not cognitively aware and unable to communicate verbally. All subjects were able to tolerate the IBS procedure without any apparent discomfort. The characteristics of the subjects are shown in Table 3. In this study population, 12 patients had scoliosis and 7 of these had spinal fusions; the degree of scoliosis was not documented. All patients with scoliosis tolerated the stacking and 6 of the 12 stacked greater than 200%.

Table 3. Patients' characteristics

#	SN	Diagnosis	Age (y)	Sex	Mass (kg)	%	NPPV	Aware	Walk
1	1	DMD	18	M	57.3	10	Yes	Yes	No
2	2	Cri-Du-Chat	5	M	11.7	< 5	No	No	No
3	7	CP	3	M	13.5	10	Yes	No	No
4	8	Rett syndrome	7	F	26.0	50	No	No	No
5	31	Multicystic encephalomalacia	6	M	38.2	95	Yes	No	No
6	18	Facioscapulo-humeral dystrophy	16	F	43.4	< 5	No	Yes	Yes
7	19	SMA	12	M	33.6	10	Yes	Yes	No
8	20	Congenital fiber type disproportion	15	F	62.7	75	No	Yes	Yes
9	21	Charcot Marie Tooth Type 1A	4	F	19.4	50	No	Yes	No
10	22	DMD	13	M	55.0	50	No	Yes	No
11	23	DMD	13	M	77.0	95	No	Yes	No
12	24	DMD	16	M	59.4	25	Yes	Yes	No
13	25	DMD	13	M	54.0	75	No	Yes	No
14	26	CP	6	M	43.6	95	No	No	No
15	27	Batten's disease	5	M	27.4	95	No	No	No
16	28	Hypoxic brain injury	11	M	37.7	50	No	No	No
17	29	C1C2 partial spinal cord injury	16	F	40.2	< 5	Yes	Yes	Yes
18	30	DMD	15	M	64.3	50	Yes	Yes	No
19	32	Becker Muscular Dystrophy	16	M	52.8	10	No	Yes	Yes
20	33	DMD	4	M	18.8	50	No	Yes	Yes
21	38	Seizure disorder	6	F	16.8	< 5	No	No	No
22	39	DMD	13	M	78.9	95	No	Yes	No
23	41	Limb Girdle Muscular Dystrophy 21	19	M	76.5	50	No	Yes	No

 # = Patient number, SN = Study number, DMD = Duchenne Muscular Dystrophy, CP = Cerebral Palsy, SMA = Spinal Muscular Atrophy, % = weight to age percentiles, NPPV = noninvasive positive pressure ventilation at night, Aware = cognitively aware and able to communicate, Walk = able to ambulate vs. wheelchair dependant.

Breath Stacking

The average time of valve closure was 14.3 (2.91) seconds. The average number of stacked breaths was 4.5 (3.61) with a range of 0-17 breaths**.** Figure 3 is an example of successful breath stacking. After the first tidal volume the patient stacked 5 successive breaths, showing that a significant increase in lung volume can be achieved with the breath stacking mask.

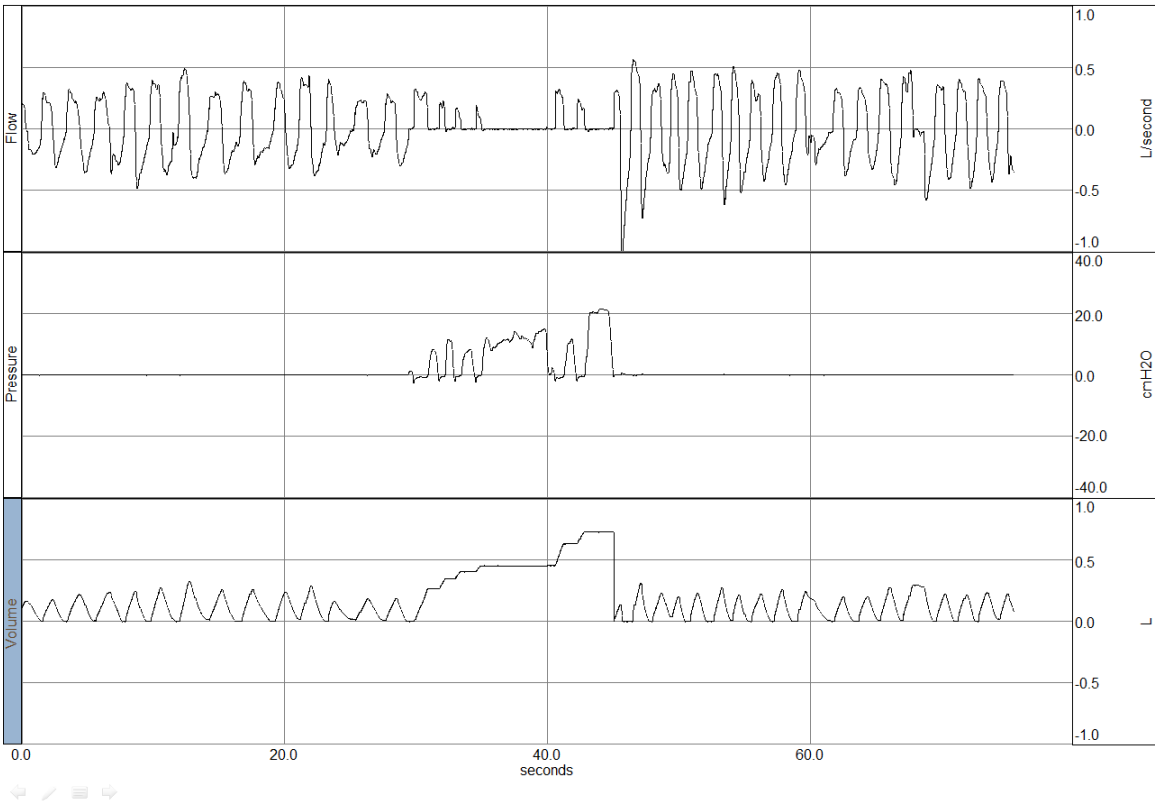

Figure 3 Screen capture from a subject who performed successful breath stacking.
The top tracing shows the airflow (l/s). During valve closure airflow is only during inspiration. The middle tracing shows the pressure (cmH_20). During valve closure the peak pressure increases. The bottom tracing shows the volume (l) with tidal volume per breaths evident (in liters). Breath stacking is measured after the first tidal breath.

However, not every child successfully stacked successive breaths. Unsuccessful stacking efforts were not necessarily obvious without the visual display of breath volumes. Figure 4 shows an example of unsuccessful volume stacking. There are

pressure changes in the mask when the valve is closed, but this did not result in breath stacking, likely because the subject held his breath.

