Assessment of Pulmonary Function in Childhood Neuromuscular Weakness

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Abstract

Children with neuromuscular weakness may have severe or progressive weakness that results in pulmonary restriction. Weakness can also result in spinal deformity that worsens the pulmonary restriction. Corrective spinal surgery carries significant respiratory risk. Accurate respiratory assessment is important for pre-operative risk assessment.

Aims: 1) to evaluate the current clinical practice of pulmonary function testing and their role in respiratory assessment in children with neuromuscular weakness undergoing corrective spinal surgery and 2) to develop a precise method of predicting pulmonary function tests in children with neuromuscular weakness.

Methods: A retrospective review of pulmonary function in children with neuromuscular weakness undergoing corrective spinal surgery was undertaken to determine the use of pulmonary function tests in pre-operative assessment, and the impact of surgery on pulmonary function. Inaccuracies in prediction of normal values of pulmonary function in this group, and in children with neuromuscular weakness across Australia were identified. A new method of prediction of pulmonary function that is precise, reproducible and is an accurate predictor of height and pulmonary function was developed. This method was tested in children with Duchenne muscular dystrophy. The effect of intelligence and behaviour on performance of pulmonary function tests in Duchenne muscular dystrophy was investigated.

Results: Pulmonary function tests are the main respiratory assessment tool used pre-operatively in children with neuromuscular weakness undergoing corrective spinal surgery. Pulmonary function falls acutely by 11.14% following corrective spinal surgery, but the rate of decline in pulmonary function is slowed post-operatively from 5.14%/year to 0.99% per year. Estimation of height and pulmonary function is imprecise in this group, and throughout Australia. Ulna length measurement is an accurate and reproducible measurement that can be used to precisely predict height ($R^2$: males 0.96, females 0.94) and pulmonary function ($R^2$ for forced vital capacity: males 0.86, females 0.83) in children with neuromuscular weakness. It is readily measured in children with Duchenne muscular dystrophy. Ulna growth charts have been developed. Children who have an Asian background are anthropometrically
distinct and in females prediction equations are significantly different ($p$ for forced vital capacity: 0.009). Intelligence (for forced vital capacity: $r=0.49$, $p=0.003$) but not behaviour ($p$ 0.070-0.90) influences the performance of pulmonary function tests in children with Duchenne muscular dystrophy, and computerised visual incentives tend to improve the results ($p$ 0.06).

**Conclusion:** Pulmonary function tests are an important component of pre-operative respiratory risk assessment in children with neuromuscular weakness, and pulmonary function is altered by corrective spinal surgery. The ulna length is a precise predictor of height and pulmonary function and it is easily measured in children with neuromuscular weakness. When performing pulmonary function tests in children with Duchenne muscular dystrophy, intelligence may impact on the performance of the test, and computerised visual incentives may facilitate teaching the technique required.
Declaration

This is to certify that:
i) The thesis comprises only my original work towards the MD,
ii) due acknowledgement has been made in the text to all other material used,
iii) The thesis is less than 40 000 words in length, exclusive of tables, maps, references and appendices.

Preface

The work was carried out in collaboration with A/Prof Colin Robertson who provided advice and supervision of the progress of the work throughout.

Acknowledgements

I am grateful for the advice and support of my supervisor, Colin Robertson throughout all phases of work towards this thesis. I am appreciative of the research assistance provided by Johanna Kappers, Kate Briggs, Antonia Stewart, Alison Boynton and Grant Betts. I would like to acknowledge the statistical advice and assistance provided by John Carlin and Suzzanah Vidmar and the patience and support provided by the staff of the respiratory departments of the Royal Children’s Hospital in Melbourne, and the Sydney Children’s Hospital.
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Introduction

Neuromuscular disorders are an important cause of respiratory morbidity and mortality in childhood.\textsuperscript{1-3} The group constitutes a diverse range of pathologies and clinical phenotypes.\textsuperscript{4} Although similarities exist, there are important differences in the time of onset, severity, distribution of weakness, progression of disease and related comorbidities that influence the respiratory status and the need for, and timing of interventions.\textsuperscript{5,6}

Children with neuromuscular weakness can develop a restrictive pulmonary defect.\textsuperscript{1,7-10} Weakness commonly leads to spinal deformity that compounds pulmonary restriction.\textsuperscript{1-3,11} Both muscle weakness and the spinal deformity may be progressive, leading to respiratory decline.\textsuperscript{10,12-16} Respiratory compromise is a common cause of morbidity and mortality and respiratory failure is the cause of death in 55-90\% of children with Duchenne muscular dystrophy.\textsuperscript{17,18} Progressive weakness may result in sleep-disordered breathing and respiratory failure. Thorough respiratory assessment is essential in monitoring progress, pre-operative risk assessment, guiding investigations for sleep-disordered breathing and prognostication.\textsuperscript{19-26} In recent times, techniques to assist in mucociliary clearance have evolved, and home-based non-invasive ventilation for sleep-disordered breathing and respiratory failure has expanded.\textsuperscript{1,27-29}

Neuropathic spinal deformity forms as a result of muscle weakness and its secondary effects on the bones.\textsuperscript{6} It is often relentlessly progressive and requires surgical fixation to improve quality of life and minimise the requirements for nursing care.\textsuperscript{14,30-34} Corrective spinal surgery is a major procedure that carries great risk.\textsuperscript{28,29,34-38} Pre-operative risk evaluation and planning of management strategies is essential in improving outcomes. The peri-operative use of techniques to assist mucociliary clearance and non-invasive ventilatory support may reduce operative risk.
Pulmonary function tests are currently the main respiratory assessment tool used in clinical practice, but have some limitations. Lung growth occurs throughout childhood, and normal pulmonary function parameters relate to height. Predicted values of pulmonary function tests take the expected growth of childhood into account and provide a comparison to normals. Children with neuromuscular weakness are often unable to stand to have their height measured, or have spinal deformities making height measurement inaccurate. Arm span has been substituted but is imprecise in the presence of weakness, joint or spinal deformity. No better method of prediction of pulmonary function currently exists. Performance of pulmonary function tests is effort dependent and the technique required is complex requiring understanding, concentration and practice.

The aims of this work are 1) to evaluate the current clinical practice of pulmonary function testing and their role in respiratory assessment in children with neuromuscular weakness undergoing corrective spinal surgery and 2) to develop a precise method of predicting pulmonary function tests in children with neuromuscular weakness.
2

Background

This chapter provides a structure with which to consider neuromuscular disorders as a whole and to outline the important similarities and differences between the neuromuscular disorders that are common in childhood. The pathogenesis, progression and treatment of spinal deformities, and how weakness and spinal deformity impact on the developing respiratory system will be addressed. The nature of the respiratory compromise, its assessment and the techniques available to assist mucociliary clearance and provide respiratory support will be outlined.

Neuromuscular Disorders

Neuromuscular disorders are a group of conditions that affect the anterior horn cells of the spinal cord, peripheral nerves, neuromuscular junctions or the muscles themselves.\textsuperscript{4,46} The common feature of all neuromuscular disorders is muscle weakness. Disorders of the central nervous system are not generally included, although weakness is frequently present, and many of the same principals apply. There is variation in the clinical and investigative features of the various neuromuscular disorders, and some clinical diversity between children with the same disorder. The effect muscle weakness has on the body relates closely to the age of onset of symptoms and signs, the distribution of affected muscles, the rate of progression of disease and the severity of weakness.\textsuperscript{4}

Neuromuscular disorders are classified by the site primarily affected.\textsuperscript{4,46} An overview of the classification is shown in Table 1. It is useful to think of neuromuscular disorders in the subgroups of this classification, as it assists with the diagnostic
Table 1: Overview of the classification of the more common childhood neuromuscular disorders.

<table>
<thead>
<tr>
<th>Anterior Horn Cell Disorders</th>
<th>Neuromuscular junction Disorders</th>
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<tbody>
<tr>
<td><strong>Spinal Muscular Atrophy</strong></td>
<td><strong>Myasthenia Gravis</strong></td>
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<tr>
<td>Type I</td>
<td>Neonatal</td>
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<td>II</td>
<td>Infantile</td>
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<td>III</td>
<td>Adult</td>
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<td>Botulism</td>
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<td>Multifocal Motor Neuropathy</td>
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<th>Axonal</th>
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<td>Guillain Barre Syndrome</td>
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<td>Subacute</td>
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<td>Chronic Inflammatory Demyelinating Neuropathy</td>
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<td>Hereditary</td>
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<td>Autoimmune</td>
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<td>Dysproteinaemia</td>
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<td>Toxin</td>
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<td>Dysproteinaemia</td>
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<td>Becker Muscular Dystrophy</td>
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<td>Limb Girdle Muscular Dystrophy</td>
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<td>Fasioscapulohumeral Muscular Dystrophy</td>
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<td>Occulopharyngeal Muscular Dystrophy</td>
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<td>Emery Dreifuss Syndrome</td>
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<td>Congenital Muscular Dystrophy</td>
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<td>Nemaline (Rod) Myopathy</td>
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<td>Multicore Myopathy</td>
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<td>Myotubular (Centronuclear) Myopathy</td>
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<td>Disorders of glucose metabolism</td>
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<td>Hypothyroidism</td>
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process. The pattern of disease, age of onset and family history provide diagnostic clues. Clinical signs vary in relation to the primary site affected. Upper motor neurone signs, such as hypertonia, hyperreflexia and positive plantar responses are not generally a feature, as the primary lesion is not a central one. Tone and power are typically reduced. Reflexes are reduced in anterior horn cell disorders and motor neuropathies. Reflexes may be normal in other neuromuscular disorders, but can be reduced if severe weakness is a feature. Fasciculations may be seen in anterior horn cell disorders. Sensory or autonomic deficits may be present in the peripheral neuropathies affecting sensory or autonomic neurones respectively. Clinical signs may be intermittent and fatigable in the neuromuscular junction disorder myasthenia gravis. In other neuromuscular disorders, clinical signs are static or progressive. Muscle atrophy frequently results. The rate of progression and presence or absence of coomorbidities, such as cardiac or neurological disease, can also assist in diagnosis.

Several investigations may assist with attaining a specific diagnosis. Table 2 provides an outline of the examination and investigative findings typically found in the subgroups of neuromuscular disorders. When muscles are damaged, creatinine phosphokinase is released into the blood stream. It can be greatly elevated when inflammation of muscle occurs, such as in the inflammatory myopathies. It is generally normal in the neuropathies and neuromuscular junction disorders. Nerve conduction studies, electromyography and biopsies are important tools in differentiating diseases of the nerve from those of the muscle.

Nerve conduction studies are performed by applying maximal electrical stimuli to motor or sensory nerves and recording evoked responses. In peripheral neuropathies with axonal damage normal to near normal velocities with reduced amplitudes are seen. In peripheral neuropathies with predominant demyelination the conduction velocity is markedly reduced. Electromyography uses random sampling of action potentials from several areas of a muscle to localise, amplify, record and measure electrical activity at rest (insertional activity) and the activity produced by voluntary contraction (interference pattern). In diseases of muscle, the average amplitude of individual motor units is decreased. There is a reduction in the mean duration of motor potentials, and polyphasic potentials are more frequent. Diseases of upper and lower motor neurons have a reduction in the density pattern of activity on maximal
Table 2: Clinical features which assist in localising neuromuscular disorders.

<table>
<thead>
<tr>
<th></th>
<th>Anterior Horn Cell Disorder</th>
<th>Peripheral Neuropathy</th>
<th>Neuromuscular Junction Disorder</th>
<th>Myopathy</th>
</tr>
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<tr>
<td>Muscle atrophy</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>+++</td>
<td>rare</td>
<td>-</td>
<td>-</td>
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<td>Sensory changes</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
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<td>Reflexes</td>
<td>Normal or ↓</td>
<td>Decreased or absent</td>
<td>Normal</td>
<td>Normal unless very weak</td>
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<tr>
<td>Creatinine phosphokinase Level</td>
<td>Normal to ↑</td>
<td>Normal</td>
<td>Normal</td>
<td>↑ to ↑↑↑</td>
</tr>
<tr>
<td>Nerve conduction studies</td>
<td>↓ CMAP*</td>
<td>Demyelinating diseases - slowed conduction velocity Axonal diseases - ↓ CMAP* amplitudes</td>
<td>CMAP* amplitude decrement with repetitive stimulation</td>
<td>Normal</td>
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<tr>
<td>Electromyogram</td>
<td>MUP↑↑ amplitude and duration</td>
<td>MUP↑↑ amplitude and duration</td>
<td>MUP↑↑ amplitude and duration</td>
<td>MUP↑↑ amplitude and duration</td>
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<tr>
<td>Muscle Biopsy</td>
<td>Grouped atrophy Type grouping Angulated fibres</td>
<td>Grouped atrophy Type grouping Angulated fibres</td>
<td>Normal</td>
<td>Specific biopsy findings depend on aetiology</td>
</tr>
</tbody>
</table>

*Compound muscle action potential; †Motor unit potential.

Adapted from Anderson, et al. 1999"
contraction. The mean duration of individual motor unit potentials is increased. In diseases of the peripheral nerve or anterior horn cell the amplitude is reduced. Nerve biopsy can aid in the differentiation between axonal and demyelinating neuropathies. Selection of an appropriate nerve is essential to ensure that the biopsied nerve is involved, and is accessible. Muscle biopsy can also be diagnostic. Site selection should consider disease activity in the prospective muscle so that the disease process is not “burned out,” and useful information can be obtained. Special stains are often required, as many muscle disorders appear similar.

Many neuromuscular disorders have associated genetic abnormalities that may lead to a specific diagnosis, and aid in genetic counselling. Molecular genetics is currently undergoing dramatic expansion. As new mutations are found many of the conditions displaying clinical diversity have been found to have several underlying genetic mutations leading to their phenotype. Our understanding of these conditions, and subgroup classification is likely to be further modified as more discoveries are made.

**Anterior Horn Cell Disorders**

Motor neurone disorders affect the efferent motor neurones arising in the anterior horns of the spinal cord and brain stem. Their axons supply voluntary muscles. These disorders lead to signs of lower motor neurone dysfunction, such as hypotonia, hyporeflexia, negative plantar responses, muscle weakness and wasting. Fasciculations are common. Poliomyelitis and Spinal muscular atrophy are important motor neurone disorders of childhood.

Poliomyelitis is an infectious disease that was a major cause of anterior horn cell damage and dysfunction in the past. Routine vaccination has made it rare in first world communities. Cases are usually associated with live virus vaccination. It remains problematic in developing countries where subsequent weakness and paralysis, including respiratory paralysis are not uncommon. Ninety percent of infections are asymptomatic or have only minor malaise. One to five percent of infections develop weakness. Any anterior horn cell of the spinal cord or cranial
nerves may be involved, and distribution varies. The most widespread forms are seen in infants. Treatment is supportive.\textsuperscript{47,50}

Spinal muscular atrophy is caused by degeneration of anterior horn cells in the spinal cord and brainstem, leading to symmetric weakness.\textsuperscript{47,51} Fasciculations are often confined to the tongue. Muscle weakness tends to be stable for prolonged periods unlike many of the relentlessly progressive neuromuscular disorders.\textsuperscript{52} Children are mentally alert. Three phenotypes exist:\textsuperscript{47,51,53}

\textit{SMA Type I} (Werdnig-Hoffman disease) begins before 6 months of age and may be evident in utero.\textsuperscript{47,51,53} Motor milestones are not reached. Children do not sit unassisted. Respiratory muscles are weak, leading to recurrent respiratory infections, and death from respiratory failure, generally before 2 years of age.

\textit{SMA Type II} (Intermediate Type SMA) presents between 6 and 18 months. Motor milestones are delayed.\textsuperscript{53} Children often sit, but do not stand unassisted or walk. Respiratory muscle weakness leads to recurrent chest infections and death by the second decade. Progressive paralytic scoliosis is common and hastens respiratory decline.\textsuperscript{52}

\textit{SMA Type III} (Kugelberg-Welander Disease) presents after 18 months of age when motor milestones are no longer gained or are lost.\textsuperscript{4} Children do walk, but differences in motor function between these children and their peers become apparent. Respiratory compromise and repeated respiratory infections occur as weakness progresses, and this eventually leads to death in young adulthood. Neuropathic scoliosis is common and hastens respiratory decline.\textsuperscript{52}

Spinal muscular atrophy is the second most frequent autosomal recessive disease of childhood, affecting 1/6000-8000 live births.\textsuperscript{53} Rare cohorts of autosomal dominant inheritance exist.\textsuperscript{47} Families with multiple children affected usually show concordance for disease severity, but there are occasionally different phenotypes within the same family.\textsuperscript{47,51,53} Genetic mutations may be found in the Survival Motor Neuron or Neuronal Apoptosis Inhibitory Protein locuses on chromosomeSq11.2-13.3.\textsuperscript{53,54}
Peripheral Neuropathies

The peripheral neuropathies are a mixed group of disorders that primarily affect peripheral nerves. The distribution varies and may be distal or proximal, symmetrical or asymmetrical. Motor, sensory or autonomic nerves may be affected alone or in combination. There may be only one or several nerves involved, leading to further classification:55,56

*Mononeuropathy:* focal involvement of a single nerve trunk.

*Mononeuritis multiplex:* simultaneous or sequential involvement of individual, non-contiguous nerve trunks, either partially or completely, evolving over days to years.

*Polyneuropathy:* widespread nerve involvement.

Clinical symptoms and signs follow the distribution of nerve(s) involved, and relate to the type of nerve affected.55 Motor neuropathies have reduced reflexes and weakness, whereas sensory and autonomic neuropathies have good preservation of reflexes and strength. Nerve conduction studies are frequently diagnostic. Peripheral neuropathies can be inherited or acquired. The inherited neuropathies most commonly seen in childhood are Charcot-Marie Tooth Disease and Fredreich's Ataxia. Secondary neuropathies include the inflammatory neuropathies, and those secondary to toxins or metabolic disorders that are rare in childhood, and may be elicited from history or investigation of systemic disorders.

Charcot-Marie Tooth disease is the most common inherited peripheral neuropathy. It affects 1/2500 children.56 The onset of Charcot-Marie Tooth disease ranges from infancy to the teenage years.47 There is progressive, distal sensory loss, and loss of deep tendon reflexes. As the disease progresses, there is muscle atrophy, hammertoes, pes cavus, champagne legs, and if severe, wasting of the intrinsic muscles of the hands.47,53 Scoliosis occurs in 10-30%, but respiratory failure is seldom seen.52 Four types are recognized:47,53
Type I is due to demyelination leading to reduced nerve conduction velocities. Nerve biopsy shows onion bulb formations due to demyelination and remyelination.

Type II is due to axonal damage leading to reduced amplitudes on nerve conduction studies.

Type III (Dejerine-Sottas Syndrome) is a severe demyelinating form. Patients also have short stature and a characteristic facial appearance.

The X-linked form has both demyelinating and axonal features.

The inheritance patterns seen in Charcot-Marie-Tooth disease vary and may be autosomal dominant, autosomal recessive or X-linked. There is not a simple correlation between genotype and phenotype, or inheritance pattern. Genetic defects have been found in peripheral myelin protein 22 (22q11.2), myelin protein 0 (1q22-23), connexin 32 (X chromosome) or early growth response 2 gene (10q21.1-22.1) locuses.

Friedreich’s Ataxia is a spinocerebellar degenerative disease that begins before 20 years of age. Clinical features include progressive ataxia, dysarthria, decreased proprioception and/or vibration sense, muscle weakness and absent deep tendon reflexes. Kyphoscoliosis, cardiomyopathy and pes cavus are not uncommon. Inheritance is autosomal recessive, and the underlying genetic defect is a triplet repeat mutation of the mitochondrial protein frataxin encoded on 9q21.

Guillain-Barré Syndrome (or acute inflammatory demyelinating polyneuropathy) and chronic inflammatory demyelinating polyneuropathy occur in all age groups. Both are thought to be immune mediated, and generally follow viral illnesses. Ascending, symmetric weakness, paraesthesia and areflexia are seen. Both conditions are multifocal demyelinating neuropathies and can be distinguished from hereditary neuropathies by nerve conduction studies. Chronic inflammatory demyelinating polyneuropathy differs from Guillain-Barré Syndrome in that it continues to progress for longer than eight weeks from its onset, and is responsive to prednisolone. Both
conditions respond to intravenous immunoglobulin and plasmapheresis. Respiratory failure can occur but spinal deformity is seldom present.

**Disorders of the Neuromuscular Junction**

Conduction of nerve impulses to the muscle occurs across the neuromuscular junction. Disorders of the neuromuscular junction occur when there is an intrinsic abnormality of nerve to muscle transmission or blockade of this transmission.

Myasthenia gravis is the most common neuromuscular junction disorder. There are three types:

1. Autoimmune myasthenia gravis
2. Transient neonatal myasthenia gravis
3. Congenital myasthenia gravis

Acetylcholine (ACh) is released from nerve terminals upon stimulation of the nerve. It travels across the synaptic cleft to the post-synaptic muscle membrane, where it combines with ACh receptors stimulating them. When a number of receptors are stimulated the muscle membrane is depolarised, resulting in an action potential and muscle contraction. The ACh that does not quickly combine with ACh receptors is degraded by acetylcholinesterase (which is present within the synaptic cleft) to choline and acetate. The nerve terminal takes up the choline where it is reused to make more ACh. In autoimmune myasthenia gravis, anticholinesterase antibodies are present. These antibodies prevent the action of acetylcholinesterase so that ACh is not broken down in the synaptic cleft, and choline is not reutilised. This results in a reduction of ACh released with further nerve stimulation leading to a decremental response in muscle contraction. ACh receptors become down regulated due to slow and incomplete degradation of ACh.

Autoimmune myasthenia gravis normally begins in adulthood, but in 10-15% of patients it begins in childhood or adolescence. Clinically, there is increased fatigability, ptosis, diplopia and limb weakness. Crises can occur and cause
respiratory compromise or failure. In adults with autoimmune myasthenia gravis 85-90% have measurable anticholinesterase receptor antibodies, but this is far less common in childhood. The Tensilon test is diagnostic; an anticholinesterase inhibitor is administered resulting in clinical improvement in autoimmune myasthenia gravis, but not other neuropathies. Diagnosis is confirmed by repetitive nerve stimulation. In autoimmune myasthenia gravis, a greater than 10% decrement of the compound muscle action potential is found. Adults with autoimmune myasthenia gravis commonly have associated thymomas, and thymectomy is advocated as it may lead to long-term clinical improvement. In childhood thymectomy remains controversial, as there is little controlled data on its benefit. Anticholinesterase inhibitors relieve symptoms, but do not alter the long-term course. Plasma exchange, intravenous immunoglobulin, prednisolone, azathioprine and cyclophosphamide are effective in those with disabling ocular or significant systemic symptoms.85,86

Neonatal myasthenia gravis can be seen in newborns of mothers with autoimmune myasthenia gravis.87 It results from trans-placental transfer of anticholinesterase antibodies to the foetus. Affected neonates can have weakness and hypotonia within the first 3 days of post-natal life, leading to feeding difficulties and a weak cry. Respiratory failure is rare and treatment is supportive. Full recovery is expected within 2-3 weeks, as maternal antibodies are degraded.