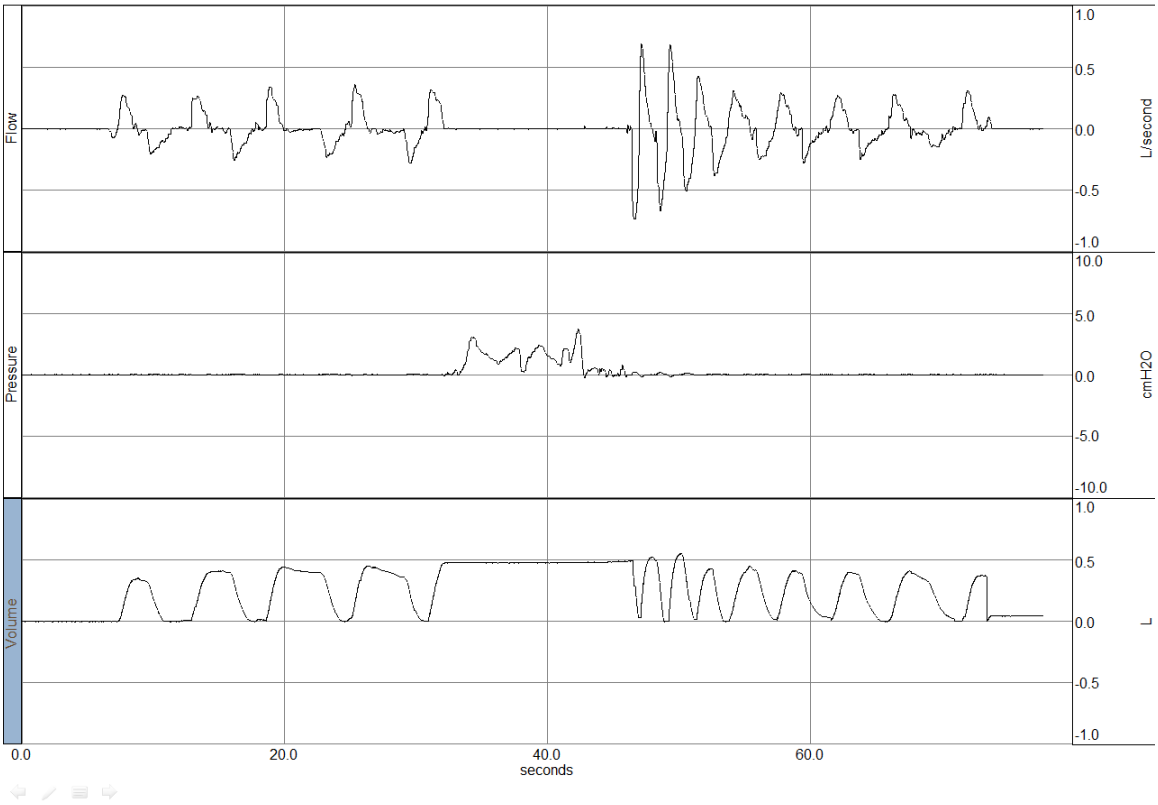

Figure 4 Screen capture from a subject who was unsuccessful in breath stacking.
The top tracing shows the airflow (l/s). During valve closure there is no inspiratory airflow. The middle tracing shows the pressure (cm H_20). Positive pressure changes inside the mask indicate some expiratory effort against the closed valve. The bottom tracing shows the volume (l) with tidal volume per breath evident (in liters).

The average (SD) tidal volume before stacking was 277 (131) ml with a range between 29 and 598 ml, derived from all measurements (i.e. not from average data). Table 4 shows the IBS volume and IBS ratio for each subject using the mean of the three trials.

Table 4. Individual breath stacking volumes

Study Number	Average Vt (ml) before stacking	IBS Volume (ml)	IBS (ml/kg)	IBS Ratio
1	397	96	1.7	24%
2	141	-32	-2.7	-23%
7	135	385	28.5	285%
8	181	494	19.0	273%
31	74	-11	-0.3	-14%
18	402	199	4.6	49%
19	378	643	19.1	170%
20	375	703	11.2	188%
21	209	567	29.2	271%
22	362	472	8.6	130%
23	403	961	2.5	239%
24	323	617	10.4	191%
25	255	730	13.5	286%
26	182	2,278	52.2	1255%
27	80	-59	-2.2	-74%
28	282	895	23.7	317%
29	258	397	9.9	154%
30	247	664	10.3	269%
32	317	688	13.0	217%
33	398	959	51.0	241%
38	60	-35	-2.1	-59%
39	376	939	11.9	250%
41	527	1,223	16.0	232%

Figure 5 shows the IBS volume for the sham and actual breath stacking procedure. The mean (SD) IBS volume was 599 (558) ml with a range between -141 to 2916 ml. (Note that the IBS volume was calculated by subtracting the average tidal volume before intervention from the maximum stacked volume; therefore subjects who stacked zero volume had negative values in the IBS calculation.) The mean (SD) IBS volume was 732 (524) ml when the four non-stacking patients were omitted. The increase in volume with IBS was statistically significant with and without the inclusion of the non-stacking patients' ($p < 0.001$).

Figure 6 shows the data expressed relative to body mass. The mean change in sham volume was 5.7 (84) ml with a range between -171 to 299 ml. Figure 7 shows the IBS volume for each patient. Figure 8 shows the IBS volume normalized to body weight for each patient. The mean (SD) IBS volume normalized to body mass was 14.7 (14.7) ml/kg with a range from - 2.7 to 52.2 ml/kg. The mean change in volume during the 15 seconds of sham maneuver, normalized to body mass, was 0.31 (4.0) ml/kg with a range of -8.8 to 15.9 ml/kg.

Successful Breath Stacking

Four of the 23 children were not able to stack at all, i.e. they had negative values for IBS volume (Table 4). Using the definition of effective stacking, (i.e. IBS of twice the average tidal volume), only 12 children stacked effectively (Table 4). These 12 children varied in age, diagnosis, and cognitive status.

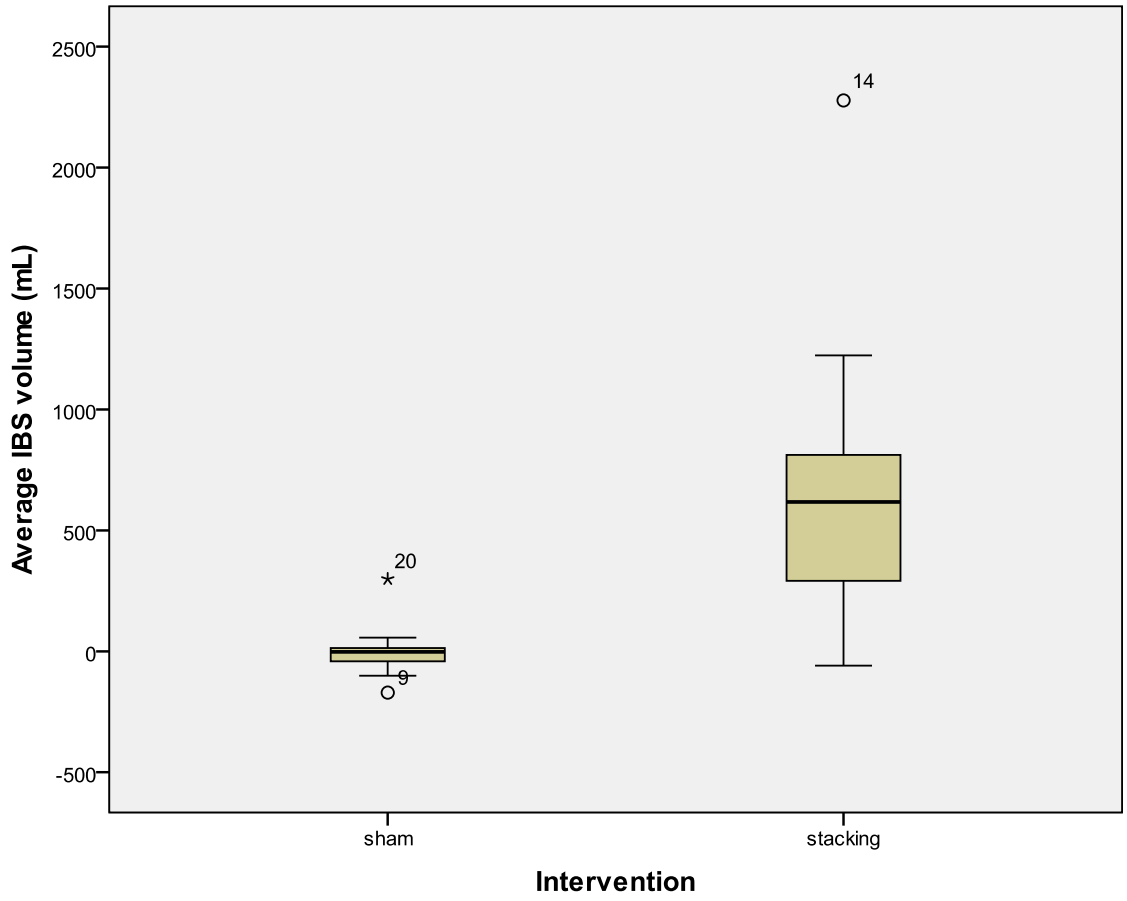

Figure 5 Box and Whisker plot of average IBS volumes by intervention.
IBS volume is shown in ml. The stacking intervention shows a significantly greater increase in volume compared to the sham ($p<0.001$).