Congenital Myasthenia Gravis is a rare, heterogeneous group of hereditary disorders of neuromuscular transmission.84,87 This group of disorders is persistent and usually non-progressive. Remissions and crises are rare. It includes end-plate acetylcholinesterase deficiency, slow channel syndrome, defects of acetylcholine synthesis or mobilisation and congenital deficiency of acetylcholine receptors.

Infantile botulism is generally caused by ingestion of the Clostridium botulinum organism, which colonises the intestinal tract and produces toxin.87 The toxin destroys the terminal twigs of cholinergic nerves, which take several months to regenerate.89 In children and adults, it is generally the toxin that is ingested from food contaminated with spores.87,89 The clinical syndrome varies from mild weakness to severe, life-threatening paralysis. Ocular, bulbar, limb and respiratory muscle weakness are
common. EMG confirms the diagnosis, and treatment is supportive, as neither antibiotics nor anti-toxin influence the disease course.\textsuperscript{47}

**Disorders of Muscle**

Disorders that primarily involve muscle lead to hypotonia, weakness and muscle atrophy.\textsuperscript{60} If weakness is severe, reflexes may be reduced or absent, but plantar responses will remain negative. The conditions primarily affecting muscle are classified by aetiology and histology. Congenital muscular dystrophies are genetically determined myopathies, not associated with specific ultra structural abnormalities, but with dystrophic changes on muscle biopsy (increased connective tissue, degenerating and regenerating muscle fibres and marked variation in fibre size). Inflammatory myopathies are autoimune in nature, and are associated with other autoimmune diseases. Hereditary myopathies have distinct histological features and are recognized as genetic from kindred analysis.

**Congenital Muscular Dystrophies**

Duchenne Muscular Dystrophy (DMD) generally presents between 3 and 5 years of age with progressive proximal weakness.\textsuperscript{4,52} Children have difficulty walking, frequently fall over, or are unable to progress through motor milestones, such as walking up steps, jumping or skipping.\textsuperscript{4} Weakness progresses throughout childhood, and mobility is lost by 12 years.\textsuperscript{4,52} Muscles, particularly of the calf, demonstrate pseudohypertrophy.\textsuperscript{52,61} Serum creatinine phosphokinase levels are greatly elevated.\textsuperscript{4} Mild mental impairment is generally present, and intelligence quotients are an average of one standard deviation below normal.\textsuperscript{4} Lung volumes increase at a slower rate, plateau earlier, at a lower level, and decline faster than in normal children.\textsuperscript{62} In teenage years, when wheelchair bound, paralytic scoliosis and hip dislocation become prominent.\textsuperscript{52} Death occurs usually in the second or third decade from respiratory failure.\textsuperscript{52} Cardiomyopathy is often present, and can lead to mortality. Patients are at risk of malignant hyperthermia. The incidence is 1/3500.\textsuperscript{4} Inheritance is X-linked recessive.\textsuperscript{63} Prednisolone can be used to preserve muscle strength in the short term, which maintains mobility for a longer period.\textsuperscript{51}
Becker Muscular Dystrophy (BMD) is usually diagnosed between 5 and 10 years of age. It begins with myalgias, muscle cramps and sometimes episodes of myoglobinuria. Progression is slow. Contractures and spinal deformities are infrequent. Immobility is rare before 15 years, and respiratory compromise does not become significant until adulthood. Death from respiratory failure is usually in mid-adult life. Intelligence is normal. Inheritance is X-linked recessive.

Dystrophin is a large cytoplasmic protein that is absent in DMD and reduced or abnormal in BMD. In DMD, "nonsense" mutations in the dystrophin gene lead to a frame shift that results in minimal production of a very abnormal, non-functional protein that does not resemble dystrophin. In BMD, a "missense" mutation occurs by removing or altering a triplet, without frame shifting, resulting in an abnormal dystrophin being produced, usually in a reduced amount. Approximately 60-70% of children with DMD and BMD have demonstrable mutations in the dystrophin gene. When molecular genetics are not included in diagnostic testing, approximately 40% of children diagnosed as BMD may in fact be misclassified as DMD. Dystrophin associated proteins may also have mutations. These proteins are present in muscles, the brain, and the heart.

Myotonic dystrophy is the second most common muscular dystrophy. It is a multi-system disorder. Clinically, patients have myotonia (increased muscle electrical irritability with reduced capability to relax), weakness and wasting of facial and limb muscles, frontal balding, cataracts, gonadal atrophy and cardiac conduction defects. Forty-seven per cent develop scoliosis. Patients are at risk of malignant hyperthermia. The genetic defect is an expansion of CTG repeats at the 3' end of a gene believed to encode a kinase (chromosome 19q13.1). Normal individuals have 5-30 repeats; those with Myotonic Dystrophy have more than 50 repeats. Inheritance is autosomal dominant and shows anticipation through the mother, so that disease severity increases in successive generations.

Limb girdle muscular dystrophies present with wasting and weakness of the pelvic and shoulder girdles. Serum creatinine phosphokinase is usually elevated. Type 1 limb girdle muscular dystrophy is autosomal dominant. Type 2 is autosomal recessive. There are at least eight different subtypes and each is due to a mutation.
affecting a sarcoglycan subunit, caplain (a calcium activated protease), or dysferlin (a protein with unknown function). Different mutations in these proteins lead to the broad variation in clinical phenotypes. Those with nonsense mutations leading to stop codons cause more severe phenotypes.

Emery-Dreifuss dystrophy has proximal muscle weakness but its predominant distinguishing feature is extensive joint contractures developing early in the course. There are often cardiac conduction disturbances that can lead to lethal arrhythmias. It is X-linked recessive and due to a mutation in the gene that encodes emerin, a nuclear protein of unknown function.

Congenital muscular dystrophies with central nervous system involvement include Fukuyama congenital muscular dystrophy, Walker-Warburg syndrome and Muscle-eye-brain disease. These conditions are associated with structural brain abnormalities, severe mental retardation and seizures. The remaining Congenital muscular dystrophies are without central nervous system involvement and are classified according to presence or absence of merosin. Congenital muscular dystrophies with merosin deficiency have a more severe course and have abnormal lucency of cerebral white matter on magnetic resonance imaging. They also have abnormal nerve conduction studies and evoked potentials. Congenital muscular dystrophies without merosin deficiency do not have these abnormalities.

Fascioscapulohumeral dystrophy is a heterogeneous group of disorders affecting 3-4 patients per million. The onset is variable between infancy and young adulthood. Children present with a weak smile, incomplete eyelid closure and decreased facial wrinkles. The lower lip protrudes, and there is inability to whistle or drink through a straw. Weakness of the trapezius, rhomboids and levator scapulae cause the scapulae to leave the chest wall when the arms are raised. Eventually shoulder abduction is lost due to instability of the scapulae. Some patients have weakness of the wrist extensors or anterior tibial muscles. Spinal deformity is common and includes paralytic scoliosis or hyperlordosis, alone or in combination. Inheritance is autosomal dominant. The involved gene is located at 4q35.
Inflammatory Myopathies

Dermatomyositis is an autoimmune mediated, systemic inflammatory disorder. It generally begins acutely with a violaceous rash of the eyelids, malar areas, and extensor surfaces of the knuckles and elbows. Children are often unwell, and may have temperatures and lethargy. Muscle tenderness is present in fifty per cent. A symmetric proximal weakness and atrophy ensues. The muscles of facial expression and extraocular muscles are spared. In some, progressive weakness and contractures occur, and it is fatal in 10%. In others it has a benign course. Scoliosis can occur, particularly when the onset is in early childhood. Generally the illness is only progressive for 1-3 years before becoming static, often with full recovery.

Dermatomyositis is caused by an idiopathic complement medicated microvasculopathy. It is associated with other autoimmune disorders, particularly mixed connective tissue disease. Calcinosis is not uncommon. In the early phases of dermatomyositis the erythrocyte sedimentation rate is elevated in fifty per cent, and the serum creatinine phosphokinase is usually modestly elevated. Electromyography shows myopathic changes. Muscle biopsy shows perivascular infiltration with B cells and CD4+ cells, without necrotic muscle fibres. Treatment consists of immunosuppression with prednisolone. Most respond well. When this is not effective, or when side effects are problematic, azathioprine, methotrexate or plasmapheresis may be useful.

Polymyositis is autoimmune and associated with other autoimmune disorders. It is more subacute and no rash occurs. It is often diagnosed later in its course. The clinical features are otherwise similar to dermatomyositis. The erythrocyte sedimentation rate may be elevated, and the serum creatinine phosphokinase is generally modestly elevated. Electromyography shows myopathic changes, and muscle biopsy shows cytotoxic T cell infiltration around healthy fibres and myofibres undergoing various stages of phagocytosis and necrosis. Treatment is similar to dermatomyositis.
Hereditary Myopathies

Hereditary myopathies are a heterogeneous group of hereditary muscle disorders with prominent muscle weakness and atrophy. Myopathies have traditionally been classified according to histological appearance. Children with the same diagnosis may have different genotypes, leading to different phenotypic presentations. Weakness is usually proximal and symmetrical. The legs are generally more severely affected than the arms. The course is usually slowly progressive. Onset can be in utero, in infancy, or later in life. Some are not diagnosed until adulthood. Children with these conditions have long, thin faces and high arched palates. Development of contractures, hip dislocations, foot deformities and kyphoscoliosis is not uncommon. Respiratory muscle weakness and respiratory failure often causes morbidity. Some hereditary myopathies involve other tissues, including cardiac muscle. Longevity varies with different phenotypes, but death is often due to respiratory failure.

Nemaline (Rod) myopathy presents in early childhood with hypotonia and developmental delay. Children have a narrow face, high arched palate and thin extremities. The voice often has a nasal quality. Children may learn to walk, but often later than their peers. Tenequinovarus and kyphoscoliosis often develop. The course is highly variable, but usually slowly progressive. Serum creatine phosphokinase is mildly elevated. Electromyography shows myopathic features. Muscle biopsy is diagnostic. Rod-like structures are seen which tend to group peripherally. There is type I muscle fibre predominance and atrophy. Four different genetic mutations, leading to different phenotypes, have been discovered. Inheritance can be autosomal dominant or X-linked dominant.

Central core disease presents in infancy with hypotonia and delayed motor milestones. Children never walk. Congenital hip dislocations, pes cavus, pes planus, tenequinoovarus and kyphoscoliosis are common. Weakness is slowly progressive. Deep tendon reflexes are generally preserved. The serum creatinine phosphokinase is normal or mildly elevated. The electromyogram shows myopathic disturbance. Muscle biopsy is diagnostic. Oxidative enzyme stains reveal discrete lucent areas in the centres of muscle fibres. Electron microscopy shows the cores to be devoid of mitochondria. The cores are predominantly in type I muscle fibres, which are the
predominant muscle type present. Inheritance is usually autosomal dominant. The genetic defect is a mutation in the gene encoding the ryanodine receptor. Malignant hyperthermia is also associated with mutations in the ryanodine receptor and patients are at risk of this. Myotubular (Centro-nuclear) myopathy has a variable, but usually early age of onset. Weakness involves proximal and distal muscles, facial muscles, and extraocular muscles. Deep tendon reflexes are decreased or absent. Seizures sometimes occur. Inheritance can be autosomal dominant, recessive or X-linked. Muscle biopsy shows muscle fibres all have central nuclei that are often lined up, and surrounded by a clear area with reduced enhancement with oxidative enzymes. There is type I muscle fibre predominance and atrophy.

Other rare hereditary myopathies are clinically similar, although the age of onset of symptoms and rates of progression vary, as do inheritance patterns. Their names are related mainly to their histological appearance: congenital fibre type disproportion, multicare disease, focal loss of cross striations, sarcotubular myopathy, reducing body myopathy and fingerprint body myopathy.

Clinical Variation

The effect muscle weakness has on the body in the short and long-term relates to its age of onset, distribution, severity and rate of progression. Weakness that is predominantly distal, has its greatest impact on mobility, which impedes quality of life. Predominantly proximal weakness, affecting the trunk has greater effects on the developing body. The earlier the onset, and the greater the severity and progression of proximal weakness, the greater the impact weakness will have on the growing spine and lungs. The vertebral column undergoes rapid growth during puberty, and the more severe the weakness present during this period, the more likely the development of spinal deformity, and the greater the severity of that deformity. The lungs grow throughout childhood, and earlier onset, greater severity and progression of proximal weakness lead to a greater impact on the growing thoracic cage and lungs, which do not grow to their potential, resulting in an earlier and more rapid decline in lung
function. Weakness in bulbar muscles may lead to recurrent aspiration. Table 3 summarises the usual age of onset of symptoms, distribution, progression of weakness and comorbidities particularly associated with many of the more common neuromuscular disorders.

Comorbidities have the potential to impact upon the respiratory, skeletal and other systems. Muscles other than the voluntary skeletal muscles may be affected. Cardiac muscle is not infrequently involved, leading to arrhythmias and cardiac failure. Nervous tissue involvement may lead to secondary involvement of other structures, such as the joint.

**Effects of Muscle Weakness**

Muscle weakness may limit motor development or if progressive, may lead to loss of motor milestones. Mobility is frequently impaired and this may necessitate the use of a wheelchair or other motor aids. Many motor tasks may still not be possible, leading to an impaired quality of life. Weakness of the muscles of the trunk can lead to spinal deformity and respiratory compromise. Sleep-disordered breathing may result from respiratory muscle weakness or loss of tone of the muscles of the upper airway or both. Respiratory failure and death may result, particularly when the weakness is progressive or the course is complicated by comorbidities or infections.

**Spinal Deformity**

Spinal deformity is common in many neuromuscular disorders. The spine is most vulnerable to deformity in young, pre-pubertal children, when the spine is growing, and the impact of weakness and bony remodelling is at its greatest. The most severe spinal deformities occur when truncal weakness begins in early childhood.

Muscle strength and tone support the spine. Without it, the spine is able to move unchecked, and its stability is reliant solely on bony stability. Contractures develop when movement is limited and the same posture is adopted for long periods, without
Table 3: Comparison of some important clinical features of neuromuscular disorders common in childhood.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Onset</th>
<th>Distribution</th>
<th>Progression</th>
<th>Common Specific Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Spinal Muscular Atrophy</em></td>
<td>1 - &lt;6 months</td>
<td></td>
<td>Rapid</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>II - 6-18 months</td>
<td></td>
<td>Relentless</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>III - &gt;18 months</td>
<td></td>
<td>Slow</td>
<td>-</td>
</tr>
<tr>
<td><em>Polio myelitis</em></td>
<td>Acute</td>
<td>Variable</td>
<td>Periods of stability but eventually progressive</td>
<td>-</td>
</tr>
<tr>
<td><em>Charcot Marie Tooth Disease</em></td>
<td>Infancy to teenage years</td>
<td>Peripheral</td>
<td>Slowly progresses more proximally</td>
<td>Joint deformity</td>
</tr>
<tr>
<td><em>Freidrick’s Ataxia</em></td>
<td>&lt;20 years</td>
<td>Peripheral</td>
<td>Slowly progressive</td>
<td>Cardiomyopathy</td>
</tr>
<tr>
<td><em>Inflammatory neuropathies</em></td>
<td>Acute</td>
<td>Generalised</td>
<td>Initially rapid followed by slow improvement</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>± resolution</td>
<td>-</td>
</tr>
<tr>
<td><em>Auto-immune myasthenia gravis</em></td>
<td>Adolescence - adulthood</td>
<td>Generalised</td>
<td>Usually intermittent, but occasionally</td>
<td>Thymomas</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>progressive weakness</td>
<td></td>
</tr>
<tr>
<td><em>Congenital Myasthenia Gravis</em></td>
<td>Infancy - early childhood</td>
<td>Generalised</td>
<td>Persistent and non-progressive</td>
<td>-</td>
</tr>
<tr>
<td><em>Duchenne Muscular Dystrophy</em></td>
<td>3-5 years</td>
<td>Generalised</td>
<td>Relentlessly progressive</td>
<td>Cardiomyopathy and conduction disturbance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Disorder</td>
<td>Age of Onset</td>
<td>Type of Muscle Involvement</td>
<td>Course of Disease</td>
<td>Associated Conditions</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-----------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>Becker Muscular Dystrophy</td>
<td>5-10 years</td>
<td>Generalised</td>
<td>Slowly progressive</td>
<td>Cardiomyopathy and conduction disturbance</td>
</tr>
<tr>
<td>Limb Girdle Muscular Dystrophy</td>
<td>Childhood - early adulthood</td>
<td>Predominant involvement is limb girdles, but other muscles may be affected Generalised</td>
<td>Variable</td>
<td>-</td>
</tr>
<tr>
<td>Myotonic Dystrophy</td>
<td>Neonatal - adulthood</td>
<td>Generalised</td>
<td>Variable</td>
<td>Cardiac conduction defects Malignant hyperthermia</td>
</tr>
<tr>
<td>Fasioscapulohumeral Muscular Dystrophy</td>
<td>Infant - adulthood</td>
<td>Predominantly face and upper limb girdle, but other muscles may be affected Generalised</td>
<td>Slowly progressive</td>
<td>-</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>Acute onset in childhood</td>
<td>Generalised</td>
<td>Slowly progressive</td>
<td>Rashes Auto-immune disorders</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>Childhood - early adulthood</td>
<td>Generalised</td>
<td>Slowly progressive</td>
<td>Auto-immune disorders</td>
</tr>
<tr>
<td>Nemaline Myopathy</td>
<td>Early childhood</td>
<td>Generalised</td>
<td>Slowly progressive</td>
<td>-</td>
</tr>
<tr>
<td>Central Core Disease</td>
<td>Infancy</td>
<td>Generalised</td>
<td>Severe progression</td>
<td>Malignant hyperthermia</td>
</tr>
<tr>
<td>Myotubular Myopathy</td>
<td>Childhood</td>
<td>Generalised</td>
<td>Variable</td>
<td>Seizures</td>
</tr>
</tbody>
</table>
placing joints through a variety of movements on a regular basis.\textsuperscript{52} Weakness limits movement. Weak children use certain postures to overcome weakness and assist with particular functions. Contracture progression may be slowed by continual movement of joints by physiotherapy. Hip contractures are common in neuromuscular weakness and generally progress asymmetrically altering the sitting posture and leading to pelvic tilt.\textsuperscript{5}

The sacrum forms the posterior wall of the pelvis. The spinal column sits on the sacrum, and its take-off is perpendicular to the pelvis. It relies on the pelvis for a stable base. Pelvic obliquity is failure of the pelvis to remain horizontal to the sitting surface.\textsuperscript{6} When pelvic obliquity exists, the spinal column still arises perpendicular to the pelvis, but this is not perpendicular to the sitting surface. To maintain an upright posture, the head must lie vertically above the pelvis. The spinal column must curve back towards a position centred above the pelvis to achieve this with pelvic obliquity. This is known as a compensatory curve.\textsuperscript{6} Pelvic obliquity is often also associated with a rotational deformity at the lumbosacral junction.

Bone is constantly remodelling. New bone formation is related to the workload of the bone and availability of metabolites. In immobilised children, weight bearing and workload are reduced, resulting in osteoporosis.\textsuperscript{6} Vitamin D is absorbed from the diet or through the skin from ultraviolet light exposure. Children with neuromuscular weakness are generally less active and spend less time in sunlight. Malnutrition is common. Osteomalacia occurs when vitamin D deficiency is present. It leads to a reduction in new bone formation, and reduced bone strength. The combination of osteoporosis and osteomalacia commonly results in weakened bone structure.\textsuperscript{6}

Any degree of spinal curvature places asymmetric forces on vertebral end plates. Bony remodelling begins to remodel the spine into the position it holds. The weakened bone structure collapses on the concave side of the curve, and overgrowth of bone occurs on the convex side.\textsuperscript{6} Rotation often develops as the forces placed on the spine alter. Remodelling leads to permanent disk, vertebral and facet joint alterations. The pattern of scoliosis is variable, unlike that seen in idiopathic scoliosis. It can include long or short curves, kyphosis or lordosis and variable degrees of rotation.\textsuperscript{6,76}
Children with proximal and truncal weakness (such as Spinal muscular atrophy and Duchenne muscular dystrophy) have a greater propensity towards spinal deformity. In Duchenne muscular dystrophy, equinovarus, knee and hip flexion contractures occur early. The centre of gravity while standing then lies posterior to the knees, and anterior to the hips, causing further flexion of the knee and hip joints. A compensatory lordosis of the lower spine develops. This seems to be protective against scoliosis by locking the facet joints to prevent lateral bending. As muscle weakness progresses, the ability to walk is lost, and children become wheelchair bound. The hips are placed in a position of greater flexion at most times, and contractures occur or progress.

Children with fascioscapulohumeral muscular dystrophy develop predominant hip extensor weakness. Hyper lordosis occurs to overcome this weakness and allow mobility to continue. Fixation in this situation is not generally performed as it usually results in loss of ambulation. In Emery Dreifuss muscular dystrophy contractures develop early and may be extensive and involve the hip joints. Once the deformity occurs, bony remodelling eventually evolves. In some neuromuscular disorders, the spinal deformity is independent of muscle strength. Scoliosis is seen in Friedreich’s Ataxia, but it is non-progressive, and unrelated to muscle weakness.