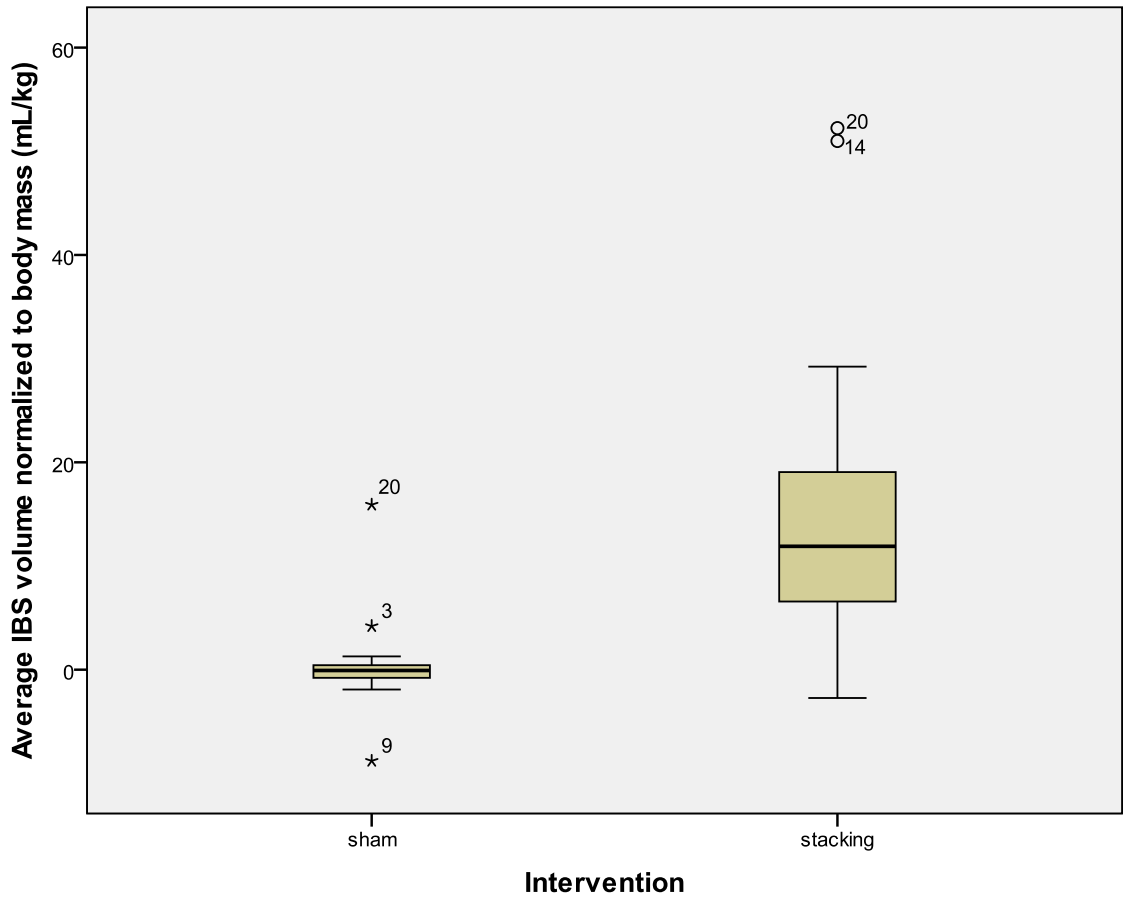

Figure 6 Box and Whisker plot of normalized IBS by intervention.
IBS volume is shown normalized to body mass (ml/kg). The stacking intervention shows a significantly greater increase in volume compared to the sham ($p<0.001$).

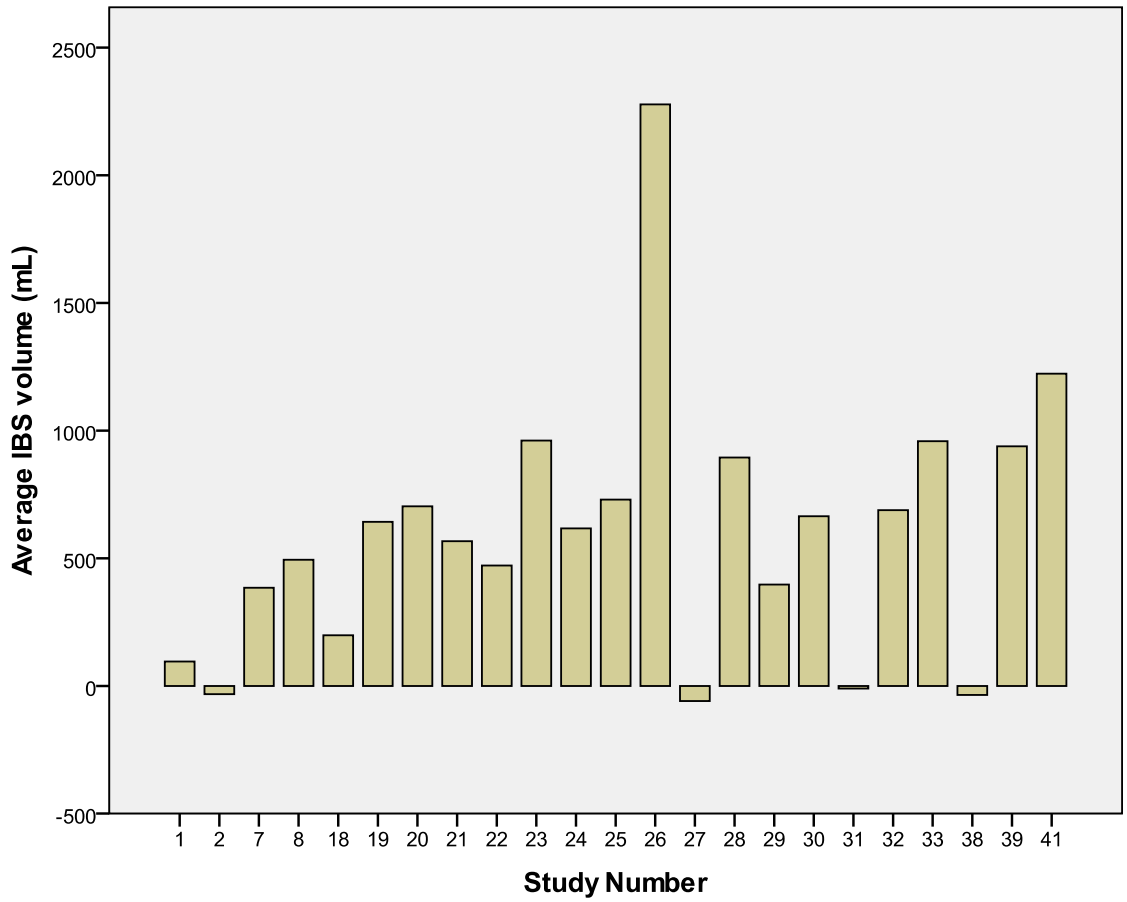

Figure 7 Average IBS volume per subject.

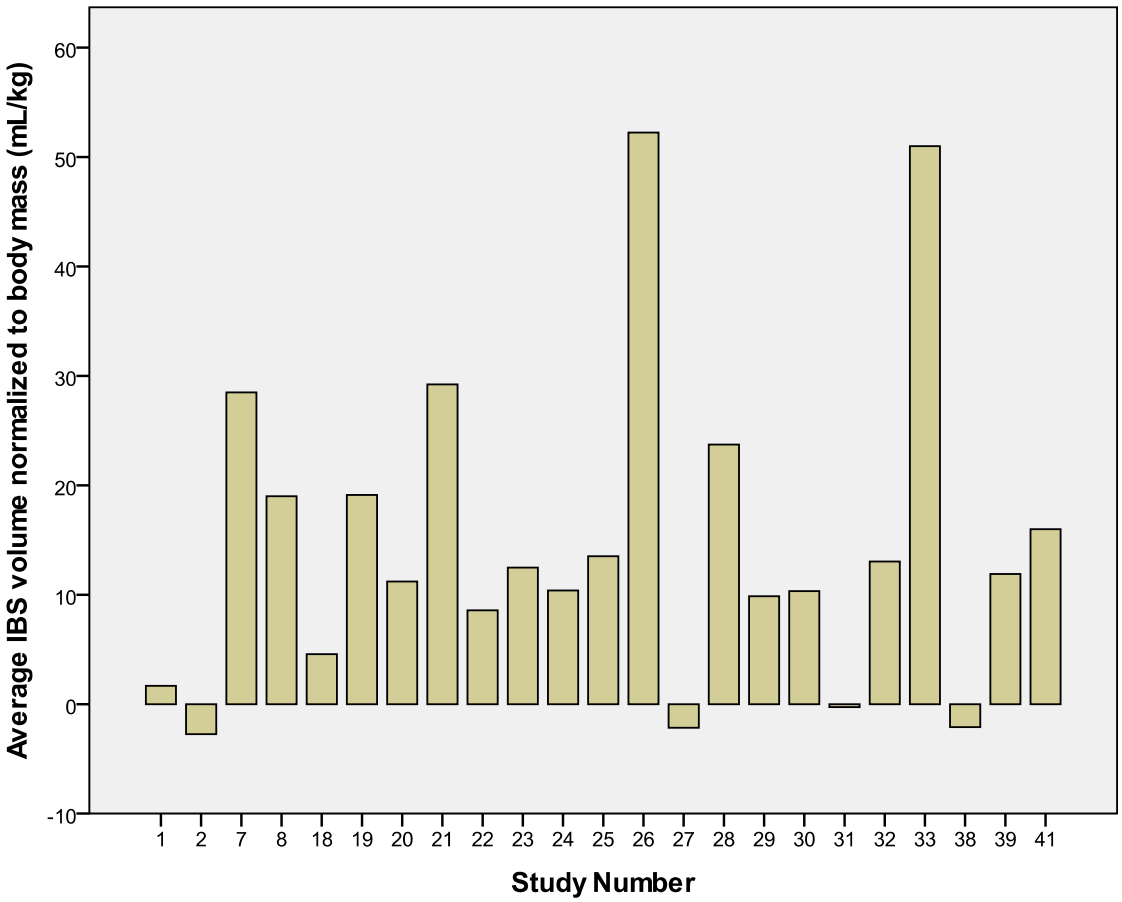

Figure 8 Average normalized IBS volume per subject.

Respiratory Parameters and IBS

Table 5 shows the respiratory parameters that were measured prior to and after intervention (sham or real IBS). The sham IBS did not have any effect on respiratory parameters while the IBS intervention resulted in small but significant increased tidal volume, increased breath frequency, and total ventilation. In the four children who failed to stack at all, there was no significant change in the Vt and RR post sham or stacking. There were no significant changes in oxygen saturation or clinical respiratory score as a result of the IBS intervention.

Table 5. Respiratory parameters before and after IBS

	Sham IBS		IBS	
	Pre	**Post**	**Pre**	**Post**
Vt	303 (141)	289 (128)	277 (131)	310 (148) **
RR	26 (10.3)	26 (10.4)	27 (9.2)	28 (10.6) *
V	7433 (4931)	6934 (3323)	6783 (3062)	7963 (3467) **
0_2	96 (3.6)	96 (2.5)	96 (3.2)	96 (3.0)
CRS	2 (1.3)	2 (1.1)	2 (1.3)	2 (1.2)

Vt = tidal volume (ml), RR = respiratory rate (breaths per minute), V =minute ventilation (ml/min), 0_2 saturation (%), CRS = clinical respiratory score. Values are mean (SD). *p <0 .05, **p <0 .001 (paired t-test)

Oxygen saturation was measured continuously in 3 patients to evaluate whether point midstream saturations were valid (Figure 9). There were no significant changes in the pre- and post-intervention continuous saturations over the course of the sham or stacking maneuvers, thus validating the point measurements.

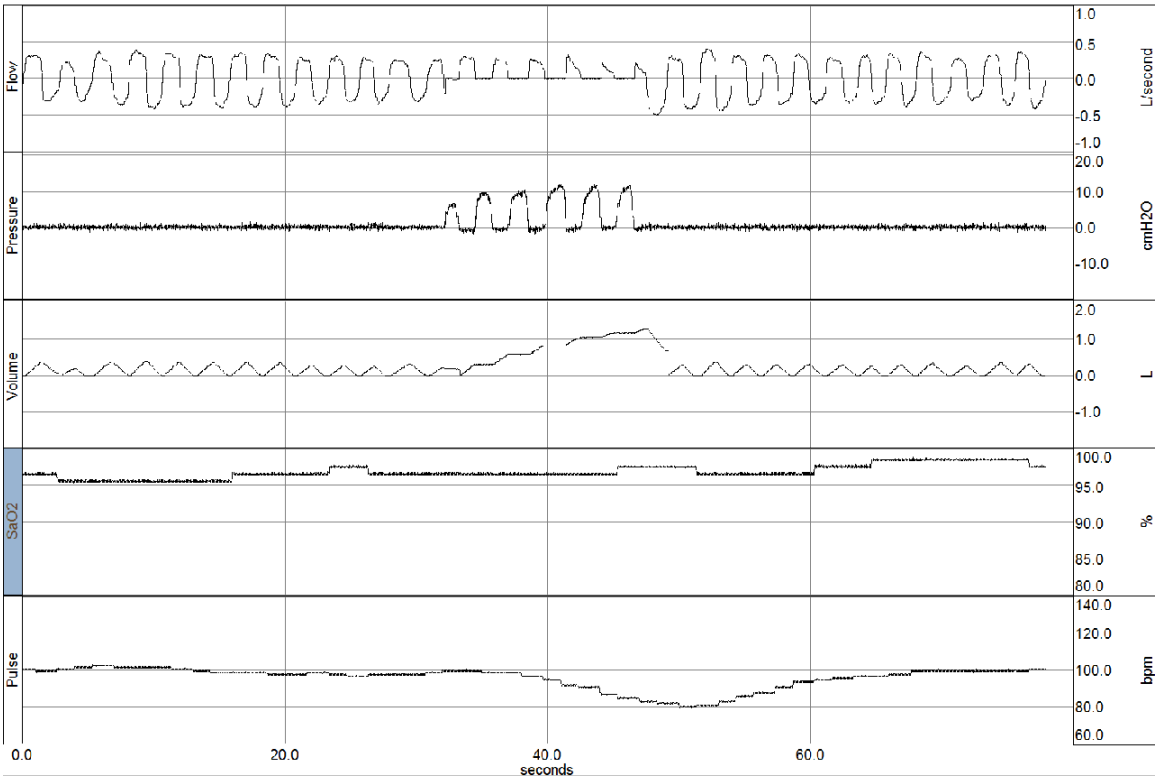

Figure 9 Example of continuous oxygen saturation during successful stacking.
The top tracing shows the airflow through the mask in liters per second. During valve closure airflow is only during inspiration. The second tracing shows the pressure changes within the mask in cmH_20. During valve closure the pressure increases within the mask. The third tracing shows the tidal volume breaths in liters and then five stacked breaths during valve closure. The fourth tracing shows the continuous oxygen saturations in %. The fifth tracing shows heart rate in beats/min.

Breath Stacking Failure

To explain the complete failure to stack in the 4 patients with negative IBS values, various factors were considered as possible candidates. Gender, ambulatory status, muscle strength, nocturnal ventilation, respiratory medications pre intervention, or whether they were an inpatient versus an outpatient did not account for the failure to stack. Also, the breath stacking failure was not related to when they were studied during the time of data collection.

The only consistent finding among these 4 subjects was a mean Vt prior to IBS that was smaller than the dead space of the mask. In fact, the four subjects appeared to hold their breath during the valve closure. The dead space in the mask was measured at 158 ml and the average Vt of the 4 patients was 88 ml (range 29-145). It is likely that these children were not even able to open the valve on the mask to stack. One other child had a Vt of 135 ml, i.e. below the dead space, however this child did manage to stack 285%. Analyzing the individual IBS during three successive interventions instead of the average IBS for each child, two of the patients who failed based on average IBS did stack a small amount (22 and 54 %) on one occasion.

Of the 7 children who did stack, but not above the 200 %, three reached ≥170 %. All 7 were cognitively aware and were between the ages of 12-18 years. Although the study was not designed to detect differences between sub-groups, an exploratory analysis was performed to detect trends for consideration in future research. The potential influence of cognitive status, diagnosis and age were examined. Because of reduced sample size in the subgroups, this analysis is subject to a greater risk of type II error. Analyzing the individual IBS during intervention in the three children who almost reached the defined cut-off, 2 of the 7 children did stack > 200% on one occasion and 1 child stacked > 200 % on two occasions.

Cognitive Status and IBS

When the mean change in volume with the breath stacking was compared to the cognitive status of the children, no statistical significance was observed between those children that were cognitively aware and able to verbalize and those that were not (Figure 10). On average the IBS volume was greater in the cognitively aware subjects and there

was less variability in the observed changes compared with the group of cognitively impaired. Four of the eight unaware children stacked greater than 200% and the other four did not stack at all. Eight of the fifteen cognitively aware children did stack greater than 200%. The cognitively aware children also tended to be the older children.