Spinal deformities often begin before loss of ambulation. It is present prior to loss of ambulation in fifteen per cent of children with Duchenne muscular dystrophy. While ambulatory, spinal deformity is generally mild and slowly progressive. Enough muscle strength is maintained to walk and to provide some spinal support. Mobility slows progression of contractures and allows exposure to sunlight. Contractures are often present, but not severe. The pelvis is generally stable. With loss of ambulation, movement of joints become less frequent, and contractures progress. Pelvic obliquity occurs. Bony condition worsens. Muscle strength continues to decline and spinal support is reduced. Spinal deformities worsen and permanent changes begin with remodelling of bone. In children with conditions that never gain ambulation (such as Spinal muscular atrophy type 1), spinal deformity begins early in life, sometimes in utero. Progression is quick, and severe deformity results. Loss of ambulation prior to the pubertal growth spurt is associated with more rapid and severe progression of scoliosis than that seen in older individuals. The younger the
child at loss of ambulation and onset of scoliosis, the greater the potential for progression.\textsuperscript{5,6,79,80}

Bracing, wheelchair modification and seating aids have been tried without success to slow progression of spinal deformity.\textsuperscript{6,30,37,81} The advantages of these techniques are that they assist with seating, and therefore, mobility and cosmesis. They are useful when corrective spinal surgery is not possible. The disadvantages are that these techniques often lead to a false belief that scoliosis progression will be slowed, and delay surgery in children with deteriorating respiratory status and a gradually increasing surgical risk.\textsuperscript{37,81} Thoracolumbar orthotic devices place pressure on the rib cage and abdomen that restrict thoracic cage and diaphragmatic movement.\textsuperscript{11,81,82} They can cause pressure areas and loss of skin integrity.\textsuperscript{5,6}

Progression of an untreated neuromuscular spinal deformity leads to pain, reduced sitting balance and an increase in mortality.\textsuperscript{32,83} When the scoliotic curve reaches forty degrees, truncal balance is lost necessitating the use of the upper limbs to maintain an upright position while seated.\textsuperscript{30} This reduces the functional capabilities of the upper limbs. Corrective spinal surgery leads to improved seating without the use of belts or lateral supports.\textsuperscript{14,30,31} It increases bimanual upper extremity freedom, which enhances the ability to interact with the environment and perform activities of daily living.\textsuperscript{14,31} Nursing care is generally simplified.\textsuperscript{14,31} Both patients and carers are generally satisfied that corrective spinal surgery improves quality of life and ease of nursing care.\textsuperscript{30,33}

**Respiratory Compromise**

Neuromuscular disorders involving the thoracic cage lead to a reduction in chest wall muscle contraction. These muscles eventually become fibrotic, shortened and stiffened.\textsuperscript{84} Articular contractures develop reducing chest wall compliance.\textsuperscript{8,84,85} Expansion of the lungs becomes incomplete and areas of microatelectasis occur. Muscle weakness generally does not improve over time, and areas of microatelectasis become chronic and lead to scarring and reduced pulmonary compliance.\textsuperscript{8,86-88} The reduction in pulmonary compliance is compounded by reduced elasticity and reduced
surfactant production from breathing at lower lung volumes. Recurrent episodes of aspiration or infection may also contribute. These changes lead to an alteration in gas distribution, and ventilation-perfusion mismatch.

Maintenance of chest wall and pulmonary compliance is dependent upon continued mobility. It is thought that reduction in compliance of both the chest wall and lungs may be slowed by continued expansion in the form of sighs. Sighs also stimulate the production and distribution of surfactant. In the early stages when children continue to breathe without assistance, physiotherapy is valuable. When ventilatory assistance is required, sighs can be instigated regularly. There is anecdotal evidence that this slows the fall in vital capacity by improving lung and chest wall compliance. However, hyperinsufflations were not found to alter pulmonary compliance in 10 patients with various neuromuscular disorders in the short-term.

In most neuromuscular disorders, including Duchenne muscular dystrophy and Spinal muscular atrophy, the muscles of expiration are affected earlier and more severely than those of inspiration. Expiration occurs passively due to the elastic recoil of the lung if pulmonary compliance is reasonable. Symptoms are often absent when the muscles of inspiration maintain good strength, and pulmonary compliance remains reasonable. The muscles of expiration are of great importance in the generation of cough. In other neuromuscular disorders, including Nemaline myopathy, the muscles of inspiration and expiration are affected equally, leading to an earlier onset of respiratory failure.

Weakness of the muscles of inspiration, including the diaphragm, is generally not seen until mobility is lost. Once the muscles of inspiration are weakened, symptoms begin. Shortness of breath on exertion and tachypnoea are not seen in the immobilised child. Nocturnal symptoms of orthopnea and sleep disordered breathing resulting in hypersonolence are more common, but not consistent.

As inspiratory muscle weakness advances, respiration during the day becomes more difficult. Abdominal and accessory muscles gain increasing importance in the provision of respiration leading to abdominal breathing. These muscles are also weakened. As weakness progresses, the muscles of respiration and accessory muscles
are unable to provide adequate strength to maintain ventilation. Children develop methods to overcome the weakness so that breathing occurs as efficiently as possible. In advanced stages of respiratory failure, some children use a rocking motion to press their abdomen against a supporting strap, which pushes the abdominal contents superiorly, raises the diaphragm and aids with expiration. Rocking back from the strap releases the pressure on abdominal contents, allowing them to fall with gravity, and aiding in inspiration.

A deformed and immobilised spine further restricts chest wall movement and compliance. It diminishes the efficiency of chest wall musculature by altering the length of the muscle and, therefore, their mechanical advantage. Scoliosis leads to compression of the ribs and chest wall on the concave side of the curve, with resultant compression of the underlying lung, and microatelectasis. On the convex side, the chest wall is held in a more expanded position. Gas distribution within the lungs is asymmetrical and ventilation-perfusion mismatch occurs. Lordosis results in a narrowed anterior-posterior chest cavity, with resultant compression of the underlying lung and atelectasis. Kyphosis reduces chest wall compliance. Bracing reduces lung function further by restricting chest wall and often diaphragmatic movement.

The combination of respiratory muscle weakness and spinal deformity that places these muscles at a mechanical disadvantage leads to a greater degree of pulmonary restriction and respiratory compromise than either component would alone.

**Sleep-Disordered Breathing**

Many of the first manifestations of respiratory compromise occur during sleep. During non-rapid eye movement sleep, the phasic activity of many medullary and pontine neurones is suppressed, including those innervating the hypoglossal motor neurones. Upper airway muscle tone is reduced leading to an increase in upper airway resistance, a reduction in tidal volume and hypoventilation. These changes are amplified during rapid eye movement sleep. The ventilatory response to hypercarbia is reduced to two thirds during rapid eye movement sleep.
During sleep children with neuromuscular weakness can get upper airways obstruction or hypoventilation. Increased upper airway resistance and obstruction can occur due to atonia in the already weak upper airway musculature and inability of weakened respiratory muscles to overcome the obstruction. Once the muscles of inspiration begin to weaken, breathing becomes more dependent on accessory muscles. During rapid eye movement sleep, these become atonic, and hypopnoeas begin to appear. Hypopnoeas are not truly central, but lack of movement of the weakened muscles occurs which mimics a central hypopnoea. Apnoeas appear as weakness progresses. Obstructive sleep apnoea severity may increase if obesity is present, and this is common in immobilised adolescents with Duchenne muscular dystrophy. Both “central” and obstructive apnoeas are evident on polysomnography.

During periods of hypopnoea and apnoea, hypoxemia and hypercarbia can occur. The severity of blood gas alterations relates to the severity and duration of the hypopnoea or apnoea, but can be striking. The child’s ventilatory response to the blood gas alterations is blunted during rapid eye movement sleep, so that marked alterations do not result in concomitant increases in minute ventilation. Many believe that the chemoreceptors adapt to the hypercarbia and hypoxemia, and the “set-point” is altered so that even during quiet sleep or wakefulness, responses to blood gas alterations are reduced compared to normal. Sleep-disordered breathing may exacerbate cardiomyopathy, daytime respiratory failure and cor pulmonale.

Orthopnea, fatigue, disturbed sleep and hypersomnolence symptoms may be present, but are often absent even when striking abnormalities exist. Daytime arterial blood gas analysis may be normal. Daytime symptoms and sleep questionnaires do not correlate well with polysomnography evidence of sleep-disordered breathing. Sleep disturbance is common even without sleep-disordered breathing, as many children with moderate or severe weakness are unable to turn themselves without waking, or require a caregiver to turn them, necessitating periods of wakefulness and reduced sleep quality. This may contribute to daytime tiredness.

Daytime measures have been found of some use in predicting sleep hypoventilation. In Duchenne muscular dystrophy, forced expiratory volume in
one second (FEV₁) <40% predicted is a sensitive, but non-specific indicator of sleep-disordered breathing. Arterial carbon dioxide levels (PaCO₂) ≥45 millimetres of mercury (mmHg) is sensitive and more specific (75%), base excess ≥4 millimoles per litre (mmol/l) is highly specific, but not sensitive (55%). It has been recommended in Duchenne muscular dystrophy, that PaCO₂ be measured when FEV₁ falls below 40% predicted, and polysomnography be performed if PaCO₂ is ≥45mmHg, particularly if the base excess is ≥4mmol/l. In a mixed group of children with neuromuscular weakness, an inspiratory vital capacity of <60% and a PaCO₂ of >40mmHg were found to be sensitive (97% and 92% respectively) and specific (88% and 72% respectively) for sleep-disordered breathing. Maximum inspiratory capacity <4 kilopascals was also predictive of sleep-disordered breathing but was less sensitive (87%) and specific (43%). Others have investigated an association between daytime measures and polysomnography findings in neuromuscular weakness, and been unable to demonstrate one. Sleep-disordered breathing has been found to occur prior to loss of ambulation, and when vital capacity is >70% predicted. Diagnosis depends on polysomnography, which is a time-consuming, inconvenient and expensive test.

**Respiratory Failure**

The respiratory muscles weaken with progression of the underlying neuromuscular disorder, leading to intrusion of the features of sleep-disordered breathing into daytime hours. When sleep-disordered breathing is present, the muscles of respiration need to work harder to overcome upper airway resistance, which places them under greater strain. This tires the weakening muscles. Upper airways resistance and obstruction may begin to occur during wakefulness, particularly if bulbar dysfunction is prominent. Hypoventilation due to insufficient effort by the weakened muscles of respiration eventually ensues. Spinal deformities that place respiratory muscles at a mechanical disadvantage worsen this. Respiratory chemoreceptors become accustomed to hypercarbia and hypoxia that occur during sleep disordered breathing, altering their “set-point.” This blunts the normal response of increasing minute ventilation in response to blood gas abnormalities. Hypercarbia, and hypoxia are not seen until late in the course of
disease. Areas of microatelectasis enlarge. The reduced compliance leads to an increased resistance to ventilation, which necessitates greater respiratory effort to overcome it and provide adequate ventilation. This puts further strain on the weakened muscles of respiration that are unable to cope with the additional effort required. Respiratory failure follows.

An effective cough requires a maximal inspiration to at least sixty per cent of total lung capacity, closure of the glottis, maintenance of glottal competence against rising expiratory pressure, and build up of expiratory pressure until the glottis is suddenly opened in conjunction with a maximal forceful expiration. Children with neuromuscular weakness may have deficits in each step of this pathway. Inspiratory muscle weakness impedes the maximal volume of air inspired. Weakness of the glottis impedes its competence, especially when expiratory pressure builds behind it. Expiratory muscle weakness impedes a maximal forced expiration when the glottis suddenly opens. Infections reduce the strength of muscles further.

Acute events such as upper respiratory tract infections or episodes of aspiration, put additional strain on the weakened muscles of respiration and can decompensate an already marginal system, causing death. Upper respiratory tract infections cause airway inflammation and increased secretion production. Secretions are moved centrally by airway cilia, bringing them to larger airways. An effective cough expels them from the larger airways. If they are not cleared, they cause obstruction, collapse, secondary infection and eventually scarring. Recognition and rapid intervention are essential to improve quality of life, reduce lung scarring and prolong longevity. Recurrent pneumonia secondary to upper respiratory tract infections is generally seen when the vital capacity falls below 30% predicted, or 1000 millilitres (ml). Risk of respiratory failure is considered high when the vital capacity is <800ml, the peak cough flow <270 litres per minute or there is a history of repeated chest infections.

Airway cilia can be damaged in lower respiratory tract infections. After an acute infection, they would generally return to normal function. If recurrent respiratory tract infections occur, scarring ensues, and cilia function is lost. Aspiration can result from weakness of the pharyngeal or laryngeal muscles or an incoordinate swallow. Each is common in children with neuromuscular disorders. Aspirated saliva,
food or gastric contents are noxious to the respiratory membranes, and lead to inflammation, increased secretion production and ciliary damage.

In children with progressive weakness involving the muscles of respiration indolent progression to respiratory failure is the norm even without acute events such as infection or aspiration that may hasten its progression. Respiratory failure is the cause of death in 55-90% of children with Duchenne muscular dystrophy.17,18

**Respiratory Assessment**

Respiratory assessment is essential in monitoring progress and guiding management of children with neuromuscular weakness. There are multiple respiratory assessment tools available.

**Spirometry**

Children with neuromuscular weakness and weakened muscles of respiration have reduced movement of the chest wall, which restricts the underlying lungs. A restrictive pulmonary defect is seen on spirometry. Reduced total lung capacity, vital capacity and functional residual capacity are seen.8,26,27 The degree of reduction is closely linked to the degree of muscle weakness. The residual volume is increased due to weakness of the expiratory muscles. A reduction in flow rates parallels the reduction in lung volumes, but reductions are more marked in the effort-dependent parts of the curve.

Vital capacity is dependent on inspiratory muscle strength and lung and thoracic cage size. In normal individuals, lungs grow throughout childhood. Vital capacity increases from birth until 19 years of age, after which it begins to fall at an average of 1-1.2% per year.41 In children with neuromuscular disorders lung growth is reduced. Vital capacity increases at a slower rate.34 The peak vital capacity is reached earlier, and is lower than that seen in normal individuals. The earlier the onset of respiratory muscle weakness and a restrictive pulmonary defect, the less lung growth will occur, and the
earlier and lower the peak vital capacity will be. Once the peak is reached, fall in vital capacity is much faster in children with neuromuscular weakness than in normal individuals.20

In children with Duchenne muscular dystrophy the vital capacity and other pulmonary volumes show a pathognomonic pattern of ascending, plateau and descending phases.62 Jenkins34 found that the observed vital capacity continues to climb for some time after the vital capacity % predicted begins to fall. This occurs because, although lung volumes are continuing to increase, they are doing so at a much slower rate than those of normal children, and disparity with predicted values is seen even before lung volumes begin to decline.109

The age of acquisition of the peak vital capacity, and the peak volume reached has prognostic implications. The lower and the earlier the peak vital capacity is reached, the worse the respiratory prognosis, and the shorter the lifespan. In Duchenne muscular dystrophy, the age at which the vital capacity falls below one litre is the best single predictor of subsequent survival.109 The peak vital capacity is reached between 10 and 15 years of age.62 If the peak is greater than 2.5 litres, the average rate of decline is 4.1% per year. If the peak is less than 1.7 litres, the average rate of decline is 9.6% per year.114 In Spinal muscular atrophy type 1, muscle weakness and restrictive defects are seen before the end of the first year of life, the peak vital capacity is reached very early and is very low. The respiratory system is unable to cope with stresses, and recurrent pneumonia and death occur in the first two years of life.115

Peak vital capacity is also related to the progression of spinal deformity and other orthopaedic complications.116 Rapid and severe progression of a spinal deformity in Duchenne muscular dystrophy is associated with a peak vital capacity of less than 1900ml, which occurs before 14 years of age.117
Maximal Inspiratory and Expiratory Pressures

Maximal inspiratory (MIP) and expiratory (MEP) pressures are used to better define inspiratory and expiratory muscle strength, respectively.\textsuperscript{118,119} Children are asked to make a maximal inspiration against a pressure transducer, and the MIP is the maximum pressure generated. A maximal expiration against the pressure transducer measures the MEP. Maximal inspiratory pressure can be measured at either residual volume or functional residual capacity.\textsuperscript{119,20,118,120} The pressures obtained at functional residual capacity tend to be higher than those obtained at residual volume. MEP is generally measured at total lung capacity. Both measures can be used to quantitate disease severity. Performing MIPS and MEPS requires cooperation, motivation and coordination, as well as the ability to form a seal around a mouthpiece. Submaximal and variable results are not uncommon.\textsuperscript{23}

In many neuromuscular conditions, the muscles of expiration are weakened earlier and more severely than those of inspiration. This can be demonstrated by an earlier decline in MEP than MIP. It occurs in Duchenne muscular dystrophy,\textsuperscript{20} Becker muscular dystrophy,\textsuperscript{80} Myotonic dystrophy,\textsuperscript{121} Fascioscapulohumeral muscular dystrophy,\textsuperscript{122} Hereditary motor and sensory neuropathies\textsuperscript{91} and Spinal muscular atrophy.\textsuperscript{91} Normally, after the first year of life, the MIP is very similar to that of adults (80-120 centimetres of water).\textsuperscript{118} In Duchenne muscular dystrophy, MEP is usually reduced by the age of 7 years but MIP is preserved until 13 years. Hypercarbia appears when MIP falls below 30 centimetres of water (cmH\textsubscript{2}O) or 30% predicted.\textsuperscript{10,20}

Sniff Inspiratory Pressures

The pressure generated in the nose or oesophagus when performing a maximal sniff provides a measure of inspiratory muscle strength.\textsuperscript{22,123,123} Sniff oesophageal pressure is measured by placing a balloon within the oesophagus that contains a pressure transducer. Sniff oesophageal pressure is higher than maximal inspiratory pressure, has a narrower range of normal values, and is more reproducible. It may, therefore be more useful in detecting mild to moderate inspiratory muscle weakness, but this technique is invasive.
Sniff nasal inspiratory pressure is measured by placing a plug in one nostril, which has a small catheter containing a pressure transducer inserted through it, then performing maximal sniffs.\textsuperscript{21-23,123-125} Sniff nasal inspiratory pressure is higher than maximal inspiratory pressure, and is higher in boys than girls.\textsuperscript{23} Nasal transducers are far less invasive than oesophageal transducers. Nasal transducer use is limited in the presence of anatomical abnormalities of the nose or septum, or nasal mucosal congestion.

The pressures generated by both methods are comparable.\textsuperscript{124,126-128} Sniff nasal inspiratory pressure is a useful additional test to maximal inspiratory pressure, in assessment of inspiratory muscle strength when the maximal inspiratory pressure is reduced. It eliminates the need for a mouthpiece in those with neuromuscular weakness who may find creating a seal difficult.\textsuperscript{21,23}

**Transdiaphragmatic Pressures**

Transdiaphragmatic pressures (Pdi) may be measured in a similar way to SNIFF oesophageal pressures, except that the pressure transducer in the mid-oesophagus also has an attached pressure transducer in the stomach.\textsuperscript{120,124} The Pdi is measured as the electrical difference between the two transducers, and can be measured during a MIP, MEP of SNIFF manoeuvre. Measurement of the Pdi is invasive and has more variability than that obtained during a SNIFF manoeuvre, even in adults.\textsuperscript{124}

**Peak Cough Flow**

Subjective audible assessment of cough is not accurate. It has been postulated that cough is the most important respiratory assessment to perform pre-operatively in children with neuromuscular weakness, as post-operative morbidity and mortality is often related to ability to clear secretions, rather than simple lung function.\textsuperscript{129}

A peak cough flow is obtained by coughing into a peak flow meter and measuring the maximum flow. Normal cough flows are greater than 300l/min.\textsuperscript{1} Peak cough flow is reduced by any inspiratory muscle weakness that reduces the vital capacity below
fifty per cent predicted or by weakness of the expiratory muscles. Normal mucociliary clearance is achieved if the peak cough flow exceeds 270l/min.130 160-270l/min is considered marginal, and <160l/min is unsatisfactory for effective mucociliary clearance. When the peak cough flow is <270l/min, it is likely to fall below 160l/min during acute infections.131

**Cough Spirometry**

Cough spirometry is performed by performing a maximal forced expiratory manoeuvre, inspiring, then performing several consecutive coughs, without inspiring again, usually until functional residual capacity is reached.129,132-134 Cough spikes overlie the flow-volume loop. Cough transients occur when the peak of the cough spikes are higher than the flow-volume loop. This is normal. If expiratory muscle weakness is prominent, cough volumes will not exceed the flow-volume loop, and cough transients will be absent. This has been noted in motor neurone disease and muscular dystrophy.

In motor neurone disease, lack of cough transients is associated with mortality within 18 months, and a reduced maximal expiratory pressure.112 In muscular dystrophy, the maximal expiratory pressure has been found to exceed 60cmH₂O in patients who exhibit cough transients, but be <40cmH₂O in those without cough transients. There is considerable overlap in the measurements of expiratory flow between those who can and cannot elicit cough transients.129

Cough spirometry has not been used widely, and is not yet a standard assessment tool in neuromuscular weakness. Further research is needed to better define normal values, and its ability to predict outcomes.

**Arterial Blood Gases**

Despite a restrictive pulmonary defect, arterial blood gas analysis generally remains normal during the day until respiratory muscle weakness is severe.10 Sleep-disordered breathing is often the first manifestation of marginal respiratory status, and
hypercarnia and hypoxia are generally first seen during rapid eye movement and later in non-rapid eye movement sleep. When sleep-disordered breathing worsens in severity, hypercapnia may spill over into the daytime, particularly in the early morning. Once inspiratory muscle strength declines markedly, atelectasis begins causing ventilation perfusion defects. Recurrent infection or aspiration can lead to scarring and compound ventilation-perfusion mismatch. Daytime arterial blood gas analysis often remains normal until the mismatch is widespread.

**Polysomnography**

Overnight polysomnography involves extensive monitoring of blood gas alterations, respiratory effort and airflow during a night of sleep. This is used to determine sleep architecture, evidence of sleep-disordered breathing, and physiological consequences of sleep disordered breathing. It distinguishes upper airway resistance, and partial (obstructive hypopnoea) or complete (obstructive apnoea) airway obstruction from central events. It is useful in diagnosing hypoventilation. When weakness is severe, muscle movements may be undetectable at times, giving the appearance of "central" events, although the origin may be weakness. This particularly occurs when weak muscles are unable to overcome upper airway obstruction. Polysomnography testing defines the presence and type of sleep-disordered breathing, and guides the use of ventilatory support.