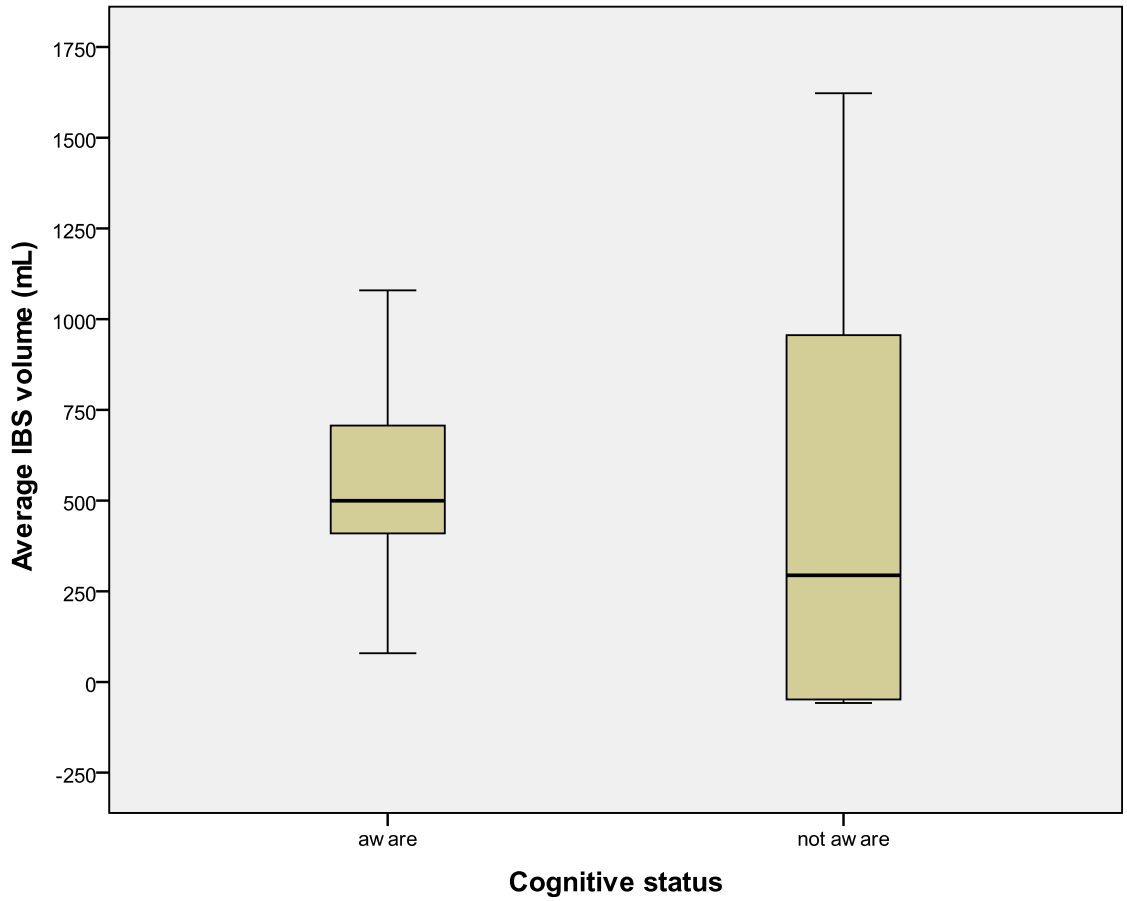

Figure 10 Average IBS volume by cognitive status.
Aware = cognitively aware and able to verbalize and not aware = not cognitively aware and unable to verbalize.

The mean change in volume with stacking was then normalized to body weight as the main contributor to tidal volume is body mass (Sprynarova, Parizkova, & Bunc, 1987). Again, no significant relation was found between normalized stacked volumes when compared to the cognitive status.

Diagnosis and IBS

IBS volume was not significantly different between the categories of diagnosis in these children (Figure 11). The median change in volume was similar in all three groups.

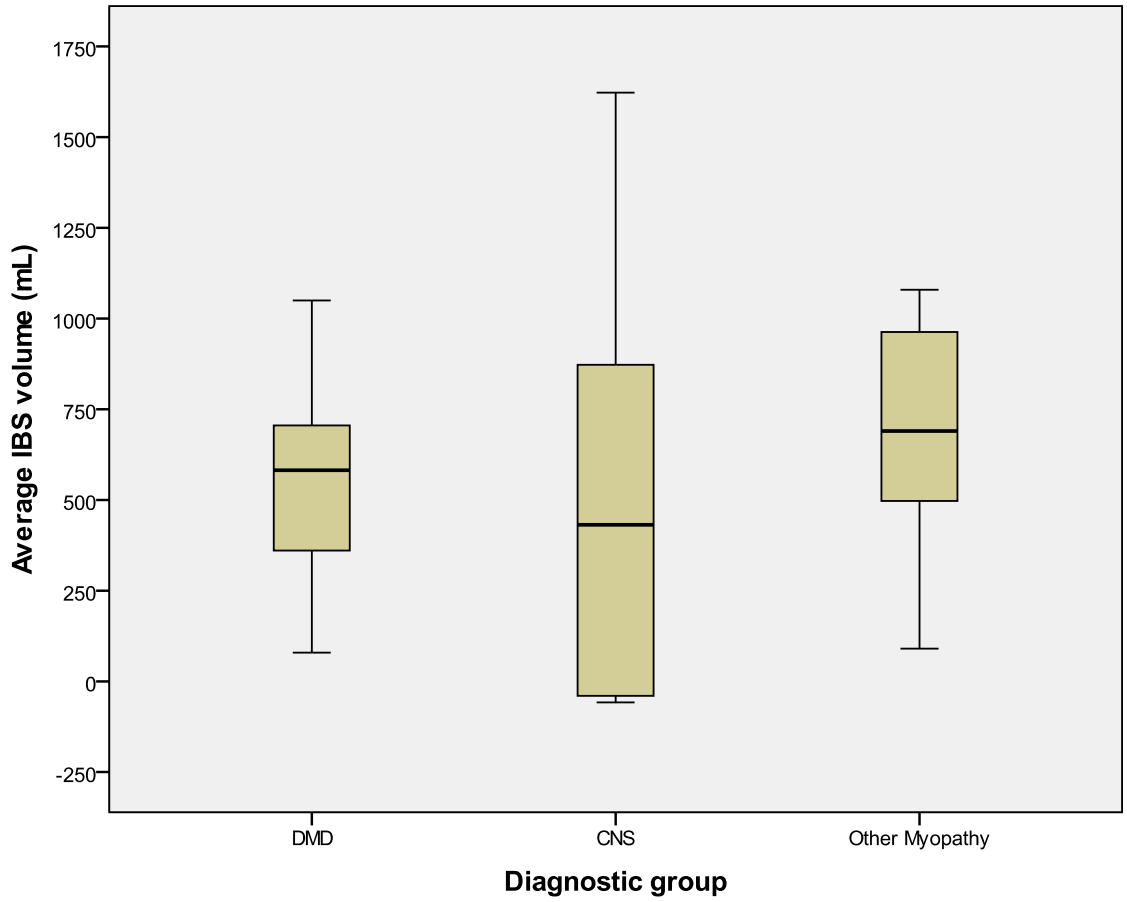

Figure 11 Average IBS volume by diagnostic group.
DMD = Duchenne Muscular Dystrophy, CNS = Central Nervous System Disorders, Other Myopathy = Other Myopathies.

The mean change in volume with stacking was then normalized to body weight as the main contributor to tidal volume is body mass (Sprynarova et al., 1987). Again, no significance was found between these normalized stacked volumes when compared to the cognitive status in the children.

Age and IBS

There was a trend to stack less volume at a higher age but the correlation was not statistically significant. An age related change in IBS may be present but the current study may have been underpowered to reveal it (Figure 12).