Polysomnography is indicated when nocturnal symptoms or daytime hypersomnia is present, although there is not good evidence that the two correlate well. In Duchenne muscular dystrophy, daytime predictors of sleep-disordered breathing have been better defined, and PaCO₂ should be measured when the FEV₁ falls below 40% predicted, and polysomnography should be performed if the PaCO₂ is ≥45mmHg, particularly if the base excess is ≥4mmol/l. In other neuromuscular disorders, polysomnography is indicated when the inspiratory vital capacity is <60% or the PaCO₂ is >40mmHg. The American Thoracic Society recommends that polysomnography be undertaken yearly from the time a child with Duchenne muscular dystrophy becomes wheelchair-bound or when clinically indicated.
Management

Management of neuromuscular disorders remains mainly supportive. The disorders themselves may be static, intermittent or progressive, but little can be offered to alter the course of the disease process. Physical therapies aim to maintain function and quality of life for the longest possible period. The multidisciplinary approach that includes psychological, nutritional, neurological, orthopaedic and respiratory modalities is offered in most centres, and has particular advantages in coordinating the child’s care. Molecular genetics may broaden therapeutic options in the future, but genetic modification is many years away.

Specific

For children with Duchenne muscular dystrophy, glucocorticoids offer a temporary delay in the progression of weakness, and lead to improved muscle mass and strength over an 18 month period; this results in symptomatic improvement, and may prolong ambulation. The mechanism of action is unknown, but is not thought to relate to immnosuppression, as azathioprine does not have a beneficial effect. Deflazacort, an oxazoline derivative of prednisone also improves muscle strength. The side-effects of these drugs, and particularly the associated weight gain, frequently outweigh their small clinical benefits and lead to cessation of treatment. The use of glucocorticoids are not known to alter respiratory decline.

Glucocorticoids and other immunosuppressive agents are also useful in the treatment of inflammatory myopathies. Most respond well. When this is not effective, or when side effects are problematic, azathioprine, methotrexate or plasmapheresis may be useful.

Corrective Spinal Surgery

The decision to perform corrective spinal surgery is difficult. It is a balance between expected deterioration in spinal deformity and functional abilities, the morbidity it
causes and the risk associated with the operation. Early stabilisation reduces the operative risk.\textsuperscript{37,144} The greater the deformity at operation, the more rigid the spinal column becomes, the more complex and dangerous the operation and the smaller the chance of a lasting stable correction.\textsuperscript{76}

Spinal deformity and pelvic obliquity are associated with significant morbidity and reduction in functional capabilities. Scoliosis causes pain, leads to truncal instability and difficulty in sitting.\textsuperscript{5} Once the Cobb angle reaches forty degrees, truncal balance is lost, and the hands are need to stabilise the trunk, limiting mobility.\textsuperscript{30} Cosmetic concerns may be raised, and skin integrity may become compromised over bony prominences.\textsuperscript{6,81} Scoliotic deformities are generally associated with rotation causing the rib cage to be skewed and worsening pulmonary restriction.\textsuperscript{37}

The natural history of spinal deformity in neuromuscular weakness must be known to predict deterioration and assist with timing corrections. Ninety-five percent of children with Duchenne muscular dystrophy develop progressive scoliosis. Oda, \textit{et al}\textsuperscript{12} studied the natural history of scoliosis in Duchenne muscular dystrophy and categorised spinal deformities into three types:

\textit{Type 1} has concomitant kyphosis and pelvic obliquity. Curves reach 30 degrees before 15 years of age and rapidly progress thereafter.

\textit{Type 2} curves are associated with hyperlordosis. Progression is not uniform. Those that have a stable pelvis and double lateral curves have minimal progression. Those with long thoracolumbar curves are slowly progressive and those with single lumbar curves may progress slowly or suddenly.

\textit{Type 3} have curves less than 30 degrees and minimal progression.

Yamishita, \textit{et al},\textsuperscript{117} found that a peak vital capacity of less than 1900ml, or its occurrence before 14 years of age was associated with more severe, progressive spinal deformities, requiring early surgical intervention. In general it is recommended that spinal fixation be undertaken when the Cobb angle reaches 50 degrees in the ambulatory patient, or 30 degrees in the non-ambulatory patient.\textsuperscript{145}
Risks Associated With Corrective Spinal Surgery

Corrective spinal surgery carries significant risk.\textsuperscript{28,29} Complication rates range from 44-62%.\textsuperscript{38} Long segment fixations are usually required, increasing anaesthetic times and risk. Malignant hyperthermia is not uncommon.\textsuperscript{5,6} Death occurs in 1-9%, mainly due to haemodynamic or pulmonary complications.\textsuperscript{37,77} Respiratory compromise generally contributes the greatest anaesthetic risk.\textsuperscript{34,37,38} Cardiac involvement is present in many neuromuscular disorders and may manifest as defective conduction and/or contraction. Haemodynamic risks are high. Blood loss is increased by poor nutritional status, poor bone quality and the need for long segment fixations, necessitating a prolonged procedure.\textsuperscript{6,37} Coagulation disorders have been reported in Duchenne muscular dystrophy and may be present in other neuromuscular disorders.\textsuperscript{146}

Neurological complications occur in 0.5-17% of children undergoing corrective spinal surgery, depending on the underlying condition, the type of surgery, the severity of the curve and the degree of correction obtained.\textsuperscript{6} Electrophysiological or somatosensory monitoring is now being used to minimise neurological complications.\textsuperscript{6,77,145}

Malnutrition increases the risk of skin ulcers and wound infections.\textsuperscript{79} Despite advances in nutritional care, and liberal use of antibiotics, wound infections occur in 26%.\textsuperscript{37,77} Post-operatively, a period of immobility may be necessary. Rod procedures require several weeks of immobilisation, and external fixation. Segmental spinal surgery does not require immobilisation or external fixation. The longer the period of immobilisation, the greater the risk of pulmonary collapse and infection, progression of muscle weakness, and occurrence of pressure areas and skin breakdown.

Hardware failure is not uncommon. It is more common with Harrington rods than with segmental spinal fixation, and is often related to poor bone quality. Segmental spinal fixation provides multiple fixation sites to distribute corrective forces over many spinal levels.\textsuperscript{77} Hardware failure may simply take the form of failure of a single screw or wire, or be a pseudoarthrosis, or implant failure requiring further surgery.\textsuperscript{77,81}
Curvatures are usually long, and may progress at either end of the fixation if the repair is not extended far beyond the end of the curve. In order to prevent progressive spinal deformity above or below the fixating device, it should extend from at least the forth-thoracic vertebrae to the forth lumbar vertebrae.\textsuperscript{37} Controversy exists about whether this extension is adequate, and some would advocate even longer fixations.\textsuperscript{28,29} Post-operatively, the curve should be less than 35 degrees to prevent ongoing curve progression.\textsuperscript{33}

Creating a rigid spine creates a long lever arm that is difficult for weak muscles to control.\textsuperscript{5,77} It often leads to some decline in function, including decline in gross motor skills, transfer ability, self-feeding, hygiene, dressing, independent toileting and ambulation. Both lordosis and lateral trunk sway are used to compensate for proximal weakness and assist with ambulation, so fixation is often best deferred until ambulation is lost.

**Pre-operative Respiratory Evaluation**

During anaesthesia, arterial blood gases worsen due to the effect of the anaesthesia on the chest wall and diaphragm.\textsuperscript{147,148} This results in alteration in the distribution of inspired gas and ventilation-perfusion mismatch. General anaesthetics also reduce hypoxic pulmonary vasoconstriction, which worsens gas exchange. These effects persist into the early post-operative period but generally return to pre-operative levels within 24 hours. Procedures involving the upper abdomen or thoracic cavity have prolonged pulmonary dysfunction. The mechanism for this is not known, but does not appear to be solely due to pain.\textsuperscript{148,149}

Invariably children with neuromuscular weakness need operations, such as orthopaedic surgery, tracheostomy insertion or other procedures. The anaesthetic risk is great, particularly from a respiratory viewpoint. Jenkins\textsuperscript{34} found that pre-operative vital capacity (VC) is the best predictor of the post-operative clinical course in patients with Duchenne muscular dystrophy. No patient with a pre-operative VC >45% predicted required post-operative ventilation, all those with a pre-operative VC <35% predicted required post-operative ventilatory support, and 2/3 of those with a pre-operative VC <30% predicted had serious post-operative pulmonary
complications. Padman\textsuperscript{35} found that pre-operative VC is related to post-operative pulmonary complications, and need for post-operative ventilatory assistance. Cambridge\textsuperscript{14} and Jenkins\textsuperscript{34} have suggested that the VC % predicted must be greater than 35% to undertake surgical intervention for spinal deformity in Duchenne muscular dystrophy. Corrective spinal surgery has been successfully performed on a child with Spinal muscular atrophy with a VC as low as 640ml.\textsuperscript{150} Pre-operative hypercapnia increases the risk of post-operative pulmonary complications.\textsuperscript{147}

Use of non-invasive ventilatory support is likely to improve anaesthetic risk in those with marginal respiratory status, and many are now beginning ventilatory support prior to surgery in high-risk patients. Assisted cough techniques as well as air stacking and glossopharyngeal breathing are being taught pre-operatively to improve post-operative respiratory recovery.\textsuperscript{150-152} In the past, surgery was not recommended for those with a VC <35% predicted. With the use of ventilatory support and assisted cough, this recommendation may alter significantly. There remains a significant risk that a child undergoing corrective spinal surgery may become dependent upon ventilation, and the difficult decision of removing the ventilator or placing a tracheostomy may need to be faced. Non-invasive ventilatory support may facilitate weaning from a ventilator. A great deal more research needs to be done to further delineate the role of ventilatory support in children with neuromuscular disorders in the peri-operative period in order to modify recommendations in the current era.

**Operative Procedures**

Corrective spinal surgery has a great impact on quality of life and ease of nursing care in children with neuromuscular weakness.\textsuperscript{14,30-33} It aims to produce a balanced spinal position in both the sagittal and coronal planes over a stable pelvis.\textsuperscript{6,77,81}

The posterior only or the combined anterior and posterior routes can be used to achieve spinal fixation. The combined approach may be performed in one or two stages. Its advantages are that it allows release of the disk spaces anteriorly and improves mobility of the spine for correction. It is best used in situations where there has been extensive remodelling leading to fixed deformities.\textsuperscript{81} It yields twice as much correction of pelvic obliquity as the posterior only approach.\textsuperscript{77} The disadvantages are
that it significantly increases operative time, blood loss, and the period of immobility post-operatively and that to achieve a thoracic anterior approach, the diaphragm must be breached. This increases operative respiratory risk, causes pleuritic chest pain and prolongs recovery. Most surgeons use the posterior only approach in children with neuromuscular weakness.5,7,7,144,153,154

Harrington rod fixation was the first advocated procedure for posterior only fixation. Attachments are not segmental and great forces are placed on the rods and osteoporotic bone. Pseudoarthrosis occurs in 15%.30,155 Post-operatively, external fixation is required which can lead to prolonged immobilisation, pulmonary atelectasis, pressure areas and progression of muscle weakness.5

Segmental spinal fixation allows primary post-operative stability without external support and provides greater correction of pelvic obliquity by applying transversal forces. Attachments are made to each vertebra, distributing its forces along the entire spinal length. This reduces the forces placed on osteopenic bone.77 Adding cross fixators assists in correcting rotational deformity. Correction of 51-74% can be expected.30,32,33,37,38,81,144,145,154,155

Luque first developed the technique for segmental spinal fixation using two contoured rods that fix intimately to each laminar surface with sublaminar wires. The rods extend to the first sacral vertebrae. Several modifications of his technique have been advocated. The gliding Luque technique allows some growth for approximately 3 years by sliding lengthwise.77,79,156

Many have advocated pelvic fixation to correct pelvic obliquity.30,33,38,81,155,157 It leads to increased blood loss, longer operation times, and hardware failure is possible.32 Correction of pelvic obliquity by approximately 67-84% can be expected.37,38,154 Post-operatively children no longer have mobility at the lumbo-sacral junction, and find leaning in their chair and transfers more difficult.32 Galveston developed a technique for pelvic fixation in which the pelvic portions of the rods are implanted into the ileum.158 This technique has led to sacroiliac joint erosion occurring several years post-operatively, in approximately fifty per cent causing pain and radiolucency.30,77,157

Many techniques of pelvic fixation have been developed to overcome this.30,33,38,81,155,157
Controversy exists about whether pelvic fixation is necessary. Many believe that fixation to the lower lumbar vertebrae provides an equal result. It allows for better mobility post-operatively, is quicker and has less blood loss. Correction of pelvic obliquity of 48-50% can still be expected.\textsuperscript{31,145,159} Others believe that pelvic fixation is required for long-term stability.\textsuperscript{81,160} Whitaker, \textit{et al}\textsuperscript{12} suggests excluding the pelvis from fixation if pelvic obliquity is less than fifteen degrees, there are no problematic lower extremity contractures, and there is potential for ambulation post-operatively.

After corrective spinal surgery, if hip contractures have not been released, the legs are unable to sit comfortably on the chair, and pressure is not distributed evenly, leading to ongoing problems of pressure areas and loss of skin integrity, tendon release operations are generally performed, but not at the time of spinal surgery.\textsuperscript{164} Operative risks associated with corrective spinal surgery and prolonged anaesthetic times negate further procedures.

\section*{Respiratory Management}

\textbf{Techniques to Aid Mucociliary Clearance}

Many techniques have been developed to enhance mucociliary clearance. If the peak cough flow is greater than 2701/min, frequent coughing and percussion physiotherapy are used to assist with mucociliary clearance.\textsuperscript{1,8} Assisted cough is now being used in many centres when the peak cough flow is marginal. It requires cooperation and often the assistance of a caregiver. The child takes the deepest breath possible and holds it briefly. As the glottis opens, an abdominal thrust is applied (usually by a caregiver, but occasionally by the patient). Peak cough flows above 2701/min can generally be achieved. This technique needs to be learned prior to the chest infection for its effective usage when needed. It can be successful in gaining effective mucociliary clearance in children who would otherwise have marginal clearance. It may be inadequate in children with obesity or scoliosis.\textsuperscript{1,27}

Glossopharyngeal breathing is performed by using the glossopharyngeal muscles to direct “gulped” air through the glottis.\textsuperscript{1} This is repeated for several consecutive breaths without releasing air between breaths to allow air to be “stacked” prior to a
cough. It allows more air to be held in the lungs than a single breath is able to obtain when the inspiratory muscles are weak. It requires training, but can greatly increase the peak cough flow. Effective mucociliary clearance may be gained. This technique cannot be used if a tracheostomy is present due to air escape.

Ventilatory support may be offered during acute events if mucociliary clearance remains marginal despite simple measures. The early home use of oximetry and non-invasive ventilatory support in those with marginal mucociliary clearance can significantly reduce the incidence of respiratory hospitalisations and prolong survival in children with Duchenne muscular dystrophy.\textsuperscript{130} Ventilatory support may be provided by invasive or non-invasive techniques.

Patients using a ventilator can learn air stacking.\textsuperscript{127} The inspiratory pressure is raised to 30-50cmH\{2}O for several consecutive breaths. Each breath is retained rather than expired. Once the lungs are filled with air, the glottis is opened and a maximal assisted or unassisted cough is performed simultaneously. The amount of air stacked will depend on compliance of the lung and chest wall. The peak cough flow will be significantly improved. This technique must be learned and practiced while well.

When mucociliary clearance remains inadequate despite air stacking and assisted cough, mechanical insufflation-exsufflation has been used.\textsuperscript{11,152} This involves air stacking by increasing peak inspiratory pressures on the ventilator to 30-50cmH\{2}O for several breaths, and then reducing the ventilator pressure to a negative value so that air is drawn forcefully out of the lungs as the glottis opens. This technique can be used with careful instruction and cooperation in conjunction with ventilator use. It can also be used in indolent respiratory failure to assist with mucociliary clearance. No detrimental effects have yet been identified, but this technique is not widely accepted.

Some advocate the intrapulmonary percussive ventilator.\textsuperscript{152} It delivers high frequency bursts of gas to the lower airways to decrease the viscosity of respiratory tract secretions and mobilise them cephalad. It has been used at times of acute infection to improve mucociliary clearance. It can be used in conjunction with assisted cough, air stacking or mechanical insufflation-exsufflation.
Invasive ventilatory support via and endotracheal tube or tracheostomy offers an effective method of large airway secretion clearance in the form of suctioning. Unfortunately, its invasive nature often requires the use of anaesthetic agents that take control away from the child. Speech is more difficult and tracheostomy is not cosmetically appealing.

Management of Respiratory Failure

Several factors need to be considered in planning respiratory management. Quality of life should remain of utmost importance. Maintenance of compliance of the chest wall and lungs, and of muscle strength is important for longevity. Decisions about ventilatory support and its type are difficult and need to be made in conjunction with the child and family.

Physiotherapy

Physiotherapy is advocated by most. Deep inspirations may assist in maintaining compliance of the chest wall and lungs and also aid mucociliary clearance. Physiotherapists are often employed to teach effective cough, assisted cough, glossopharyngeal breathing and air stacking techniques. The techniques learnt while well are of great importance during acute respiratory illness.

Respiratory Muscle Training

Respiratory muscle training remains controversial. It is thought that training respiratory muscles may improve muscle strength, that these muscles will then cope better with acute illness, and that it may slow progression of chronic respiratory failure. Concerns have been raised about the possibility of muscle fatigue, and the detrimental effects this may have on a marginal respiratory system. This concern now seems to be dispelled, as many have used such training with benefit.

Generally the training consists of repetitive inspiring against a resistance, voluntary hyperventilation or a combination of these techniques with exercise. Improvement
in maximal inspiratory pressure lasting up to 24 months has been found in Duchenne muscular dystrophy. The benefit seems greatest in those who have less severe disease represented by a vital capacity >25% predicted. Others have not found any significant benefit. Ill effects have not been found. Further controlled evidence is needed to better define any benefit respiratory muscle training may have on respiratory infection frequency and its long-term impact. 

**Ventilatory Support**

Options for ventilatory support in children with neuromuscular disorders have expanded in recent times. Portable bilevel positive airway pressure machines are now available for home use, and modes of use are expanding. The decision to start ventilatory support, and its timing is difficult. Ventilatory support is generally first required during sleep.

Phillips, et al found that fifty per cent of patients with vital capacity <1000ml require ventilatory support within 25 months, and all required this within 50 months. Hypercapnia is found in 80% of patients with a maximal inspiratory pressure <30cmH₂O. In poliomyelitis, hypercarbia is generally seen when the forced vital capacity falls below 55% predicted. The relationship between vital capacity and hypoventilation is not always clear, and respiratory muscle strength (maximal inspiratory and expiratory pressures and sniff inspiratory pressures) may be a better indicator. Polysomnography is the only definitive indicator of sleep-disordered breathing which can be used to guide the use of ventilatory support.

Nocturnal ventilatory support reduces sleep related hypopnoeas and apnoeas, improves sleep architecture and quality, and can lead to improved daytime blood gases. Two theories of the mechanism by which this occurs exist: 1) resetting the chemoreceptors which now have long periods of normal oxygen and carbon dioxide levels, or 2) resting the respiratory muscles which gives them relief from fatigue. Provision of nocturnal ventilatory support for respiratory failure improves quality of life and longevity. Survival is prolonged in tracheotomized patients (7.6 ± 6.2 years; mean ± standard deviation) and those using non-invasive ventilation (4.5 ± 3.6 years).
Daytime ventilatory support should be considered when daytime respiratory symptoms, or significant hypercarbia despite nocturnal ventilation dictates this is necessary. Continuous ventilatory support is suggested when patients request this or support is required for 16 hours a day or more. This is generally seen in Duchenne muscular dystrophy when the vital capacity falls below 12% predicted.\textsuperscript{152,178,179} Mohr, \textit{et al}\textsuperscript{180} and Hukins, \textit{et al}\textsuperscript{105} found that although hypercarbia improved with non-invasive ventilation, vital capacity continued to decline.

Raphael, \textit{et al}\textsuperscript{181} conducted a prospective randomised controlled trial of the provision of "preventative" ventilatory support to children with Duchenne muscular dystrophy and a vital capacity 20-50% predicted. After a mean 52 month follow-up the trial was aborted due to reduced survival with "preventive" non-invasive ventilation. "Preventative" non-invasive ventilation had reduced survival with a relative risk of ten when adjusted for social and echocardiogram differences between the "preventative" and treatment groups. There were several confounding factors present in this study. Cardiac disease was significantly higher in non-invasive ventilation group (37% versus 23%), and polysomnography was not performed in any children to determine which children had sleep-disordered breathing. As a result of this trial, "preventive" ventilatory support is not generally recommended, but most centres conduct polysomnography and treat with ventilatory support when sleep-disordered breathing is present.

\textbf{Types of Ventilatory Support}

Non-invasive ventilation has revolutionised the treatment of respiratory failure from neuromuscular weakness. The poliomyelitis epidemic of 1931 claimed many lives due to respiratory failure.\textsuperscript{182} The invention of negative pressure ventilation revolutionised treatment, and saved lives. Many further advances have been made in non-invasive ventilation since this time, and a broad variety of techniques are now available.

\textbf{Negative Pressure Ventilation}

Negative pressure ventilation was the first form of non-invasive ventilation. It uses a chamber (iron lung), body garment, wrap or chest shell which surrounds or covers the
chest. Air is forcefully removed from around the chest, causing the pressure around the chest to become negative. This forces the chest to expand, and draw in air leading to inspiration. The pressure in the chamber is then normalised. The chest relaxes and passive expiration occurs.

The iron lung encases the body in a large container. Within this container sub-atmospheric pressure can be generated. The disadvantages are that many find it claustrophobic, movement is limited which may lead to musculoskeletal problems, and the machine is large and cumbersome. Air leaks may occur. In an effort to overcome the restricted mobility and claustrophobia, body wraps and garments have been made that encase only the upper torso. The chest shell is a contoured plastic shell with a foam seal that fits over the anterior chest and abdomen. It is flexible enough for sitting, standing and reclining. It is far less efficient than the other negative pressure ventilators, and not recommended for those with high ventilatory requirements.

Negative pressure ventilation allows adequate ventilation in those with reasonable chest wall and lung compliance, but is limited when compliance is reduced in situations such as obesity, scoliosis or scarring. It has the potential risk of increasing upper airways obstruction during sleep, as upper airway muscle movements remain phasic and negative pressure ventilators are not patient driven and may not be synchronous with the patient. Compared to non-invasive positive ventilation, patients using negative pressure body ventilation are more likely to require tracheostomy insertion, hospitalisation and death occurs more commonly. Negative pressure ventilation becomes less effective as lung volumes and compliance decrease with age or progression of disease.

**Abdominal Displacement Ventilation**

Abdominal displacement ventilation uses pressure placed intermittently on the abdomen to raise the abdominal contents against the diaphragm, causing active exhalation, followed by removal of this pressure and passive inspiration. The devices used include an abdominal corset (pneumobelt) and the rocking bed.
The pneumobelt is an abdominal corset that contains an air-filled bladder. This bladder can be inflated and deflated under the control of a ventilator. A trunk angle of 30 degrees or greater is required. Inflation of the bladder forces the abdominal contents superiorly against the diaphragm, causing expiration. Deflation allows the abdominal contents to move inferiorly away from the diaphragm, allowing expansion of the chest and inspiration. It can increase tidal volumes by up to 1200ml. It is most efficient in the sitting and standing positions but is inadequate in the presence of scoliosis or obesity. It cannot be used in the presence of abdominal pathology. It is best used as a supplement to other forms of nocturnal non-invasive ventilation.

The rocking bed uses a similar concept. The patient’s bed is set in a head to toe rocking motion. It uses the effect of gravity on the abdominal contents to assist ventilation. When the rocking motion raises the head with respect to the feet, the abdominal contents move with gravity away from the diaphragm to assist inspiration. When the bed rocks in the opposite direction, the abdominal contents move superiorly against the diaphragm, aiding expiration. Its use is often associated with obstructive sleep apnoeas; so many are moving away from beginning this form of therapy.

Positive Pressure Ventilation

Positive pressure ventilation forces air into the airway under pressure to a preset pressure or volume. It can be achieved non-invasively by mask or mouthpiece or invasively via an endotracheal tube or tracheostomy. To achieve positive pressure ventilation non-invasively, a variety of delivery appliances exist. The choice of appliance is based on comfort, ease and accuracy of ventilation, and the occurrence of complications.

Non-Invasive Positive Pressure Ventilation

Non-invasive positive pressure ventilation can be used to prevent tracheal intubation, facilitate extubation, aid in weaning from ventilatory support, for support during acute respiratory tract infections or to provide respiratory support during sedation for invasive medical procedures.
Nasal non-invasive ventilation is an effective method of providing ventilatory support.\textsuperscript{1} It is particularly useful in those with jaw contractures preventing insertion of a mouthpiece, or persistent air leak. It is preferred in many centres. A nasal mask is applied and fixed with a strap around the head. Air leak can occur through the mouth, so that closure of the mouth elicits the most constant and consistent ventilation. In those who have difficulty keeping the mouth closed due to weakness or habit, a chin strap may be used or the pressures can be adjusted to compensate for air leakage.\textsuperscript{1,187} Pressure areas on the bridge of the nose are not uncommon, but recent expansion in the variety of masks available and their fixation means most are able to find a mask that fits comfortably, provides a good seal and does not lead to pressure areas. In addition to the standard masks, bubble, gel, mini masks and nasal pillows now exist.\textsuperscript{182} Several masks may need to be tried in order to find the most comfortable, the best seal, and the least skin irritation.

Mouthpiece non-invasive ventilation uses a mouthpiece that needs to be held in the mouth by the muscles of mastication.\textsuperscript{187} A lip seal can be used if air leaks around the mouthpiece are a persistent problem. Air escape may occur through the nasopharynx, and patients need to learn palatal control to prevent such escape. If nasal air escape cannot be overcome by training, a nose clip or plugs may be used. If air leaks remain a problem, high ventilatory volumes may be used.\textsuperscript{1}

For those in whom air leaks or skin breakdown remain and issue, oronasal or facial masks can be used.\textsuperscript{185} Some find these claustrophobic. Pressure areas can remain an issue, but rarely does it warrant changing to invasive ventilation, and air leaks are less frequently problematic. The masks carry a theoretical increased risk of aspiration, particularly if the patient vomits and when the patient is too weak to remove the mask himself.

Non-invasive positive pressure ventilation has several potential complications, including irritation of the skin and skin breakdown, aerophagia and increased risk of aspiration.\textsuperscript{182-184,189} Those who use non-invasive positive pressure ventilation for prolonged periods may suffer alteration of the bony structure of the midface, especially in young, growing faces.\textsuperscript{190} Those with mouth ventilation have difficulty with speech, and often secretion control.\textsuperscript{182-184,189} Non-invasive positive pressure
ventilation can be patient driven and does not potentiate upper airways obstruction. Negative pressure ventilation may. It allows preservation of airway protective mechanisms, speech and swallowing. Many have found that despite the benefits of non-invasive ventilation, tracheostomy may eventually become necessary in a large proportion of patients. Others have not found this necessary. This may reflect to some extent the experience and beliefs of caregivers involved.

**Invasive Positive Pressure Ventilation**

Invasive ventilation can be through an endotracheal tube or tracheostomy. Endotracheal tubes are limited to acute use as they often require sedation in order that they be tolerated and have potential long-term complications. They negate the ability to speak, and take control away from the patient. Tracheostomy is still recommended in many centres for both secretion management and ventilatory support. Ventilation is accurate and not limited by air leak through an open mouth or around the mask. There is no dependence on muscle strength for mouth closure or holding a mouthpiece. There are no pressure area concerns, and airway stability is the norm. Secretions can be easily suctioned without cooperation from the patient or the learning of a difficult technique. Mechanical insufflation-exsufflation and air stacking may be used.

Although tracheostomy-related mortality rates have diminished, they remain higher than the mortality rates associated with non-invasive ventilation. Tracheostomy has an overall complication rate of 40% in children. Complications include lower respiratory tract infections, infections of the stoma, chest pain, lack of adequate humidification, mucous plugging, granulomas, haemorrhages, tracheal fistulas and tracheal stenosis. Although patients may learn to change their own tracheostomy tubes, many are too weak to perform this, and a caregiver is always required in the case of an emergency tracheostomy tube change.

There are ethical considerations that need to be deliberated when discussing performance of a tracheostomy with the patient family. This needs to include the care of the tracheostomy, its potential complications, the need for a prolonged hospital stay during training for care of the tacheostomy, and the requirements for caregivers in the home. Recruitment and retention of caregivers in the home is
frequently very difficult, and may limit discharge to the home setting, and readmissions. Tracheostomies may be useful when bulbar dysfunction and secretion control are difficult, but use is generally limited due to their affect on quality of life.

**Modes of Positive Pressure Ventilation**

Almost any mode of ventilation that can be used with an endotracheal tube in place can also be used non-invasively.\(^{94,182}\) The most common modes used are continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BPAP).\(^ {187}\) Ventilation can be volume or pressure limited, and spontaneous, timed, triggered or assisted ventilation can be provided. CPAP is mainly used for upper airways obstruction and increased resistance. BPAP is generally used when weakened muscles are unable to overcome upper airways obstruction with the use of CPAP, or when hypoventilation occurs. The high pressures required to overcome reduced chest wall and lung compliance may limit home BPAP use. Even higher pressures may be required for air stacking. Home-based machines may not be able to provide these and children may require admission to intensive care units during periods of acute infection.

Whether invasive or non-invasive nocturnal ventilation is used, sleep disordered breathing is likely to worsen if muscle weakness is progressive and the period of time requiring ventilation is likely to extend. It is also likely to worsen with acute respiratory events.\(^ {195}\) This has obvious implications for quality of life, and the decision to proceed along this path must be carefully discussed with the patient and their carer. Some will decide not to undergo this treatment, others will insist upon it. Many would persist with non-invasive ventilation even when fully ventilator dependent. Others would elect to insert a tracheostomy at this stage. If a tracheostomy is inserted, the potential for sustaining life for a prolonged period exists. The quality of life needs to be addressed again before embarking on this pathway.\(^ {176}\) Despite the benefits for quality of life and longevity, 25% of physicians still do not discuss the option of long-term ventilation with their Duchenne muscular dystrophy patients, often because of a perceived poor quality of life outcome (52%). When it is discussed, the physicians modify their discussions to influence the outcome.\(^ {176}\)
When negative pressure ventilation was used for poliomyelitis over a 24 year period, the forced vital capacity was found to fall at a rate of 5ml per year. In a three year follow up of non-invasive positive pressure ventilation for poliomyelitis, the forced vital capacity increased by a mean of 90ml per year. In Duchenne muscular dystrophy, the rate of decline of forced vital capacity is more rapid than that seen in poliomyelitis. Boys with Duchenne muscular dystrophy have been found to have an ongoing decline in forced vital capacity of 60ml per year over a two-year period on positive pressure non-invasive ventilation.

Patient acceptance is important in any decision about the mode of ventilation to use. Those with non-invasive positive pressure ventilation are more likely to experience improved well-being, independence and ability to perform daily activities than those with tracheostomy or negative pressure ventilation. Tracheostomy ventilation is more difficult to deliver in the home than non-invasive ventilation.

**Conclusion**

Neuromuscular disorders are a diverse group of conditions that result in weakness. The age of onset, distribution, severity and progression of weakness varies between the conditions, and there is a broad spectrum of disease severity within the same condition. Weakness and spinal deformities have a major impact on the developing respiratory system. Timing of operative intervention needs to be a careful balance of benefits and risk, with special consideration to respiratory risk. The variability between and within the neuromuscular disorders and their interplay with spinal deformity makes prognostication for individual children difficult, and necessitates thorough respiratory investigation.

Both neuromuscular weakness and spinal deformity cause significant respiratory compromise. This leads to sleep-disordered breathing, respiratory failure and eventually death in many. A vast array of respiratory assessment tools is available for use, but no tool used alone is adequate. Techniques are available to aid mucociliary clearance and respiratory support can be provided by non-invasive or
invasive ventilation, leading to improved quality of life and longevity. The use of these techniques and supports may also reduce operative risk if used appropriately.
Methods

Respiratory compromise and spinal deformity are major causes of morbidity and mortality in neuromuscular weakness. A vast array of respiratory assessment tools is now available, for pre-operative pulmonary risk assessment, guiding investigative pathways for sleep-disordered breathing and for the instigation of ventilatory support and teaching techniques to assist mucociliary clearance.

The aims of this work are 1) to evaluate the current clinical practice of pulmonary function testing and their role in respiratory risk assessment in children with neuromuscular weakness undergoing corrective spinal surgery and 2) to develop a precise method of predicting pulmonary function tests in children with neuromuscular weakness. The methods used to achieve these aims and the reasons for choosing the methods are described in detail to allow critical evaluation of the results obtained, their limitations, and the conclusions drawn.

Pulmonary Function Test Use in Clinical Practice

Identification of respiratory assessment tools commonly used and relied upon in clinical practice in neuromuscular weakness requires evaluation of clinical practice. Children with neuromuscular weakness are likely to undergo some degree of respiratory assessment on multiple occasions throughout childhood. A situation where extensive respiratory assessment is important in management decisions provides an opportunity to identify the respiratory assessments commonly used, how they are interpreted, their impact on management decisions and any deficiencies they may have.
Spinal deformity is common in neuromuscular weakness. Respiratory decline in neuromuscular weakness is due to a combination of progressive weakness of the respiratory muscles, and progression of the spinal deformity, leading to pulmonary restriction.\textsuperscript{3} Corrective spinal surgery carries significant respiratory risk, and the decision to operate and timing of operations are a careful balance of the benefits in quality of life and ease of nursing care and the risks involved with the procedure.\textsuperscript{14,31}\textsuperscript{31} A significant proportion of the risk has a respiratory origin.

Corrective spinal surgery was used as the model of a situation that commonly arises in neuromuscular weakness, carries significant respiratory risk and in which the respiratory status of the patient may alter management plans. This component of the research aimed to identify how respiratory function tests were used in clinical practice in children with neuromuscular weakness undergoing corrective spinal surgery, and how they relate to respiratory outcomes.

**Study Design**

A retrospective review of children with neuromuscular weakness undergoing corrective spinal surgery between April 1976 and June 2002 at the Royal Children’s Hospital, Melbourne was undertaken. Children were identified from a comprehensive database of children with Duchenne muscular dystrophy and Spinal muscular atrophy and from a computer based medical records search of discharge diagnoses.

An extensive review of each medical record was undertaken for disease type, diagnostic method, age and mobility at time of surgery, and recurrent chest infections. Scoliosis type and level was recorded, but the severity and presence of kyphotic, lordotic or rotational deformities were seldom documented.

Pre-operative respiratory assessments used were identified where documented, and evidence of their interpretation, respiratory specialist consultation and alteration in management plans as a result of the pre-operative investigations was sought. The operative procedure used and anaesthetic time was noted. Details of the operation, post-operative complications and the need for respiratory support were collected.
All pulmonary function tests ever performed by each child were recorded. The height, method of height estimation and observed values of forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were recorded. Predicted values were calculated using the equations of Zapletal, et al. as two different spirometers and prediction equations had been used within this period. Pulmonary function tests were considered pre-operative if they were performed in the 31 days prior to surgery. All post-operative pulmonary function tests were performed at least 30 days after surgery.

Statistical Analysis

Data was collected into an Access '97 database. Stata 7.0 was used for statistical analysis. An association between post-operative need for respiratory support and mobility, chest infections, pre-operative FVC % predicted and age at surgery were sought using ANOVA.

In examining the rates of decline of pulmonary function it was found that not all children had ≥2 pulmonary function tests in the pre- and post-operative periods. The children who had ≥2 pulmonary function tests in the pre- and post-operative periods were compared to those who had ≥2 pulmonary function tests in the pre- but not the post-operative periods. The unpaired student t test was performed to evaluate any difference in age at the time of surgery or pre-operative pulmonary function.

For children who had more than two pulmonary function tests in the pre- or in the post-operative periods, the decline in FVC % predicted over time was plotted against time. A regression model was fitted to the individuals’ data, and the overall rates of decline were determined using the generalised estimating equations method to allow for repeat measures on patients. Predicted values were used as ages varied, and observed values would not take growth into account and would have less meaning. The differences in rates of decline in the pre- and post-operative periods were evaluated with the student t test.
Inaccuracy in Predicting Pulmonary Function

In children with neuromuscular weakness undergoing corrective spinal surgery, pre-operative pulmonary function tests are the main respiratory assessment tool used. In general, interpretation was by a junior medical staff member, surgeon, anaesthetist or neurologist. The predicted value of FVC was the most commonly quoted result. Much of the research guiding management of children with neuromuscular weakness uses predicted values of pulmonary function.\textsuperscript{14,34,35,105} This part of the study aimed to identify deficiencies in the prediction of pulmonary function or its interpretation.

Prediction of normal values of pulmonary function depend on accurate height measurement. Arm span can be used to estimate height.\textsuperscript{42-45,198} Height and arm span would normally increase with advancing age. Height may reduce when spinal deformity is present, but in this situation it would be an inappropriate measurement to calculate predicted values of pulmonary function from, and arm span should be used instead. The value of height or arm span used to estimate pulmonary function should steadily increase as the child’s age advances.

To identify deficits in predicting pulmonary function, inaccuracies in height or arm span measurement were sought in the group of children with neuromuscular weakness that had undergone corrective spinal surgery. As it is not possible to repeat measurements that may have occurred many years ago, this part of the research is limited to only identifying inaccuracies that resulted in a reduction in height or arm span measurement from the previous measurement. The percentage of all pulmonary function tests where height or arm span reduced with advancing age was calculated.

Nationwide Pulmonary Function Test Prediction

Pulmonary function changes throughout childhood and is related to height and age. Height has traditionally been used to predict normal values.\textsuperscript{39,40,199,200} When spinal deformity, weakness or immobility is present, height measurement is difficult and inaccurate. Height measurement becomes inaccurate in neuromuscular weakness when weakness limits mobility, or when spinal or lower limb joint deformity is
present, and in other groups of children who may perform pulmonary function tests, such as those with cerebral palsy or lower limb amputation. Arm span has generally been used to estimate height in these situations, and good prediction equations exist.\textsuperscript{42-45,198}

Accurate arm span measurement relies on consistent and precise positioning. To achieve this, the back is placed against a wall and active and full extension of the arms held at right angles to the trunk is necessary. This outstretched position must be maintained until correct positioning is confirmed and measurement can occur.\textsuperscript{32,45,201}

Forming and holding this position becomes impossible when significant weakness, joint deformity or abnormal tone exists. In these situations arm span measurement becomes imprecise. In spinal deformity, typical methods of height measurement lead to an inaccurate representation of stature. Arm span measurement in this group is also inaccurate due to the effect of spinal deformity on positioning for the measurement. Rotational, kyphotic and lordotic deformities limit the ability to place the back firmly against a vertical wall. Shoulder imbalance leads to disparity in the level of the arms from the floor, which reduces accuracy.\textsuperscript{202}

Practices in Australia are likely to reflect those of other countries where evidence-based medicine is practiced. This part of the research aimed to identify the method of height estimation and pulmonary function prediction used in children with neuromuscular weakness or spinal deformity throughout Australia. A cross-sectional survey of all tertiary paediatric respiratory laboratories in Australia was used to identify the method of height and pulmonary function prediction used, how the results are generally interpreted, and to subjectively assess if similar difficulties in height estimation arise throughout Australia. Contact by both phone and email was made to maximise response rates. The survey form used is attached in Appendix 1. Data was collected into a Microsoft Excel '97 database, and results are presented descriptively.

Much of the research guiding management of children with neuromuscular weakness uses predicted values of pulmonary function.\textsuperscript{14,34,35,105} Yet the specific method used to estimate height and predict normal values of pulmonary function tests is seldom provided. When great variation exists in the methods used, and inaccuracies are readily recognised, a more precise method needs to be sought. The following
component of the research investigates an alternative method of predicting pulmonary function that may be more accurate and reproducible in children with neuromuscular weakness and/or spinal deformity.

**Modified Method of Prediction of Height and Pulmonary Function**

There is inconsistency throughout Australia in the method of height estimation used to predict pulmonary function and most tertiary paediatric laboratories have identified inaccuracies in height estimation as a complexity in the generation of results, leading to difficulty in interpretation. There is a close relationship between height and arm span, as there is with many other body segments.\(^{42-45,198,201,203-207}\) It is likely that another body measurement may also be precise in estimating height and pulmonary function. For a measurement to be of most use in predicting pulmonary function in this group of children who are often immobilised, it should be easily accessible, and its landmarks readily identified to ensure reproducibility. A distal limb segment or long bone length would seem appropriate.

The aim of this part of the research was to identify a distal long bone or body segment measurement that could be precisely and reproducibly measured and could be used to accurately predict height and measurements of pulmonary function. The design used was a cross-sectional population-based study.

**Subjects**

Children aged between 7 and 18 years, were recruited as pulmonary function testing is generally possible in this age group. Recruitment of 100 males and 100 females in each year of age was undertaken. School sampling was used as it gives a comprehensive representation of the school-aged community and is a convenient method of sampling as many students can be approached in a small time period, making recruitment and measurements efficient. It is thought that metropolitan Melbourne would be representative of the general Australian population.
A computer-based random number generator selected schools. Recruitment of schools involved the principal of each being approached by phone and mail. At recruited schools, students aged 7 to 18 years were invited to participate using a presentation at a routine school assembly. Interested students received an information sheet, questionnaire and consent form for their parent or guardian to read and complete. See Appendix 2. The questionnaire asked for gender, date of birth, medical information, gestation at birth, medication use and racial background.

Students were excluded if the questionnaire revealed significant respiratory or systemic illness, spinal deformity, disease known to cause growth disturbance, prematurity (<35 weeks gestation), muscle weakness or abnormal tone, medications thought to alter growth, or use of asthma preventer or reliever medication in the preceding four weeks.

**Measurements**

All measurements were made in schools. Anthropometric measurements were obtained in light clothing with shoes and socks removed. The same anthropometric and spirometric equipment was used for each student. The same observer obtained all the measurements. Weight measurements were in kilograms to the nearest 100 grams. All other measurements were in centimetres (cm) to the nearest millimetre. Age was calculated in (decimal) years for the day of measurement.

Distal limb measurements were chosen because they are the most accessible in immobilized children. Although the upper arm is also accessible, landmarks are more difficult to define, which impedes reproducibility. Arm span was included so comparison could be made to the best currently available method of height estimation in this group. The Harpenden stadiometer and anthropometer and Wedderburn electronic scales were used because of their high degree of accuracy.

Each student underwent a brief medical examination of the spine for scoliosis. Those in whom scoliosis was thought likely were referred to their local doctor and were excluded from further participation.
Standing height was obtained using a portable Harpenden Stadiometer (Holtain Ltd, Crosswell, UK). The accuracy of the Harpenden Stadiometer was checked daily with a metal rule. Each student placed their feet on the base plate, together throughout their length. The back was placed firmly against the vertical plate, with the head, shoulders, buttocks and heels touching it. The head was placed in the Frankfurt horizontal plane. The head plate was lowered to sit on the vertex. Gentle vertical traction was applied to the mastoid processes as a deep inspiration was taken to obtain the measurement.

Weight was obtained by standing on zeroed Wedderburn electronic scales (Wedderburn, Southampton, UK). Weight measurement was omitted in the presence of plaster casts, and in one student who weighed in excess of the scales ability to measure (150 kilograms).

Arm span was measured on a wooden arm span stadiometer. The frame consisted of two vertical poles and a horizontal beam with measurements marked in millimetres. The frame sits neatly against the wall, and each pole is held stable by three wooden feet. Attached to the horizontal beam is a mobile vertical wooden plate that sits from 80cm to 200cm above the floor. Students were measured by standing with their back against the wall, with their head, shoulders, buttocks and heels touching the wall. The feet were vertically below the head, which was in the Frankfurt horizontal plane. The feet were together throughout their length. The arms were extended laterally so that the hands were at the same level from the floor as the shoulders. The palms faced forward. The middle finger of the right hand just touched the protruding right hand pole. The vertical plate was moved medially until it rested against the middle finger of the left hand. If a middle finger had been traumatically amputated or injured, this measurement was omitted.

Ulna length was obtained in the sitting position with the left forearm resting comfortably on a table. The palm faced downwards and the fingers were extended but together. The elbow was bent at 90-110 degrees. The proximal end of the ulna was found by palpating along its length. The tip of the styloid process was felt at the wrist by palpating down the length of the bone distally, until its end was felt. The tips of Harpenden anthropometer were placed adjacent to both end points. See Figure 1.
Figure 1: Method of ulna measurement.

Forearm measurements were made in the same position as the ulna measurement. Harpenden anthropometers were used to measure from the tip of the left middle finger to the most lateral aspect of the elbow. If the middle finger of the left hand had been traumatically amputated or injured, the right arm was substituted.

Tibia length was measured in the seated position using the Harpenden anthropometer. The right tibial plate was found by palpating along the medial boarder of the tibia until its proximal aspect was identified. The distal end was found by palpating the most distal point of the medial malleolus. See Figure 2.