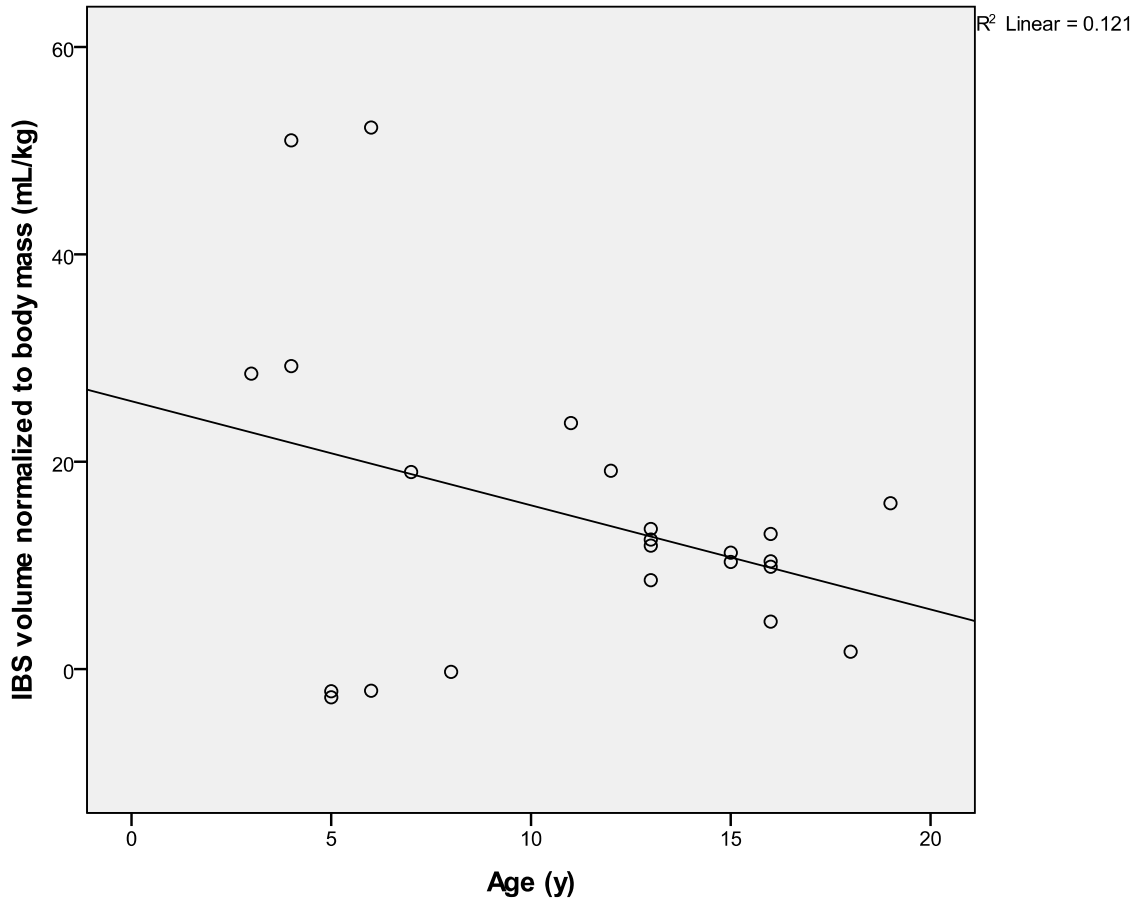

Figure 12 Relation between normalized IBS volume and age.
Pearson product moment correlation coefficient = -0.346, p=0.103.

There was no significant difference in the magnitude of either the IBS or sham volume between inpatients and outpatients.

DISCUSSION

This study has clearly shown that involuntary breath stacking with a mask and a one-way valve can achieve breath volumes above the average tidal volume, independent of the type of neuromuscular disorder or the cognitive status of the patient. The target for the stacked volume to be considered clinically meaningful was set as at least twice the average tidal volume above end inspiratory level. (IBS ratio of 200%), i.e. reaching at least that of a spontaneous sigh. In the literature, the sigh is considered an important component of breathing, resulting in an increase in pulmonary compliance and decrease in atelectasis (Perez-Padilla et al., 1983). Many of the patients with neuromuscular disease in our care may not have the strength to take intermittent deep breaths or sighs. Effective stacking was achieved in about half of the subjects in our study. Seven of the participants did stack but not at the 200 % target, although three of these came close. If one sigh or stacked breath is considered clinically meaningful it would mean that 15 out of 23 stacked volumes successfully. If a less stringent definition of effectiveness is applied, i.e. IBS >150%, then 16 or about two thirds of children reached the goal. Overall, we found that the involuntary breath stacking was efficacious in this patient population without any deleterious effects in respiration, oxygenation or clinical status, supporting our general hypothesis. However we do not know what level of IBS is clinically meaningful for the long term outcomes. A study that determines the stacked volume required to reduce or eliminate atelectasis is needed.

The one study in cooperative adults that looked at breath stacking using a mask and a one-way valve showed that significantly higher inspiratory volumes were obtained during breath stacking when compared to incentive spirometry, both pre- and post-

operatively. The authors of that study also did not find any adverse effects and concluded it could probably be used safely and effectively, particularly in uncooperative patients (Dias et al., 2008). We have extended their findings to a pediatric population which includes both cognitively aware and unaware children. The mask with the one-way valve worked well, as the cooperation of the patient was not required. This technique can therefore be used on cognitively unaware children and on children too weak to hold a mouth piece. There have been no pediatric studies to date that have tested this approach.

Four children in our study were unable to stack at all. We looked for factors which may have contributed to this failure based upon sex, disorder type, etc. All of these children were cognitively unaware and therefore unable to follow instructions. Their age ranged from 5 to 6 years. One identifiable parameter that was consistent among the four was an average Vt before stacking that was less than that of the measured dead space in the mask. This suggests that their breath efforts may have been too weak to open the valve on inspiration. Their average Vt and respiratory rate pre and post intervention did not change significantly in contrast to the children who stacked some volume. There are no masks with lower dead space or devices that can decrease the dead space. These children and those that did not stack effectively would need a bag attached to the mask and valve to augment their inspiration and assist with stacking. From this result, it is advised that prior to IBS that a tidal volume assessment be performed and if the Vt is smaller than mask dead space, then a IBS trial should be performed to assess effect.

The factor related to the effectiveness of IBS that showed a trend was age. The older the child, the less IBS volume was achieved. The progressive disorders of DMD and other myopathies were all found in the older age group, from 12 to 19 years. Over the

years, the lung compliance and muscle strength will decrease in these progressive diseases, which would explain our observation. The respective subjects were all cognitively aware and able to follow the instructions. The younger children, from 2 to 16 years of age, who stacked more volume, were all in the CNS category which is usually non – progressive. If we had enrolled a more homogeneous group of children we might have seen a relation between age or diagnostic group and IBS more clearly.

In our study, there were detectable but small effects of 15 seconds of breath stacking on respiratory parameters. The average breath frequency only increased by one breath per minute after stacking. The tidal volume also increased slightly. There is of course the possibility that dead space ventilation over a longer time, i.e. during the 2nd period of 30 seconds, did have an effect on RR and Vt. However, since this was not observed following the sham intervention the increase in minute ventilation, at least over a short term, must be related to successful stacking. An effect of a respiratory apparatus on breathing pattern has been reported, presenting as an increase in tidal volume but a decrease in frequency while the mask is on the face (Hirsch & Bishop, 1982). This may then affect the breathing pattern immediately after removal of the mask. The expected production of venous carbon dioxide production is 3 mmHg per minute (Stock et al., 1988). With our 15 seconds of stacking there would be less than 1mmHg increase in venous carbon dioxide, which would not be expected to act as a stimulus to increase ventilation.

As was expected, there was no significant drop in oxygen saturation or worsening of the clinical respiratory score after stacking, indicating that this is a safe technique.

Visual feedback of the oxygen saturation and of the IBS volumes may be of benefit to the caregiver and perhaps also to the patient when using the mask for the first time.

The present study has certain limitations. We had projected a larger group of participants but the number of hospitalized children with neuromuscular disorders with respiratory issues is quite variable. Several of these patients are admitted frequently, and while we did study some participants during three separate admissions, we decided to only include the first data set for standardization and to prevent selection bias.

The population was heterogeneous and reflected the clientele that is typically referred to the physiotherapy service for lung volume recruitment. This heterogeneity and the small number of participants in the different disease categories limited the possibilities to detect potential increased benefit within subgroups, e.g. in patients with progressive myopathies.