Lower leg length was measured by the Harpenden portable stadiometer. The student was seated beside the stadiometer, facing it. The level of the seat was set so that the knee was at a higher level than the hip. The lateral aspect of the left lower leg was firmly against the stadiometer. The foot was placed directly below the knee. The head plate of the stadiometer was brought down to rest upon the upper aspect of the knee.

To determine reproductibility of the measurements, 14 subjects were measured on two separate occasions on the same day by the first author. Both the first author and an independent observer, trained in performance of the measurements, measured another 15 subjects. The first measurement obtained by the first author was included in analysis for prediction of pulmonary function on all occasions.
Figure 2: Method of tibia measurement.

Pulmonary Function Tests (PFT) were performed in the standing position with a nose clip. A Jaeger Masterscope Spirometer with a heated pneumotac and Version 3.43 Jaeger software (Jaeger Toennies, Hoechberg, Germany) was used. Children were asked to take a maximal inspiration, followed immediately by a maximal forced expiratory manoeuvre without a pause between. A minimum of three manoeuvres was performed. Manoeuvres were considered acceptable if there was a rapid rise to peak flow and a full maximally prolonged expiratory curve²⁰⁸. Computerized visual incentives were often used for encouragement.

To ensure reproducibility, the FEV₁ and FVC of two manoeuvres were required to be within 200 millilitres of each other. The best manoeuvre was defined as the manoeuvre with the greatest sum of FEV₁ and FVC and was used for analysis.²⁰⁸ FEV₁, FVC, and mean mid expiratory flow were recorded. If acceptable and reproducible pulmonary function tests could not be obtained after several attempts, pulmonary function tests were not included in the analysis.
Statistical Analysis

A large sample was used to ensure that variation across the age range could be adequately described and results would have comparable precision to previous studies.\textsuperscript{209}

Data was double entered into two identical forms of a Microsoft Access '97 database that had built in validation checks. Stata 7.0 statistical software was used for analysis.\textsuperscript{196} Intra- and inter-observer variability was analysed by calculating the standard deviation of differences between repeated measurements by the same observer (intra-) and independent observers (inter-).\textsuperscript{210} These were used to derive the standard deviation of individual values, which was expressed as a percentage of the mean.

Exploratory analysis indicated that linear regression models were accurate in predicting height, but performed best on logarithmically transformed pulmonary function values. Linear regression equations were developed including each of the anthropometric measurements and age to predict height and logistically transformed pulmonary function.

Reference ranges for height were calculated to include 95% (two standard deviations) of normal children. For pulmonary function, reference ranges were created by back-transforming 95% prediction intervals obtained from the regression models; because linear prediction was performed in the log scale, back transformation produces a range that can be expressed in ratio terms ("% predicted") relative to the central predicted or normal values.

Ulна length was used as an example of the anthropometric measurements to develop growth charts with increasing age using the LMS method.\textsuperscript{211,212} In males, the median was 5.0, coefficient of variation 5.0 and skewness 3.0. In females, the median was 4.0, coefficient of variation 3.0 and skewness 1.0. Three, 10, 25, 50, 75, 90 and 97 centiles were derived.
The Caucasian and Asian subgroups were compared to the overall group by using interaction terms in each linear regression analysis to assess whether the pattern of the relationship between the dependent measure (height or pulmonary function) and the two independent measures of age and anthropometric measurement was similar between the two groups. A two-degree-of-freedom Wald test was used, and separate prediction equations were obtained whenever this test indicated statistical difference at the 0.05 level.

**Ethical Approval**

The study was approved by the Royal Children’s Hospital Ethics in Human Research Committee and the Department of Employment, Education and Training of Victoria. See Appendix 3 and 4. Written informed consent was obtained from parents and from children over the age of 12 years.

**Evaluation of New Prediction Equations**

For the newly developed prediction equations to be of practical use, the anthropometric measurements must be readily performed by respiratory laboratory technicians in the target group. Orthopaedic complications of neuromuscular weakness may impede performance of the anthropometric measurements that could be used to predict pulmonary function, limiting their practical use. Children with Duchenne muscular dystrophy manifest most of the orthopaedic complications of neuromuscular weakness between the ages of 6 and 18 years. The aim of this part of the research was to subjectively assess the ease of positioning, identification of landmarks and performance of each anthropometric measurements in a group of boys with Duchenne muscular dystrophy.

Limitations in the performance of the anthropometric measurements should be adequately identified with a relatively small sample. All children with Duchenne muscular dystrophy aged between 6 and 18 years attending Sydney Children’s Hospital in a 12 month period were approached.
Arm span was measured standing against a wall with the arms actively or passively extended laterally where possible. If this position was not possible, arm span measurements were made while seated in a wheelchair, with the arms held outstretched as much as possible, often passively with the assistance of a second person. The measurement was performed with a tape measure run over the skin from the tip of one middle finger posteriorly, to the tip of the other middle finger.

Measurement of the ulna, tibia and forearm were performed in an identical manner to that described in the previous part of the research. Lower leg length measurements were performed with a Harpenden anthropometer, as ankle contractures generally precluded positioning of the lower leg against the Harpenden portable stadiometer.

Data was collected into an Access '97 database. A subjective assessment of the ease of performance of each of the anthropometric measurements was made. Difficulties commonly encountered were described. A comparison between the height predicted from the anthropometric measurement in which the positioning and landmarks were best preserved in Duchenne muscular dystrophy, and the height predicted from their arm span was made by the Bland Altman method.213

The Sydney Children’s Hospital Ethics in Human Research Ethics Committee approved the research. See Appendix 5. Written informed consent was obtained from parents/guardians and children over the age of 12 years.

**Impact of Intelligence and Behaviour on Performance of Pulmonary Function Testing**

Teaching children the technique of performing pulmonary function tests adequately and reproducibly can be challenging at times. It generally involves careful verbal explanation and demonstration by paediatric respiratory laboratory staff, and it can take several attempts before the technique is learned. With many pulmonary function test systems, built-in visual incentives provide an encouragement system that can be used to increase the child’s effort and assist in teaching them the technique required.
In children with Duchenne muscular dystrophy, the mean full-scale intelligence quotient (80) is one standard deviation below the population average. Reduced intelligence or oppositional behaviour may limit a child's ability to perform pulmonary function tests. With many pulmonary function test systems, built-in computerised visual incentives provide an encouragement system that can be used to increase the child's effort, teach them the technique required and improve their technique. The effect of computerised visual incentives may be altered in those with impaired intelligence or behaviour.

The aim of this part of the research was to determine if intelligence or behaviour influence performance of pulmonary function tests in children with Duchenne muscular dystrophy and if the use of computerised visual incentives influence pulmonary function test results.

The study design was a randomised cross-over study that prospectively recruited all children with Duchenne muscular dystrophy aged between 6 and 18 years seen at Sydney Children's Hospital in a 12 month period. Children with Duchenne muscular dystrophy at this hospital have not previously performed pulmonary function tests with the assistance of computerised visual incentives.

A computer-based random number generator performed randomisation into two groups. Children randomised to group 1 first performed pulmonary function tests without visual incentives. A minimum of 3 and a maximum of 5 manoeuvres were performed. After a brief rest, these children performed pulmonary function tests with the assistance of visual incentives. Again, a minimum of 3 and a maximum of 5 manoeuvres were performed. Group 2 performed pulmonary function tests with visual incentives on the first occasion and without visual incentives on the second.

Pulmonary function tests were performed in the seated position using a nose clip. A Jaeger Masterscope Spirometer with a heated pneumotac and version 4.60 software was used. A snorkel mouthpiece was used if a good seal could not be made with a standard mouthpiece. Children were asked to take a maximal inspiration, followed immediately by a maximal forced expiratory manoeuvre without a pause between.
The technique required was demonstrated. Manoeuvres were considered acceptable if there was a rapid rise to peak flow and a full maximally prolonged expiratory curve. Reproducibility to within 200 millilitres for both FEV₁ and FVC of two of the manoeuvres was required. The manoeuvre with the greatest sum of FEV₁ and FVC was included in analysis. Predicted values of pulmonary function were calculated from the ulna length.

Full-scale, verbal and performance intelligence quotients were obtained using the Wechsler Intelligence Scales (WPPSI-R or WISC-III) when the children were aged between 6 and 14 years. Ratings of oppositional behaviour level for each child were obtained from the Connors’ parent and teacher rating scales (CPRS-R:1 and CTRS-R:1) within the 12 months prior to spirometry testing.

A questionnaire was used to assess the child’s perceived ease of performance of the pulmonary function tests with and without visual incentives. A five point visual analogue scale was used. See Appendix 5. Written informed consent was obtained from parents or guardians and children over the age of 12 years.

Statistical Analysis

The sample size of 40 children was calculated to detect a 10% difference in means between children performing pulmonary function tests with and without computerised visual incentives, with a power of 0.8 and a significance level of 0.05. The normal standard deviation for forced vital capacity is 0.102, but as these children have neuromuscular weakness and more variability is expected, two standard deviations (0.20) were used in the calculation. According to this calculation, 34 children are required to show a 10% difference in the means of each method of performing pulmonary function testing.

Data was collected into an Access '97 database. Stata 7.0 statistical software was used. Linear regression was used to assess the relationship between pulmonary function test results and full-scale, performance and verbal intelligence quotients and parent and teacher reported oppositional behaviour scores. The paired student t test was used to compare the observed and predicted values of the FEV₁ and FVC found.
with and without using visual incentives. The effect of test order was also compared using the paired student t test. Questionnaires were descriptively reported.

The Sydney Children’s Hospital Ethics in Human Research Ethics Committee approved the research. See Appendix 6. Written informed consent was obtained from parents or guardians and children over the age of 12 years.

**Summary**

A retrospective investigation of children with neuromuscular weakness undergoing corrective spinal surgery was undertaken to evaluate the clinical use of pulmonary function tests and their role in pre-operative risk assessment. A national survey of pulmonary function test prediction in childhood neuromuscular weakness and scoliosis was undertaken to assess the extent of difficulties in predicting normal values. A modified method of pulmonary function test prediction was developed and the impact of intelligence and behaviour on pulmonary function testing was then investigated.
4

Results

The aims of this work, and the methodology used to answer these aims have been outlined. Detailed results of each component of research undertaken will now be provided to allow the reader to draw their own conclusions, and identify the clinical implications and applications of the results.

Pulmonary Function Test Use in Clinical Practice

The retrospective review of children with neuromuscular weakness undergoing corrective spinal surgery identified 68 male and 10 female children. Diagnosis of the underlying neuromuscular condition was made by a neurologist in each instant and was based on family history, clinical characteristics, electrophysiological studies and muscle biopsy, as was the convention at the time. The diagnosis was confirmed by genetic studies in 27 (35%) children. Baseline characteristics of the children included in this study are summarised in Table 1.

Spinal deformities were C-shaped thoracolumbar in 42 (53.8%), S-shaped thoroacolumbar in 22 (28.2%), lumbar in 13 (16.7%), and thoracic in 1 (1.3%). The spinal fixation used was a Luque rod in 67, Harrington rod in 5 and a Unitary rod in 2 children. One child had a Dwyer anterior spinal fusion and 3 had an anterior release and posterior fusion. Pelvic fixation was performed in 58 children (74.4%). The mean anaesthetic time was 2.7 hours, with a standard deviation of 0.83 (SD 0.83; range 1.3-5.2 hours).

The pre-operative respiratory assessment tools used are shown in Table 2. Pulmonary function tests (PFT) were performed in the month before their operation in 87.2% and
Table 1: Baseline characteristics of children with neuromuscular weakness undergoing corrective spinal surgery.

<table>
<thead>
<tr>
<th>Neuromuscular Disorder (%)</th>
<th>Gender</th>
<th>Age</th>
<th>Mobility</th>
<th>Chest Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Mean</td>
<td>Range</td>
</tr>
<tr>
<td>DMD* (70.5)</td>
<td>55</td>
<td>-</td>
<td>14.4</td>
<td>10.52 – 17.1</td>
</tr>
<tr>
<td>SMA† (19.2)</td>
<td>8</td>
<td>7</td>
<td>10.8</td>
<td>7.6 – 12.8</td>
</tr>
<tr>
<td>ED‡ (1.3)</td>
<td>-</td>
<td>1</td>
<td>10.6</td>
<td>-</td>
</tr>
<tr>
<td>MD§ (1.3)</td>
<td>1</td>
<td>-</td>
<td>8.1</td>
<td>-</td>
</tr>
<tr>
<td>NM‖ (1.3)</td>
<td>1</td>
<td>-</td>
<td>12.9</td>
<td>-</td>
</tr>
<tr>
<td>CCD¶ (1.3)</td>
<td>1</td>
<td>-</td>
<td>12.9</td>
<td>-</td>
</tr>
<tr>
<td>CM** (1.3)</td>
<td>1</td>
<td>-</td>
<td>11.7</td>
<td>-</td>
</tr>
<tr>
<td>Unspecified (3.8)</td>
<td>1</td>
<td>2</td>
<td>15.3</td>
<td>14.3 – 15.8</td>
</tr>
<tr>
<td>Total (100)</td>
<td>68</td>
<td>10</td>
<td><strong>13.5</strong></td>
<td><strong>7.6-17.1</strong></td>
</tr>
</tbody>
</table>

*Duchenne muscular dystrophy, †Spinal muscular atrophy, ‡Emery Dreifuss myopathy, §Myotonic dystrophy, ‖Nemaline myopathy, ¶Central core disease, **Cap myopathy.
post-operative PFT were performed 30-90 days post-operatively in 15.4% of children. Fifteen (19.2%) children in this series had a pre-operative forced vital capacity (FVC) <35%. Three (3.8%) children had documented respiratory specialist interpretation of the respiratory investigations. Junior medical staff, surgeons, anaesthetists or neurologists interpreted all other investigations. No child had assessment of respiratory muscle strength (maximal inspiratory or expiratory pressure, or a sniff inspiratory pressure), peak cough flow or polysomnography. No child received pre-operative ventilatory support.

**Table 2:** Summary of pre-operative respiratory assessments.

<table>
<thead>
<tr>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Observations (%)</strong></td>
</tr>
<tr>
<td>FVC* (litres)</td>
</tr>
<tr>
<td>%FVC</td>
</tr>
<tr>
<td>SpO$_2$† (%)</td>
</tr>
<tr>
<td>pCO$_2$‡ (mmHg§)</td>
</tr>
</tbody>
</table>

*Forced vital capacity, †transcutaneous oxygen saturations, ‡arterial carbon dioxide level §millimters mercury.

The complications encountered in the peri-operative period (prior to discharge) and those becoming evident in the longer term are summarised in Table 3. Blood products were required in the peri-operative period in 85.9% of children. Ventilatory support was required post-operatively in 11.5% of children. Table 4 shows the level of respiratory support required. Post-operative requirement for respiratory support was associated with reduced mobility requiring a wheelchair (p=0.0002). No association was found between post-operative need for respiratory support and age at surgery (p=0.24), frequency of chest infections (p=0.22) or pre-operative FVC % predicted (p=0.05). See Figure 1.
Table 3: Complications of corrective spinal surgery.

<table>
<thead>
<tr>
<th>Peri-operative Complication</th>
<th>Number (%)</th>
<th>Long-term Complication</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>5 (6.4)</td>
<td>Neurological sequelae</td>
<td>5 (6.4)</td>
</tr>
<tr>
<td>Infection</td>
<td>5 (6.4)</td>
<td>Infection</td>
<td>2 (2.6)</td>
</tr>
<tr>
<td>Haemodynamic</td>
<td>1 (1.3)</td>
<td>Hip or pelvic pain</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>9 (11.5)</td>
<td>Back pain</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrence/progression</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of spinal deformity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hardware failure</td>
<td>2 (2.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced mobility</td>
<td>1 (1.3)</td>
</tr>
</tbody>
</table>

Table 4: Maximum level of respiratory support required.

<table>
<thead>
<tr>
<th></th>
<th>Number (%</th>
<th>Mean maximum O₂*</th>
<th>Mean maximum PIP† (cmH₂O‡)</th>
<th>Mean maximum PEEP§ (cmH₂O‡)</th>
<th>Mean duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(range)</td>
<td>(range)</td>
<td>(range)</td>
<td>(range)</td>
<td>(range)</td>
</tr>
<tr>
<td><em><em>O₂</em> therapy</em>*</td>
<td>63 (80.8)</td>
<td>3.7 litres/min</td>
<td>-</td>
<td>-</td>
<td>26.6 hours</td>
</tr>
<tr>
<td><strong>CPAP</strong></td>
<td>2 (2.6)</td>
<td>40%</td>
<td>-</td>
<td>9.5</td>
<td>58.5 hours</td>
</tr>
<tr>
<td><strong>BPAP</strong>*</td>
<td>2 (2.6)</td>
<td>25.5%</td>
<td>18</td>
<td>8</td>
<td>1- nocturnal for 2 days</td>
</tr>
<tr>
<td><strong>Invasive ventilation</strong></td>
<td>5 (6.4)</td>
<td>45.3%</td>
<td>23.2</td>
<td>4.8</td>
<td>106.7 hours</td>
</tr>
<tr>
<td></td>
<td>(40-100)</td>
<td>(13-36)</td>
<td>(3-6)</td>
<td>(2.5-408)</td>
<td></td>
</tr>
</tbody>
</table>

*Oxygen, †peak inspiratory pressure, ‡centimetres of water, §peak end expiratory pressure, ||continuous positive airway pressure, **bilevel positive airway pressure.

Only four children in this series have begun home-based non-invasive ventilation, and all four began this therapy in the last 2 years, a mean of 3.2 years (8 days - 5.2 years) following corrective spinal surgery. All were alive at the time of data collection. The use of the taught techniques to assist with mucociliary clearance was not evident in any medical history.

Rates of Decline of Pulmonary Function

A total of 361 pulmonary function tests recorded in these 78 children. Sixty-four children had ≥2 pulmonary function tests prior to surgery; 26 had ≥2 pulmonary function tests after their operation. The characteristics of the children included in
analysis of the rates of decline in the pre- and post-operative periods are summarised in Table 5. There is no statistical difference between the age at the time of surgery (p=0.16), FVC (p=0.11) or FVC % predicted (p=0.85) between the group included in both the pre- and post-operative analysis and the group considered only in the pre-operative analysis.

In the 64 children included in the pre-operative rate of decline analysis, the mean number of pre-operative pulmonary function tests performed was 3.53 (SD 1.37; range 2-8). The mean period of follow-up in the pre-operative period was 2.29 years (SD 1.75 years; range 20 days to 6.5 years). In the 26 children included in the post-operative analysis, there was a mean of 4.00 post-operative pulmonary function tests performed (SD 2.8; range 2-15). The mean period of follow-up was 4.23 years (SD 2.96 years; range 304 days – 10.7 years).

There was an acute fall from the pre-operative %FVC to that measured 30-90 days post-operative of 11.14% (6.09% in Duchenne muscular dystrophy and 15.74% in Spinal muscular atrophy). There was a reduction in the rate of decline of FVC % predicted post-operatively from 5.14 to 0.99%/year overall (p<0.01), 6.17 to 3.35%/year in Duchenne muscular dystrophy (p=0.02) and 2.33 to 0.20%/year in Spinal muscular atrophy (p=0.27). Subgroup analysis was not possible for the other neuromuscular disorders as numbers were small. The magnitude of the acute fall in FVC % predicted in the post-operative period, the change in rate of decline in FVC % predicted from the pre- to the post-operative period and 95% confidence intervals are shown in Table 6 and graphically demonstrated in Figure 2.

Subgroup analysis was undertaken for children included in this study from 1974-1991 and from 1992-2002. It was found that the pre-operative FVC, complication rates and types did not differ between the two groups, and the proportions of children requiring respiratory support were equivalent. Bilevel support was not used in the earlier group. The rates of decline in pulmonary function in the pre- and post-operative periods, the acute peri-operative fall and the reduction in rate of decline post-operatively were all similar to the whole group analysis, but the confidence intervals were wider, due to the smaller numbers of children in each group. The subgroup analysis did not add further information to the overall results.
Figure 1: Relationship between forced vital capacity percent predicted and need for respiratory support post-operatively.

*p = 0.05
**Table 5:** Characteristics of children included in the analysis for rates of decline in forced vital capacity percent predicted in the pre- and post-operative periods.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Included in Both Pre- and Post-Operative Analysis</th>
<th>Only Included in Pre-Operative Analysis</th>
<th>Only Included in Post-Operative Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMD*</td>
<td>17</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>SMA†</td>
<td>5</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Mean age of surgery (years)</td>
<td>13.2</td>
<td>13.9</td>
<td>10.3</td>
</tr>
<tr>
<td>[range]</td>
<td>[9.3-16.5]</td>
<td>[7.6-17.1]</td>
<td>[8.1-12.6]</td>
</tr>
<tr>
<td>Mean pre-operative FVC ‡ (litres)</td>
<td>1.5</td>
<td>1.7</td>
<td>-</td>
</tr>
<tr>
<td>[range]</td>
<td>[0.61-3.0]</td>
<td>[0.71-3.02]</td>
<td>-</td>
</tr>
<tr>
<td>Mean pre-operative %FVC ‖</td>
<td>48.8</td>
<td>49.7</td>
<td>-</td>
</tr>
<tr>
<td>[range]</td>
<td>[21.9-104.5]</td>
<td>[19.8-74.4]</td>
<td>-</td>
</tr>
</tbody>
</table>

DMD-Duchenne muscular dystrophy, SMA-Spinal muscular atrophy, FVC-forced vital capacity.

**Table 6:** Acute peri-operative fall in forced vital capacity percent predicted and its rate of pre- and post-operative decline.