The subjective nature of the clinical assessment presents another limitation. The categories of normal, mildly/slightly increased or decreased are quite broad and require experience to assess. Having the clinical assessments done by a single, experienced blinded observer did overcome this limitation to some degree. The cognitive status of the child may also have affected the findings, as some may have understood the process and taken a deeper breath which would affect the assessment of breathing effort and possibly cough effort. Of the 12 children who stacked effectively, 8 were cognitively aware and 4 were not which supports this consideration. A more specific scale with measurements relative to a gold standard would have been of benefit, e.g. the measurement of peak cough flow. However, many of our children were unable to perform the tests.

This highlights the limitation of using only indirect outcomes, i.e. clinical scores and oxygen saturation instead of direct measurements of lung function. Inspiratory and expiratory lung volumes measured by spirometry would have been helpful to see if successful IBS was related to respiratory mechanics, e.g. maximal static inspiratory and expiratory pressure, peak cough flow and vital capacity. However many of the participants were not only unable to follow the commands necessary to do spirometry but also unable to hold a mouthpiece due to weakness, age or cognitive status.

Measures of absolute lung volume can be done by body plethysmography, which measures the change in thoracic volume that occurs during respiratory maneuvers. This would typically require the patient to sit inside the plethysmograph with a mouthpiece and a nose clip in place. The patient must support both cheeks with their hands and be able to follow commands. This technique is therefore not feasible in most of the neuromuscular population. We did not measure upper limb mobility and strength of our subjects, but objectively only 4 may have been able to complete this test.

The assessment of diaphragmatic muscle strength with electromyography and measurement of transdiaphragmatic pressure changes require invasive procedures which were not acceptable in our population.

In subjects with limited ability to cooperate, radiographic estimates of lung volumes may be more feasible than physiological measurements. Computed tomography can provide estimates of the volume of gas in the lungs and may also be useful to detect the presence of and changes in areas of atelectasis. Because of the significant exposure to radiation and of cost this was not considered appropriate for our study.

The potential effect of IBS on outcomes over the long term would require a separate study. Since each child with a neuromuscular disorder has a different course of the disease, a within person, longitudinal investigation of patients within defined disease categories would be helpful. Our study asked whether the intervention of IBS could increase volume, which it did. We would now like to know whether there was a reduction of atelectasis, an increase in the compliance of the lungs and thorax and improvement of peak cough flow. Clinically, this should then also become apparent in a reduced need for visits to the physician, antibiotic prescriptions and hospitalizations.

This study has increased our awareness that volume stacking may not be occurring in some patients when we think it is. To change our practice, an improved clinical assessment is required because we currently do not have the technology, outside of this research study, to visualize IBS volume. Two physiotherapists should perform the initial trial of the mask, one auscultating for an increase in breath sounds and to observe if there is an increase in chest movement. Measurement of chest expansion would also be of benefit. If the patient is able to do spirometry, we should confirm that the tidal volume is larger than the dead space in the mask and that there is adequate respiratory muscle strength. In the DMD population, as patients get weaker over time, they may not benefit from this technique any longer and instead require further assisted volume recruitment with a bag, mask and one-way valve.

One practical issue related to the use of the mask and one-way valve needs mentioning. The mask is generally held in place not by the patient but by another person. This requires that the patient's head is held in a neutral position during stacking or optimal lung expansion may not be possible. Due to the different shapes of faces, air

leaks are possible, which then reduces the effect of the stacking. In our study the same research assistant did all the measurements, and was trained in the use of the breath stacking technique. If there was a leak from the mask it was evident on the computer screen and the trial could be re-started when the mask was readjusted. This was only documented once.

Training is required when IBS is implemented in the home setting. Parents and caregivers are given information regarding the basic concept of lung volume recruitment and why it is important. The technique is taught specific to the child. The physiotherapist selects a mask of appropriate size for the child's face. Parents are taught to listen for air leaks and watch the chest for movement for breaths when using the mask with their child. The parents are instructed in how many breaths their child should stack and how many cycles to do, with rests in between. A written instruction sheet is provided.

The shallow breaths and the lack of intermittent larger sighs in patients with significant muscle weakness can lead to chest wall stiffness and reduced rib cage excursions. When bigger breaths are given, this can potentially cause pain in the ankylosed costo-vertebral joints and in the stiffened tendons and ligaments of the rib cage. There is also reduced lung elasticity predisposing patients to sub segmental atelectasis. It has been postulated that a program of daily maneuvers that provide larger chest wall excursions with breath stacking could minimize this reduction in chest wall compliance that occurs with age and simultaneously improve lung compliance by reversing sub segmental atelectasis (Bach & Bianchi, 2003) through increased collateral ventilation and because of alveolar interdependence. Similar to decreased range of motion without regular limb exercise, the chest wall and lungs also require range of

motion. We did not measure chest wall compliance or formally assess discomfort during chest expansion, but none of the cognitively aware subjects expressed discomfort and the behavior of the cognitively unaware subjects also did not indicate this.

Many children with progressive neuromuscular diseases also develop scoliosis and require a spinal fusion. With progression of the scoliosis there is a worsening chest cage restriction and a further decrease of the vital capacity. Despite scoliosis surgery patients with neuromuscular disease are still likely to have deterioration of their pulmonary function (Koumbourlis, 2006). In our study, 12 of the 23 had scoliosis and 7 of these had spinal fusions; however the degree of scoliosis was not documented. Therefore we can not say how scoliosis may have affected our data.

CONCLUSION AND CLINICAL IMPLICATIONS

In conclusion, the involuntary breath stacking technique was shown to be efficacious for the generation of larger lung volumes in children with neuromuscular disease. However, approximately half of our subjects did not reach the level of a sigh with IBS and there is no evidence at present that confirms a benefit of this technique in the long term. Without our equipment the failure to stack would not necessarily have been obvious. There is a need to develop technology to indicate volumes reached with IBS, e.g. a small flow meter attached to the mask or mouthpiece.

However, since there were no adverse effects, we feel that IBS is a technique that can be used in a safe and efficient form with both cognitively aware and unaware children. This device is relatively simple, inexpensive and portable. This study reminds us that we need to improve our clinical assessment to guide the use of IBS with a mask and one-way valve.

FUTURE RESEARCH

Further investigations could be directed at the specific clinical effects of breath stacking. For example,

- using radiographic imaging to assess whether IBS decreases alveolar atelectasis,
- measuring the lung and thorax compliance,
- measuring the peak cough flow before and at the end of breath stacking.

More work is needed to determine at what level of respiratory weakness IBS is no longer efficacious and further assistance is required for successful lung volume recruitment.

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APPENDICES

Appendix A: Consent Form

Health Sciences Centre

Physiotherapy – Child Health

CHILDREN'S HOSPITAL
840 Sherbrook Street (Rm CH246)
Winnipeg, MB R3A 1S1

Ph # (204) 787-2641
Fax # (204) 787-1965

RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study: Effect of a Volume Stacking Mask on the Respiratory Status in Children.

Protocol number: _____

Principal Investigator: Heather Jenkins, CH246-840 Sherbrook St., Winnipeg, MB, R3A 1S1, Tel: (204) 787-2641
Co-Investigator: Dr. Hans Pasterkamp, CS512-840 Sherbrook St., Winnipeg, MB, R3A 1S1,
Tel.: (204) 787-4753

Sponsor: Health Sciences Centre Foundation

You are being asked to participate in a Clinical Trial (a human research study). Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision. This consent form may contain words that you do not understand. Please ask the study staff to explain any words or information that you do not clearly understand.

The study physiotherapist is receiving salary support to conduct this study.

Purpose of Study

This Clinical Trial is being conducted to study children over one year of age with central nervous system dysfunction and/or muscle weakness who are often unable to take a deep breath. You are being asked to take part in this study because you have a child over one year of age with a neuromuscular condition that requires chest physiotherapy to help clear secretions and who would benefit from deeper breaths. A total of at least twenty children will participate in this study.

The purpose of this study is to prove that significantly greater breath volumes can be achieved with the volume stacking mask. We want to find out about the conditions that may not allow an increase in breath volume by this method. We also want to determine the effect of volume stacking on oxygen uptake in the lungs and on airway clearance.

This research is being done because volume stacking masks are being used at the Winnipeg Children's Hospital and in other centres. However there is currently no information on the effect or the effectiveness of volume stacking techniques in children.