<table>
<thead>
<tr>
<th></th>
<th>Acute Peri-Operative Fall in FVC* (%predicted)</th>
<th>Pre-Operative Rate of FVC* Decline (%/year)</th>
<th>Post-Operative Rate of FVC* Decline (%/year)</th>
<th>Difference in Rates of Decline (%/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All NMD</td>
<td>11.14</td>
<td>5.14‡</td>
<td>0.99‡</td>
<td>4.15</td>
</tr>
<tr>
<td>(CI</td>
<td></td>
<td>)</td>
<td>(10.03-12.25)</td>
<td>(4.17-6.20)</td>
</tr>
<tr>
<td>DMD</td>
<td>6.09</td>
<td>6.17‡</td>
<td>3.35‡</td>
<td>2.82</td>
</tr>
<tr>
<td>(CI</td>
<td></td>
<td>)</td>
<td>(5.17-7.01)</td>
<td>(5.13-7.21)</td>
</tr>
<tr>
<td>SMA</td>
<td>15.74</td>
<td>2.33§</td>
<td>0.20§</td>
<td>2.13</td>
</tr>
<tr>
<td>(CI</td>
<td></td>
<td>)</td>
<td>(13.6-17.91)</td>
<td>(0.01-4.64)</td>
</tr>
</tbody>
</table>

*Forced vital capacity, ‡p<0.01, ‡p=0.02, §p=0.27, ‖95% confidence interval.
Figure 2: Fitted regression models of the rate of decline in forced vital capacity percent predicted before and after corrective spinal surgery. *p<0.01, †p=0.02, ‡p=0.27.
Peri-Operative Death

A 12.9 year old boy with Nemaline myopathy died in the peri-operative period from respiratory failure. Pre-operatively, he was wheelchair bound, had bulbar weakness resulting in recurrent aspiration, and had >5 chest infections requiring hospitalisation per year. He had an S-shaped thoracolumbar scoliosis with a 45 degree angle in his thoracic spine. His pre-operative oxygen saturations were 93%. His pre-operative FVC was 26.6 % predicted (788 millilitres). His corrective spinal surgery required an anaesthetic time of 5.2 hours, and he received blood products due to intra-operative losses. Post-operatively he was in respiratory failure and had an ongoing requirement for ventilatory support. He received a maximum of 100% oxygen and peak inspiratory and expiratory pressures of 18 and 6 centimetres of water, respectively for a total of 408 hours. He was successfully weaned to continuous positive airway pressure of 14 centimetres of water and 40% inspired oxygen. He failed cessation of continuous positive airway pressure on several occasions before he and his family decided to desist with ventilatory support due to his poor quality of life on continuous ventilatory support. He died 24 days post-operatively.

In considering whether this child’s peri-operative death may have been predicted from his pre-operative investigations, differences between him and the other children in this group were sought. He was the only child in the series to have Nemaline myopathy, although this in not known to increase the risk of surgery beyond other children with neuromuscular weakness. He had the most frequent recurrent chest infections. Only 3 other children had ≥ 5 chest infections per year. His oxygen saturations were the lowest recorded; all others were ≥ 95%. He did not have an arterial carbon dioxide level measured. He had the longest anaesthetic time in this series. Only four other children in this series had a FVC % predicted lower than this child (19.8-25.2) and five had an observed FVC < 788 millilitres (range: 610-760 millilitres). His respiratory reserve was likely to be marginal, and his operation occurred before non-invasive ventilation use was begun in the Royal Children’s Hospital, Melbourne.
**Inaccuracy in Predicting Pulmonary Function**

The most commonly used pre-operative respiratory assessment tool used prior to corrective spinal surgery was pulmonary function testing, which was used in 87.2% of children. The component of pulmonary function testing that was most frequently documented in the medical notes was FVC % predicted. Interpretation of the result was generally by a junior medical staff member, surgeon, anaesthetist or neurologist. A respiratory physician consultation was only documented in 3.8% of children.

Of the 361 pulmonary function tests recorded, 333 (92.2%) did not have a method of height estimation recorded and 26 (7.2%) used arm span. Thirty-four (9.4% of tests) children had a height or arm span estimation that reduced despite increasing age. This reduction ranged from 1cm to 22cm. See Figure 3.

![Figure 3](image-url)

*Figure 3:* Magnitudes of errors in height estimation that resulted in a reduced height measurement despite increasing age. n=34.
In the group of children included in the analysis of rates of decline in pulmonary function before and after corrective spinal surgery, 226 pulmonary function tests were performed prior to surgery, and 19 (8.4%) of these tests had inaccuracies of height estimation, leading to a reduced height despite an increasing age. The inaccuracies ranged from 1-12 centimeters (mean of 6.47, standard deviation 3.36). In the post-operative group, 104 pulmonary function tests were performed, and 12 (11.5%) contained inaccuracies of height estimation, that ranged from 2-17 centimeters (mean 7.75, standard deviation 4.49).

This part of the research highlights that there is imprecision within the Royal Children’s Hospital, Melbourne throughout this time period for the measurement used to estimate height and predict normal pulmonary function test values.

**Nationwide Pulmonary Function Test Prediction**

To define the extent of difficulties in predicting pulmonary function that may exist, eight tertiary paediatric laboratories in Australia were surveyed. The response rate was 100%. The total number of children performing pulmonary function tests in these laboratories each year was 227 with neuromuscular weakness and 163 with known scoliosis. The methods used to estimate height when predicting pulmonary function and how the results are interpreted in children with neuromuscular weakness or scoliosis are summarised in Table 7 and 8, respectively.

There is not standardisation of either the method of height estimation used to predict normal values of pulmonary function, nor in the way pulmonary function tests are interpreted within tertiary paediatric respiratory departments in children with neuromuscular weakness or scoliosis. Six (75%) laboratory managers identified difficulties in performing arm span measurements in children with weakness or joint deformities, and recognised significant variations between repeat measurements.
Modified Method of Prediction of Height and Pulmonary Function

Subjects

To develop a new method of prediction of normal values of pulmonary function tests, forty metropolitan Melbourne schools were approached and 27 agreed to participate. Five thousand three hundred and fifty-two questionnaires were distributed and 2810 students (53% of available students) returned a completed questionnaire and consent form. The response rate was 71% for primary school students and 33% for high school students. Four hundred and sixty-seven students were excluded on the basis of their questionnaire or scoliosis check. The reasons for exclusion are shown in Table 9. The age distribution was consistent from 7 to 18 years, with few lying outside this range. Figure 4 provides a graphical representation.
Table 7: Method of height estimation and pulmonary function interpretation used in respiratory laboratories in children with neuromuscular weakness.

<table>
<thead>
<tr>
<th>Method of Height Estimation</th>
<th>Interpretation of Pulmonary Function</th>
<th>Combined predicted and observed values</th>
<th>Mainly observed values</th>
<th>Mainly predicted values</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tape measure run posteriorly over the skin surface from the tip of one middle finger to the other</td>
<td>1 (12.5%)</td>
<td>3 (37.5%)</td>
<td>3 (37.5%)</td>
<td>7 (87.5%)</td>
<td></td>
</tr>
<tr>
<td>Tape measure run posteriorly over the skin surface from the tip of one middle finger to the midline and measurement doubled</td>
<td>-</td>
<td>1 (12.5%)</td>
<td>-</td>
<td>1 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 (12.5%)</td>
<td>4 (50.0%)</td>
<td>3 (37.5%)</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>
Table 8: Method of height estimation and pulmonary function interpretation used in respiratory laboratories in children with scoliosis.

<table>
<thead>
<tr>
<th>Method of Height Estimation</th>
<th>Combined predicted and observed values</th>
<th>Mainly observed values</th>
<th>Mainly predicted values</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tape measure run posteriorly over the skin surface from the tip of one middle finger to the other</em></td>
<td>-</td>
<td>1 (12.5%)</td>
<td>4 (50.0%)</td>
<td>5 (62.5%)</td>
</tr>
<tr>
<td><em>Arms extended laterally and arm span measured against a wall</em></td>
<td>1 (12.5%)</td>
<td>-</td>
<td>-</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td><em>Tape measure run posteriorly over the skin surface from the tip of one middle finger to the midline and measurement doubled</em></td>
<td>1 (12.5%)</td>
<td>-</td>
<td>-</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td><em>Standing height</em></td>
<td>1 (12.5%)</td>
<td>-</td>
<td>-</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td><em>Total</em></td>
<td>3 (37.5%)</td>
<td>1 (12.5%)</td>
<td>4 (50.0%)</td>
<td>8</td>
</tr>
</tbody>
</table>
Table 9: Reasons for exclusion.

<table>
<thead>
<tr>
<th>Reason for Exclusion</th>
<th>Males (%)</th>
<th>Females (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>145 (12.7)</td>
<td>102 (8.5)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>55 (4.8)</td>
<td>49 (4.1)</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>15 (1.3)</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td>Medications</td>
<td>23 (2.0)</td>
<td>9 (0.8)</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>4 (0.3)</td>
<td>7 (0.6)</td>
</tr>
<tr>
<td>Stature</td>
<td>1 (0.1)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Other</td>
<td>14 (22.5)</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>257 (22.5)</strong></td>
<td><strong>210 (17.5)</strong></td>
</tr>
</tbody>
</table>

* % of total recruited males (n=1144) and females (n=1199).

Measurement Variability

The measurement of each variable was highly reproducible. The standard deviation of intra-observer differences for repeat ulna measurements was 0.13 centimetres, corresponding to a standard deviation of 0.093 centimetres for individual values or 0.41% relative to the mean value. Intra- and inter-observer variability was calculated similarly for all repeat measurements and results are shown in Table 10.
Figure 4: Age distribution of males and females included in analysis.
Table 10: Standard deviations of intra- and inter-observer variabilities.

<table>
<thead>
<tr>
<th></th>
<th>SD* of Differences (centimetres)</th>
<th>Individual SD* (centimetres)</th>
<th>Individual SD* as % of Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-Observer Variability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>0.08</td>
<td>0.06</td>
<td>0.13</td>
</tr>
<tr>
<td>Height</td>
<td>0.23</td>
<td>0.16</td>
<td>0.11</td>
</tr>
<tr>
<td>Arm Span</td>
<td>0.57</td>
<td>0.41</td>
<td>0.27</td>
</tr>
<tr>
<td>Ulna</td>
<td>0.13</td>
<td>0.09</td>
<td>0.41</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.17</td>
<td>0.12</td>
<td>0.31</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.16</td>
<td>0.11</td>
<td>0.32</td>
</tr>
<tr>
<td>Lower Leg</td>
<td>0.10</td>
<td>0.07</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Inter-Observer Variability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>0.09</td>
<td>0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>Height</td>
<td>0.26</td>
<td>0.19</td>
<td>0.12</td>
</tr>
<tr>
<td>Arm Span</td>
<td>0.50</td>
<td>0.35</td>
<td>0.22</td>
</tr>
<tr>
<td>Ulna</td>
<td>0.21</td>
<td>0.15</td>
<td>0.61</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.15</td>
<td>0.10</td>
<td>0.25</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.23</td>
<td>0.24</td>
<td>0.65</td>
</tr>
<tr>
<td>Lower Leg</td>
<td>0.17</td>
<td>0.12</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*Standard deviation.

**Prediction of Height**

Prediction equations for height from each of the anthropometric measurements have been developed from linear regression analysis. Age was included to improve the accuracy of prediction. Weight did not significantly improve accuracy. The prediction equations and 95% reference ranges are shown in Table 11. The relationship between height and each of the anthropometric measurements is graphically represented in Figure 5-9, and include the prediction equation, ignoring age, and the reference range. The prediction equation depicted for ulna length had $R^2$ 0.95 and 0.92 respectively, compared to 0.96 and 0.94 when age is included. Table 12 provides a comparison of the precision of height estimation from ulna length, compared to the precision of height estimation from arm span in other studies.
Table 11: Prediction equations for height estimation.

<table>
<thead>
<tr>
<th>Prediction Equation for Height</th>
<th>$R^2$</th>
<th>RMSE</th>
<th>95% Reference Range (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm span</td>
<td>0.97</td>
<td>3.214</td>
<td>± 6.30</td>
</tr>
<tr>
<td>Ulna</td>
<td>0.96</td>
<td>3.896</td>
<td>± 7.64</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.97</td>
<td>3.556</td>
<td>± 7.00</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.96</td>
<td>3.791</td>
<td>± 7.43</td>
</tr>
<tr>
<td>Lower leg</td>
<td>0.98</td>
<td>3.062</td>
<td>± 6.00</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm span</td>
<td>0.91</td>
<td>4.484</td>
<td>± 8.79</td>
</tr>
<tr>
<td>Ulna</td>
<td>0.94</td>
<td>3.785</td>
<td>± 7.42</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.95</td>
<td>3.344</td>
<td>± 6.55</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.95</td>
<td>3.383</td>
<td>± 6.63</td>
</tr>
<tr>
<td>Lower leg</td>
<td>0.97</td>
<td>2.717</td>
<td>± 5.33</td>
</tr>
</tbody>
</table>

RMSE-root mean square of the error, cm-centimetres, H-height, AS-arm span, A-age, U-ulna length, F-forearm length, T-tibia length, L-lower leg length.

Table 12: Comparison between accuracy ($R^3$) of height predicted from ulna length to that predicted from arm span in other studies.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td>0.96</td>
<td>0.97</td>
<td>0.97</td>
<td>0.87</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td>0.94</td>
<td>0.97</td>
<td>0.94</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Figure 5: Relationship between height and arm span with prediction equation (excluding age), third and 97th percentiles.
Figure 6: Relationship between height and ulna length with prediction equation (excluding age), third and 97th percentiles.
Figure 7: Relationship between height and forearm length with prediction equation (excluding age), third and 97th percentiles.
Figure 8: Relationship between height and tibia length with prediction equation (excluding age), third and 97th percentiles.
Figure 9: Relationship between height and lower leg length with prediction equation (excluding age), third and 97th percentiles.
Growth Charts

Growth charts were developed for ulna length with increasing age for males and females and are shown in Figure 10.

Figure 10: Ulna length growth charts for advancing age for males and females.
Prediction of Pulmonary Function

Prediction equations for FVC, forced expiratory volume in one second (FEV₁) and mean mid-expiratory flow were developed using each of the anthropometric measurements and age as predictor variables. The prediction equations developed for each of the pulmonary function parameters using the anthropometric measurements and age are shown in Table 13-18 along with $R^2$, root mean square error and 95% reference ranges. Weight did not add to the precision of prediction equations. Prediction equations could be graphically represented for each of the anthropometric measurements, and for each of the pulmonary function test parameters using the data collected. Ulna length has been used as an example, rather than including all the possible combinations. The relationship between FVC and ulna length is graphically represented in Figure 11, ignoring age. The prediction equations depicted had $R^2$ of 0.84 and 0.79, respectively, compared with the values of 0.86 and 0.83 when age is included. Similar graphs, without the inclusion of age have been generated for FEV₁ and mean mid-expiratory flow versus ulna length; see Figure 12 and 13. An example of the use of the prediction equations using the ulna length for FVC prediction is provided in Figure 14.

Table 13: Prediction equations for pulmonary function using height and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ = exp (0.016 x H + 0.021 x A - 1.768)</td>
<td>0.89</td>
<td>0.132</td>
<td>77-130</td>
</tr>
<tr>
<td>FVC = exp (0.017 x H + 0.017 x A - 1.798)</td>
<td>0.89</td>
<td>0.137</td>
<td>76-131</td>
</tr>
<tr>
<td>MMEF = exp (0.014 x H + 0.032 x A - 1.451)</td>
<td>0.69</td>
<td>0.245</td>
<td>62-162</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ = exp (0.016 x H + 0.020 x A - 1.728)</td>
<td>0.88</td>
<td>0.133</td>
<td>80-125</td>
</tr>
<tr>
<td>FVC = exp (0.017 x H + 0.016 x A - 1.831)</td>
<td>0.86</td>
<td>0.121</td>
<td>79-127</td>
</tr>
<tr>
<td>MMEF = exp (0.012 x H + 0.039 x A - 1.164)</td>
<td>0.62</td>
<td>0.231</td>
<td>64-157</td>
</tr>
</tbody>
</table>

RMSE-Root mean square error, FEV₁-forced expiratory volume in one second, H-height, A-age, FVC-forced vital capacity, MMEF-mean mid-expiratory flow.
Table 14: Prediction equations for pulmonary function using arm span and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1135)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.014 x AS + 0.032 x A -1.512)</td>
<td>0.88</td>
<td>0.140</td>
<td>76 - 132</td>
</tr>
<tr>
<td>FVC = exp (0.015 x AS + 0.027 x A -1.543)</td>
<td>0.88</td>
<td>0.144</td>
<td>75 - 133</td>
</tr>
<tr>
<td>MMEF = exp (0.011 x AS +0.042 x A -1.216)</td>
<td>0.68</td>
<td>0.249</td>
<td>61 - 163</td>
</tr>
<tr>
<td><strong>Females (n=1198)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.010 x AS +0.047 x A - 1.148)</td>
<td>0.83</td>
<td>0.135</td>
<td>77 - 130</td>
</tr>
<tr>
<td>FVC = exp (0.010 x AS + 0.043 x A -1.182)</td>
<td>0.81</td>
<td>0.143</td>
<td>76 - 132</td>
</tr>
<tr>
<td>MMEF = exp (0.067 x AS + 0.059 x A - 0.697)</td>
<td>0.60</td>
<td>0.237</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

RMSE=Root mean square error, FEV$_1$=forced expiratory volume in one second, AS=arm span, A=age, FVC=forced vital capacity, MMEF= mean mid-expiratory flow.

Table 15: Prediction equations for pulmonary function using ulna length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.071 x U + 0.046 x A - 1.269)</td>
<td>0.86</td>
<td>0.149</td>
<td>75 - 134</td>
</tr>
<tr>
<td>FVC = exp (0.077 x U + 0.041 x A - 1.285)</td>
<td>0.86</td>
<td>0.154</td>
<td>74 - 135</td>
</tr>
<tr>
<td>MMEF = exp (0.060 x U + 0.053 x A - 1.013)</td>
<td>0.67</td>
<td>0.253</td>
<td>63 - 158</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.072 x U + 0.041 x A - 1.272)</td>
<td>0.84</td>
<td>0.127</td>
<td>78 - 128</td>
</tr>
<tr>
<td>FVC = exp (0.078 x U + 0.037 x A - 1.315)</td>
<td>0.83</td>
<td>0.135</td>
<td>78 - 128</td>
</tr>
<tr>
<td>MMEF = exp (0.053 x U + 0.054 x A - 0.806)</td>
<td>0.61</td>
<td>0.234</td>
<td>63 - 158</td>
</tr>
</tbody>
</table>

RMSE=Root mean square error, FEV$_1$=forced expiratory volume in one second, U=ulna length, A=age, FVC=forced vital capacity, MMEF= mean mid-expiratory flow.

Table 16: Prediction equations for pulmonary function using forearm length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.046 x F + 0.042 x A - 1.419)</td>
<td>0.87</td>
<td>0.145</td>
<td>75 - 133</td>
</tr>
<tr>
<td>FVC = exp (0.050 x F + 0.038 x A - 1.433)</td>
<td>0.87</td>
<td>0.150</td>
<td>75 - 134</td>
</tr>
<tr>
<td>MMEF = exp (0.067 x F - 1.659)</td>
<td>0.66</td>
<td>0.251</td>
<td>60 - 167</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.046 x F + 0.039 x A - 1.426)</td>
<td>0.85</td>
<td>0.125</td>
<td>78 - 128</td>
</tr>
<tr>
<td>FVC = exp (0.050 x F + 0.035 x A - 1.470)</td>
<td>0.84</td>
<td>0.133</td>
<td>77 - 130</td>
</tr>
<tr>
<td>MMEF = exp (0.035 x F + 0.052 x A - 0.934)</td>
<td>0.61</td>
<td>0.233</td>
<td>63 - 158</td>
</tr>
</tbody>
</table>

RMSE=Root mean square error, FEV$_1$=forced expiratory volume in one second, F=forearm, A=age, FVC=forced vital capacity, MMEF= mean mid-expiratory flow.
Table 17: Prediction equations for pulmonary function using tibia length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.039 \times T + 0.056 \times A - 1.085)$</td>
<td>0.85</td>
<td>0.153</td>
<td>74 - 135</td>
</tr>
<tr>
<td>$FVC = \exp (0.043 \times T + 0.053 \times A - 1.084)$</td>
<td>0.85</td>
<td>0.159</td>
<td>73 - 137</td>
</tr>
<tr>
<td>$MMEF = \exp (0.034 \times T + 0.062 \times A - 0.855)$</td>
<td>0.67</td>
<td>0.255</td>
<td>61 - 165</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.042 \times T + 0.046 \times A - 1.108)$</td>
<td>0.85</td>
<td>0.130</td>
<td>78 - 128</td>
</tr>
<tr>
<td>$FVC = \exp (0.046 \times T + 0.042 \times A - 1.148)$</td>
<td>0.83</td>
<td>0.137</td>
<td>76 - 131</td>
</tr>
<tr>
<td>$MMEF = \exp (0.028 \times T + 0.060 \times A - 0.630)$</td>
<td>0.60</td>
<td>0.237</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

RMSE: Root mean square error, $FEV_1$: forced expiratory volume in one second, $T$: tibia length, $A$: age, $FVC$: forced vital capacity, $MMEF$: mean mid-expiratory flow.