Study Procedures

A cushioned facemask that covers the nose and mouth of your child will be connected via a valve to a device that measures airflow (a pneumotachograph). A sensor will measure pressure inside the mask. Airflow and pressure will be recorded with a portable computer at the bedside. Breath volumes will be calculated from the airflow.

Breaths will be stacked one on top of the other when closure of the valve over 15 seconds will allow your child only to breathe in but not to breathe out. As a control, the mask will be held to the face without closing the valve. Your child will have either the stacking procedure or the control procedure as part of the morning routine chest physiotherapy and the alternate procedure as part of the afternoon routine physiotherapy session.

There will be 30 seconds of recording flow and pressure with the valve open before and after each procedure. Each set of three interventions recorded to computer will take 15 minutes at the maximum. Both interventions will be done in one day shortly before your child is expected to be discharged home.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study staff and your regular doctor first. Your child will continue to receive the routine chest physiotherapy during his/her admission to the Winnipeg Children's Hospital.

When the study is completed and all results have been analyzed we will inform you about the findings regarding volume stacking in the group of children who participated and also for your child in particular.

Risks and Discomforts

The application of a volume stacking mask may upset some children who do not understand the reason for its use. We have not found this to be a problem in children who have been treated with volume-stacking masks at the Winnipeg Children's Hospital. However, if your child should become restless or upset, the facemask will be removed. The procedure will then be tried again after a five-

minute rest. If your child still does not get used to the application of the stacking mask, the procedure will be stopped and will not be tried again.

There is no risk to not get enough oxygen during the procedure because every breath will still bring in fresh air. The short time when the valve is closed to prevent breathing out will also not cause a feeling of breathlessness because there will not be enough carbon dioxide retained during 15 seconds for that to occur.

Your child's condition may not improve but there is no reason why it would worsen because of the volume stacking mask.

Benefits

By participating in this study, you will be providing information to the study doctors that will show the effects of involuntary volume stacking for the treatment of decreased lung volumes and difficult airway clearance due to weakness. There may or may not be direct medical benefit to you from participating in this study. We hope the information learned from this study will benefit other participants in the future who have neurological and muscular disorders that cause low lung volumes and a weak cough.

Costs

All clinic and professional fees, diagnostic and laboratory tests, which will be performed as part of this study, are provided at no cost to you. There will be no cost for the study treatment that you will receive.

Payment for participation

You will receive no payment for participating in this study. There will be no extra costs for you because the study will not prolong the admission of your child to the Winnipeg Children's Hospital.

Alternatives

If you do not want to participate, your child will still receive the standard chest physiotherapy for airway clearance during the hospital admission.

Confidentiality

Information gathered in this research study may be published or presented in public forums, however you and your child's name and other identifying information will not be used or revealed. Medical records that contain your child's identity will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. Despite efforts to keep your child's personal information confidential, absolute confidentiality cannot be guaranteed.

Your child's personal information may be disclosed if required by law. All study documents related to you and your child will bear only your assigned patient number (or code) and /or initials. Computer files with you and your child's

personal information and measurements from the study will be kept in a secure place with access only to the investigators at the Winnipeg Children's Hospital.

The Health Sciences Foundation as sponsor of this project may access data files at the offices of the investigators for quality assurance. The University of Manitoba Biomedical Research Ethics Board may also review research-related records for quality assurance purposes.

All records will be kept in a locked secure area and only those persons identified will have access to these records. If any of your child's medical/research records need to be copied to any of the above, you and your child's name and all identifying information will be removed. No information revealing any personal information such as name, address or telephone number will leave the Winnipeg Children's Hospital.

The admitting physician of your child will be notified about his/her participation in this study.

Voluntary Participation/Withdrawal From the Study

Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect your child's other medical care at this site. If the investigators feel that it is in your child's best interest to withdraw from the study, they will remove him/her without your consent.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

Medical Care for Injury Related to the Study

In the case of injury or illness resulting from this study, necessary medical treatment will be available at no additional cost to you. You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) or the sponsor(s) from their legal and professional responsibilities.

Questions

You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study or if you have a research-related injury, contact the study staff, Mrs. Heather Jenkins at 787-2641, or the study doctor, Dr. Hans Pasterkamp at 787-4753.

For questions about your rights as a research participant, you may contact The University of Manitoba Biomedical Research Ethics Board at (204) 789-3389

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Statement of Consent

I have read this consent form. I have had the opportunity to discuss this research study with Mrs. Heather Jenkins and /or her study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statement or implied statements. Any relationship (such as employee, student or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my participation in this clinical trial is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that information regarding my child's personal identity will be kept confidential, but that confidentiality is not guaranteed. I authorize the inspection of my child's medical records by the Health Sciences Foundation and The University of Manitoba Biomedical Research Ethics Board.

By signing this consent form, I have not waived any of the legal rights that my child has as a participant in a research study.

I agree to being contacted in relation to this study. Yes ☐ No ☐

Parent/legal guardian's signature_____ Date _____
(day/month/year)

Parent/legal guardian's printed name: _____

Child's signature _____ Date _____
(day/month/year)

Child's printed name: _____

I, the undersigned, attest that the information in the Participant Information and Consent Form was accurately explained to and apparently understood by the participant or the participant's legally acceptable representative and that consent to participate in this study was freely given by the participant or the participant's legally acceptable representative.

Witness signature_____ Date _____
(day/month/year)

Witness printed name: _____

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name: _____Date _____
(day/month/year)

Signature: _____

Role in the study: _____

Appendix B: Assent Form

Physiotherapy – Child Health

CHILDREN'S HOSPITAL
840 Sherbrook Street (Rm CH246)
Winnipeg, MB R3A 1S1

Ph # (204) 787-2641
Fax # (204) 787-1965

ASSENT FORM

STUDY TITLE: EFFECT OF A VOLUME STACKING MASK ON THE RESPIRATORY STATUS IN CHILDREN

Investigators: Heather Jenkins, B.M.R. (PT), Dr. Hans Pasterkamp

WHY YOU ARE HERE?

The physiotherapists want to tell you about a study about children with muscle weakness. They want to see if you would like to be in this study. This form tells you about the study. If there is anything you do not understand, please ask your parent, your guardian or the study staff.

WHY ARE THEY DOING THIS STUDY?

They want to see if a special mask that you would breathe through can help you to take deeper breaths.

WHAT WILL HAPPEN TO YOU?

The study will be done on a day when you are almost ready to go home. The mask will be used when you receive your regular chest physiotherapy. The mask will be held to your face and will cover your nose and mouth. You can breathe through the mask. For a few breaths only, either during the morning or the afternoon chest physiotherapy, the mask will only allow you to breathe in but not out. This will stack one breath on top of the other. After 15 seconds, the mask will again allow you to breathe out. The mask measures your breathing and sends these measurements to a computer. The physiotherapist will also listen to your chest and use an oximeter (a finger clip that uses light) to measure your oxygen level.

Will the study hurt?

It will not hurt when they put the mask on your face.

WILL YOU GET BETTER IF YOU ARE IN THE STUDY?

This study may not make you feel better or get well. But the doctors might find out something that will help other children like you later.

WHAT IF YOU HAVE ANY QUESTIONS?

You can ask questions any time, now or later. You can talk to the physiotherapist or doctors, your family or someone else.

WHO WILL KNOW WHAT I DID IN THE STUDY?

Any information you give to the study staff will be kept private (or secret). Your name will not be on any study paper and no one but the study staff and your family doctor will know that it was you who was in the study.

DO YOU HAVE TO BE IN THE STUDY?

You do not have to be in the study. No one will be mad at you if you don't want to do this. If you don't want to be in this study, just say so. We will also ask your parents if they would like you to be in the study. Even if your parents want you to be in the study you can still say no. The physiotherapist will still take care of your chest physiotherapy. Even if you say yes now you can change your mind later. It's up to you.

Do you have any questions?

Assent

I want to take part in this study. I know I can change my mind at any time.

_____ **Verbal assent given Yes** ☐

Print name of child

Written assent if the child chooses to sign the assent.

_____ _____ _____

Signature of Child **Age** **Date**

I confirm that I have explained the study to the participant to the extent compatible with the participants understanding, and that the participant has agreed to be in the study.

_____	_____	_____
Printed name of Person obtaining assent	**Signature of Person obtaining assent**	**Date**