Table 18: Prediction equations for pulmonary function using lower leg length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.036 \times L + 0.048 \times A - 1.326)$</td>
<td>0.86</td>
<td>0.148</td>
<td>75 - 134</td>
</tr>
<tr>
<td>$FVC = \exp (0.039 \times L + 0.045 \times A - 1.345)$</td>
<td>0.86</td>
<td>0.152</td>
<td>74 - 135</td>
</tr>
<tr>
<td>$MMEF = \exp (0.030 \times L + 0.056 \times A - 1.059)$</td>
<td>0.68</td>
<td>0.252</td>
<td>61 - 164</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.038 \times L + 0.041 \times A - 1.391)$</td>
<td>0.85</td>
<td>0.124</td>
<td>78 - 128</td>
</tr>
<tr>
<td>$FVC = \exp (0.042 \times L + 0.036 \times A - 1.455)$</td>
<td>0.84</td>
<td>0.130</td>
<td>78 - 129</td>
</tr>
<tr>
<td>$MMEF = \exp (0.025 \times L + 0.057 \times A - 0.805)$</td>
<td>0.60</td>
<td>0.236</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

RMSE: Root mean square error, $FEV_1$: forced expiratory volume in one second, $L$: lower leg length, $A$: age, $FVC$: forced vital capacity, $MMEF$: mean mid-expiratory flow.
Figure 11: Forced vital capacity versus ulna length for males and females with prediction equations (excluding age) and 95% reference range.
Figure 12: Forced expiratory volume in one second versus ulna length for males and females with prediction equations (excluding age) and 95% reference range.
Figure 13: Mean mid-expiratory flow versus ulna length for males and females with prediction equations (excluding age) and 95% reference range.
\[ FVC = \exp (0.078 \times U + 0.037 \times A - 1.315) \quad \text{RMSE}=0.135 \]

<table>
<thead>
<tr>
<th>Ulna Length (centimetres)</th>
<th>Age (years)</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td></td>
<td>1.21</td>
<td>1.26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>1.31</td>
<td>1.36</td>
<td>1.41</td>
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<td></td>
<td>1.42</td>
<td>1.47</td>
<td>1.53</td>
<td>1.59</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>19</td>
<td></td>
<td>1.53</td>
<td>1.59</td>
<td>1.66</td>
<td>1.72</td>
<td>1.78</td>
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</tr>
<tr>
<td>20</td>
<td></td>
<td>1.66</td>
<td>1.72</td>
<td>1.79</td>
<td>1.85</td>
<td>1.92</td>
<td>2.00</td>
<td>2.07</td>
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<td></td>
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<tr>
<td>21</td>
<td></td>
<td>1.79</td>
<td>1.86</td>
<td>1.93</td>
<td>2.01</td>
<td>2.08</td>
<td>2.16</td>
<td>2.24</td>
<td>2.33</td>
<td>2.41</td>
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<tr>
<td>22</td>
<td></td>
<td>2.01</td>
<td>2.09</td>
<td>2.17</td>
<td>2.25</td>
<td>2.33</td>
<td>2.42</td>
<td>2.51</td>
<td>2.61</td>
<td>2.71</td>
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<tr>
<td>23</td>
<td></td>
<td>2.26</td>
<td>2.34</td>
<td>2.43</td>
<td>2.52</td>
<td>2.62</td>
<td>2.72</td>
<td>2.82</td>
<td>2.93</td>
<td>3.04</td>
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<tr>
<td>24</td>
<td></td>
<td>2.53</td>
<td>2.63</td>
<td>2.73</td>
<td>2.83</td>
<td>2.94</td>
<td>3.05</td>
<td>3.17</td>
<td>3.29</td>
<td>3.41</td>
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<td>2.95</td>
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<td>3.31</td>
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<td></td>
<td>3.58</td>
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<tr>
<td>28</td>
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<td></td>
</tr>
</tbody>
</table>

Per year of age, multiply by: \(1.0378\)
Per cm of ulna length, multiply by: \(1.0812\)

**Reference ranges:**

| 50% | Multiply or divide by: 1.095 |
| 75% | 1.168 |
| 80% | 1.189 |
| 90% | 1.248 |
| 95% | 1.302 |

*Figure 14: Method of prediction of normal forced vital capacity for females.*

Table 19 summarises the goodness of fit \(R^2\) for the prediction equations for each of the anthropometric measurements and age. This table also includes a comparison to published \(R^2\) values for prediction equations in common use. The accuracy of prediction of FEV1 and FVC from all measurements, including height, arm span and ulna lengths are comparable. The \(R^2\) ranged between 0.85-0.89 for males, and 0.81-0.88 for females.
Table 19: $R^2$ of pulmonary function prediction equations compared to previous studies using height that are commonly cited.

<table>
<thead>
<tr>
<th></th>
<th>Current study</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Height</td>
<td>Arm span</td>
<td>Ulna</td>
<td>Forearm</td>
<td>Tibia</td>
<td>Lower leg</td>
<td>Zapletal</td>
<td>Knudson</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td>n=2343</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1977&lt;sup&gt;300&lt;/sup&gt;</td>
<td>1983&lt;sup&gt;39&lt;/sup&gt;</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>0.89</td>
<td>0.88</td>
<td>0.86</td>
<td>0.87</td>
<td>0.85</td>
<td>0.86</td>
<td>0.88</td>
<td>0.70</td>
<td>0.77</td>
</tr>
<tr>
<td>FVC</td>
<td>0.89</td>
<td>0.88</td>
<td>0.86</td>
<td>0.87</td>
<td>0.85</td>
<td>0.86</td>
<td>0.92</td>
<td>0.66</td>
<td>0.80</td>
</tr>
<tr>
<td>MMEF</td>
<td>0.69</td>
<td>0.68</td>
<td>0.67</td>
<td>0.66</td>
<td>0.67</td>
<td>0.68</td>
<td>0.60</td>
<td>0.30</td>
<td>0.45</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>0.88</td>
<td>0.83</td>
<td>0.84</td>
<td>0.85</td>
<td>0.85</td>
<td>0.85</td>
<td>0.86</td>
<td>0.61</td>
<td>0.55</td>
</tr>
<tr>
<td>FVC</td>
<td>0.86</td>
<td>0.81</td>
<td>0.83</td>
<td>0.84</td>
<td>0.83</td>
<td>0.84</td>
<td>0.88</td>
<td>0.57</td>
<td>0.53</td>
</tr>
<tr>
<td>MMEF</td>
<td>0.62</td>
<td>0.60</td>
<td>0.61</td>
<td>0.61</td>
<td>0.60</td>
<td>0.60</td>
<td>0.60</td>
<td>0.10</td>
<td>0.28</td>
</tr>
</tbody>
</table>

FEV<sub>1</sub>-forced expiratory volume in one second, FVC-forced vital capacity, MMEF-mean mid-expiratory flow.
Influence of Racial Background

The racial backgrounds of included students is summarised in Table 20. The majority of children were Caucasian (n=1801) or Asian (n=307). The prediction equations developed are precise for the Caucasian sub-population. The most anthropometrically distinct sub-population was the group from Asia. Prediction equations for height in the male and female Asian subpopulation were significantly different (p<0.05) when using arm span, forearm or tibia length as independent predictors. There was no significant difference in the prediction equations when ulna length was used. The prediction equations for height in the Asian sub-population are summarized in Table 21, along with $R^2$, root mean square error and $p$ values for the difference. Separate growth charts for ulna length have not been created for the Asian population, as the prediction equations in the Asian sub-population are not significantly different to those of the overall group, and the same growth charts may be used in both populations.

Table 20: Racial backgrounds of included students.

<table>
<thead>
<tr>
<th></th>
<th><strong>Males</strong></th>
<th></th>
<th><strong>Females</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td></td>
<td>Number (%)</td>
</tr>
<tr>
<td>Anglo-Saxon</td>
<td>728 (63.6)</td>
<td>792 (66.1)</td>
<td></td>
</tr>
<tr>
<td>Mediterranean</td>
<td>103 (9.0)</td>
<td>147 (12.3)</td>
<td></td>
</tr>
<tr>
<td>South American</td>
<td>13 (1.1)</td>
<td>18 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>173 (15.1)</td>
<td>134 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>7 (0.6)</td>
<td>5 (0.4)</td>
<td></td>
</tr>
<tr>
<td>African</td>
<td>3 (0.3)</td>
<td>4 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Aboriginal</td>
<td>-</td>
<td>2 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>109 (9.5)</td>
<td>86 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (0.7)</td>
<td>11 (0.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1144</td>
<td><strong>1199</strong></td>
<td></td>
</tr>
</tbody>
</table>
Table 21: Prediction equations for height in the Asian subpopulation and p value for the difference from the overall population.

<table>
<thead>
<tr>
<th>Prediction Equation for Height</th>
<th>$R^2$</th>
<th>RMSE</th>
<th>95% Reference Range (cm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong> (n=173)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$H = 0.775 \times AS + 0.889 \times A + 21.634$</td>
<td>0.97</td>
<td>3.120</td>
<td>$\pm 6.12$</td>
<td>0.03</td>
</tr>
<tr>
<td>$H = 4.171 \times U + 1.594 \times A + 33.650$</td>
<td>0.95</td>
<td>4.367</td>
<td>$\pm 8.56$</td>
<td>0.06 (NS)</td>
</tr>
<tr>
<td>$H = 2.741 \times F + 1.353 \times A + 24.615$</td>
<td>0.96</td>
<td>3.817</td>
<td>$\pm 7.48$</td>
<td>0.16 (NS)</td>
</tr>
<tr>
<td>$H = 2.424 \times T + 2.129 \times A + 42.941$</td>
<td>0.95</td>
<td>4.153</td>
<td>$\pm 8.14$</td>
<td>0.02</td>
</tr>
<tr>
<td>$H = 2.654 \times L + 1.070 \times A + 15.290$</td>
<td>0.97</td>
<td>2.996</td>
<td>$\pm 5.87$</td>
<td>0.09 (NS)</td>
</tr>
<tr>
<td><strong>Females</strong> (n=134)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$H = 0.752 \times AS + 0.821 \times A + 25.069$</td>
<td>0.96</td>
<td>2.724</td>
<td>$\pm 5.34$</td>
<td>0.001</td>
</tr>
<tr>
<td>$H = 4.665 \times U + 1.079 \times A + 29.115$</td>
<td>0.93</td>
<td>4.294</td>
<td>$\pm 8.42$</td>
<td>0.22 (NS)</td>
</tr>
<tr>
<td>$H = 2.711 \times F + 1.230 \times A + 26.376$</td>
<td>0.95</td>
<td>3.131</td>
<td>$\pm 6.14$</td>
<td>0.002</td>
</tr>
<tr>
<td>$H = 2.782 \times T + 1.445 \times A + 37.559$</td>
<td>0.95</td>
<td>3.094</td>
<td>$\pm 6.06$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$H = 2.443 \times L + 1.374 \times A + 21.213$</td>
<td>0.97</td>
<td>3.262</td>
<td>$\pm 6.39$</td>
<td>0.33 (NS)</td>
</tr>
</tbody>
</table>

RMSE-root mean square of the error, cm-centimetres, H-height, AS-arm span, A-age, U-ulna length, F-forearm length, T-tibia length, L-lower leg length, NS-not significant.

In the female Asian sub-population the prediction equations were distinct for FEV$_1$ and FVC from arm span ($p=0.02$ and 0.009, respectively), ulna length ($p=0.03$, $p=0.009$, respectively) and forearm length ($p=0.02$, $p=0.02$, respectively). The order of the difference in the prediction from ulna measurement was approximately a 10% overestimation of both FEV$_1$ and FVC. Sub-group analysis for the other measurements and for prediction of mean mid-expiratory flow did not uncover significant differences. The prediction equations derived for the male and female Asian sub-population, their $R^2$, RMSE and reference ranges are included in Table 22 and 23.
Table 22: Prediction equations for pulmonary function for the male Asian group, and $p$ value for the difference between these and the overall equations.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.017 \times H + 0.022 \times \Lambda - 1.95)$</td>
<td>0.91</td>
<td>0.212</td>
<td>66 - 152</td>
<td>0.14</td>
</tr>
<tr>
<td>$FVC = \exp(0.019 \times H + 0.015 \times \Lambda - 2.02)$</td>
<td>0.91</td>
<td>0.123</td>
<td>79 - 128</td>
<td>0.10</td>
</tr>
<tr>
<td>$MMEF = \exp(0.015 \times H + 0.034 \times \Lambda - 1.68)$</td>
<td>0.71</td>
<td>0.245</td>
<td>62 - 162</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Arm span (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.012 \times AS + 0.042 \times \Lambda - 1.50)$</td>
<td>0.88</td>
<td>0.139</td>
<td>76 - 131</td>
<td>0.40</td>
</tr>
<tr>
<td>$FVC = \exp(0.014 \times AS + 0.037 \times \Lambda - 1.56)$</td>
<td>0.88</td>
<td>0.141</td>
<td>76 - 132</td>
<td>0.38</td>
</tr>
<tr>
<td>$MMEF = \exp(0.011 \times AS + 0.050 \times \Lambda - 1.26)$</td>
<td>0.69</td>
<td>0.251</td>
<td>61 - 164</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Ulna (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.062 \times U + 0.059 \times \Lambda - 1.25)$</td>
<td>0.86</td>
<td>0.149</td>
<td>75 - 134</td>
<td>0.14</td>
</tr>
<tr>
<td>$FVC = \exp(0.068 \times U + 0.055 \times \Lambda - 1.28)$</td>
<td>0.86</td>
<td>0.154</td>
<td>74 - 135</td>
<td>0.14</td>
</tr>
<tr>
<td>$MMEF = \exp(0.056 \times U + 0.066 \times \Lambda - 1.07)$</td>
<td>0.68</td>
<td>0.256</td>
<td>61 - 165</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Forearm (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.040 \times F + 0.056 \times \Lambda - 1.36)$</td>
<td>0.86</td>
<td>0.147</td>
<td>75 - 133</td>
<td>0.11</td>
</tr>
<tr>
<td>$FVC = \exp(0.043 \times F + 0.052 \times \Lambda - 1.39)$</td>
<td>0.86</td>
<td>0.153</td>
<td>74 - 135</td>
<td>0.12</td>
</tr>
<tr>
<td>$MMEF = \exp(0.035 \times F + 0.064 \times \Lambda - 1.16)$</td>
<td>0.68</td>
<td>0.256</td>
<td>61 - 165</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Tibia (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.034 \times T + 0.067 \times \Lambda - 1.07)$</td>
<td>0.85</td>
<td>0.153</td>
<td>74 - 135</td>
<td>0.12</td>
</tr>
<tr>
<td>$FVC = \exp(0.038 \times T + 0.064 \times \Lambda - 1.08)$</td>
<td>0.85</td>
<td>0.159</td>
<td>73 - 137</td>
<td>0.19</td>
</tr>
<tr>
<td>$MMEF = \exp(0.032 \times T + 0.072 \times \Lambda - 0.94)$</td>
<td>0.68</td>
<td>0.257</td>
<td>60 - 165</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>Lower Leg (n=168)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.037 \times L + 0.053 \times \Lambda - 1.46)$</td>
<td>0.88</td>
<td>0.140</td>
<td>76 - 132</td>
<td>0.14</td>
</tr>
<tr>
<td>$FVC = \exp(0.040 \times L + 0.050 \times \Lambda - 1.50)$</td>
<td>0.87</td>
<td>0.145</td>
<td>75 - 133</td>
<td>0.11</td>
</tr>
<tr>
<td>$MMEF = \exp(0.034 \times L + 0.059 \times \Lambda - 1.29)$</td>
<td>0.69</td>
<td>0.251</td>
<td>61 - 164</td>
<td>0.18</td>
</tr>
</tbody>
</table>

RMSE-Root mean square error, $FEV_1$-forced expiratory volume in one second, $H$-height, $\Lambda$-age, $FVC$-forced vital capacity, $MMEF$- mean mid-expiratory flow, $AS$-arm span, $U$-ulna length, $F$-forearm length, $T$-tibia length, $L$-lower leg length.
Table 23: Prediction equations for pulmonary function for the female Asian group, and $p$ value for the difference between these and the overall equations.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.013 x H + 0.032 x A - 1.55)</td>
<td>0.88</td>
<td>0.108</td>
<td>81 - 124</td>
<td>0.11</td>
</tr>
<tr>
<td>FVC = exp (0.014 x H + 0.026 x A - 1.59)</td>
<td>0.86</td>
<td>0.116</td>
<td>80 - 126</td>
<td>0.19</td>
</tr>
<tr>
<td>MMEF = exp (0.008 x H + 0.054 x A - 0.78)</td>
<td>0.56</td>
<td>0.258</td>
<td>60 - 166</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Arm span (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.010 x AS + 0.043 x A - 1.214)</td>
<td>0.86</td>
<td>0.114</td>
<td>80 - 125</td>
<td>0.02*</td>
</tr>
<tr>
<td>FVC = exp (0.011 x AS + 0.038 x A - 1.203)</td>
<td>0.84</td>
<td>0.124</td>
<td>78 - 128</td>
<td>0.009*</td>
</tr>
<tr>
<td>MMEF = exp (0.007 x AS + 0.058 x A - 0.66)</td>
<td>0.56</td>
<td>0.257</td>
<td>60 - 165</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Ulna (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.051 x U + 0.052 x A - 1.015)</td>
<td>0.84</td>
<td>0.124</td>
<td>78 - 128</td>
<td>0.03*</td>
</tr>
<tr>
<td>FVC = exp (0.054 x U + 0.048 x A - 0.987)</td>
<td>0.81</td>
<td>0.134</td>
<td>77 - 130</td>
<td>0.009*</td>
</tr>
<tr>
<td>MMEF = exp (0.036 x U + 0.062 x A - 0.056)</td>
<td>0.55</td>
<td>0.258</td>
<td>60 - 166</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Forearm (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.033 x F + 0.051 x A - 1.136)</td>
<td>0.85</td>
<td>0.120</td>
<td>79 - 127</td>
<td>0.02*</td>
</tr>
<tr>
<td>FVC = exp (0.036 x F + 0.046 x A - 1.139)</td>
<td>0.82</td>
<td>0.129</td>
<td>77 - 129</td>
<td>0.02*</td>
</tr>
<tr>
<td>MMEF = exp (0.021 x F + 0.064 x A - 0.058)</td>
<td>0.55</td>
<td>0.259</td>
<td>60 - 166</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Tibia (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.034 x T + 0.053 x A - 1.00)</td>
<td>0.85</td>
<td>0.121</td>
<td>79 - 127</td>
<td>0.39</td>
</tr>
<tr>
<td>FVC = exp (0.037 x T + 0.049 x A - 0.98)</td>
<td>0.82</td>
<td>0.130</td>
<td>78 - 129</td>
<td>0.27</td>
</tr>
<tr>
<td>MMEF = exp (0.020 x T + 0.066 x A - 0.47)</td>
<td>0.55</td>
<td>0.260</td>
<td>60 - 166</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Lower Leg (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ = exp (0.031 x L + 0.051 x A - 1.22)</td>
<td>0.86</td>
<td>0.118</td>
<td>79 - 126</td>
<td>0.15</td>
</tr>
<tr>
<td>FVC = exp (0.034 x L + 0.045 x A - 1.26)</td>
<td>0.84</td>
<td>0.124</td>
<td>78 - 128</td>
<td>0.21</td>
</tr>
<tr>
<td>MMEF = exp (0.015 x L + 0.067 x A - 0.49)</td>
<td>0.55</td>
<td>0.261</td>
<td>60 - 167</td>
<td>0.34</td>
</tr>
</tbody>
</table>

RMSE=Root mean square error, FEV$_1$=forced expiratory volume in one second, H-height, A-age, FVC=forced vital capacity, MMEF=mean mid-expiratory flow, AS-arm span, U-ulna length, F-forearm length, T-tibia length, L-lower leg length. *p<0.05.

This part of the research has identified anthropometric measurements that are precise and reproducible in the normal population, and are accurate predictors of height and pulmonary function. Racial group variation was identified in the Asian sub-population for predicting height and pulmonary function from many of the measurements. Any of the measurements investigated could be used to predict both height and pulmonary function in normal children.
Evaluation of New Prediction Equations

Ease of Positioning and Performance

To evaluate the ease of performance of the measurements in the target population, 47 Caucasian children with Duchenne muscular dystrophy underwent the limb measurements. The mean age was 12.6 years (6.0-18.6), and 42 children were wheelchair bound. All children had significant fixed ankle deformity, and 38 had significant wrist and elbow contractures. The ulna was readily accessible in all children, and the elbow could be placed at 90 degrees or greater, enabling easy identification of its proximal end. The ulna styloid process was readily identifiable in all children, and its identification was not limited by joint deformity. No strength is required as the forearm may rest on a surface, such as the tray of a wheelchair. See Figure 15. The measurement does not cross over joint spaces, as do forearm and lower leg measurement. Adequate positioning for forearm and lower leg length measurements was not possible for any child with wrist (38 children, 80.8%) or ankle deformities (47 children, 100%), respectively. Tibia measurement became more difficult when severe equinovarus deformity of the ankle existed (5 children, 10.6%), obscuring the tip of the medial malleolus. See Figure 16 and 17. These findings lead to the recommendation that ulna length is used to predict height and pulmonary function in children with neuromuscular weakness.

![Image](image_url)

*Figure 15:* The ulna remains accessible in wheelchair bound children and its end points are readily identifiable despite significant joint contractures.
Figure 16: Measurement of the tibia is difficult in the presence of severe equinovarus deformity of the ankle.

Figure 17: Identification of the distal end of the medial malleolus is difficult in the presence of severe equinovarus deformity of the ankle.
Relationship Between Height Predicted from Ulna Length and Arm Span

The correlation coefficient between the height predicted from ulna length and that predicted from arm span in children with Duchenne muscular dystrophy is 0.86. The Bland Altman 95% limits of agreement are -14.71 to 22.40 centimetres. Figure 18 is the Bland Altman plot for the difference in height predicted form the two measurements compared to the mean predicted height. This plot graphically demonstrates the poor correlation between the height predicted from ulna and arm span measurements and that there is a tendency for arm span to overestimate height in children with Duchenne muscular dystrophy, particularly as size increases, when joint and spinal deformities are more common and severe.

Figure 18: Bland Altman plot for the difference in height estimation from ulna length and arm span in children with Duchenne muscular dystrophy.
Effect of Intelligence and Behaviour on Pulmonary Function Tests in Duchenne Muscular Dystrophy

To assess the effect of intelligence and behaviour on the performance of pulmonary function tests in children with Duchenne muscular dystrophy, 47 boys mean aged 12.6 years (6.0-18.6) were recruited. The diagnosis of Duchenne muscular dystrophy was made by a neurologist in all cases. The mean FEV₁ was 1.74 litres per second (range 0.45-4.22) and mean FVC 1.82 litres (range 0.69-4.36). The mean full-scale intelligence quotient (IQ) was 84.7 (range: 42-131), performance IQ was 90.6 (range: 46-139) and verbal was IQ 85.6 (range: 46-131). The mean parent reported oppositional behaviour score was 56.3 (range: 39-87) and teacher reported oppositional behaviour score was 56.9 (range: 45-90).

All children were able to perform pulmonary function tests adequately and meet reproducibility criteria with careful explanation and demonstration by experienced respiratory laboratory scientists and the use of computerised visual incentives. Only one child could not adequately perform the test without the use of computerised visual incentives (age 16.5 years, IQ 62, FVC 16.9%), but he was quickly able to learn the technique when computerised visual incentives were used.

An association was found between FEV₁ % predicted and FVC % predicted to full-scale (r=0.50, p=0.002; r=0.49, p=0.003), performance (r=0.68, p<0.0005; r=0.68, p<0.0005) and verbal (r=0.39, p=0.043; r=0.36, p=0.037) IQ. See Figure 19. There is no association with parent (p=0.77, p=0.70) or teacher (p=0.90, p=0.90) reported oppositional behaviour scores. There is a non-significant trend towards and improved FVC (p=0.06) if spirometry was performed with visual incentives first. See Figure 20. There was no other significant effect of visual incentives, and no significant first test effect (p=0.17, p=0.60).
Figure 19: Association of forced expiratory volume in one second percent predicted and forced vital capacity percent predicted to full-scale, performance and verbal intelligence quotients.

The questionnaire showed that 88.6% of children found performance of pulmonary function tests easier with the use of computerised visual incentives. No child found performing the tests very hard, with or without visual incentives, but 6.8% found it hard with incentives, and 18.2% found it hard without incentives. Performance of the test was reported as easy or very easy with incentives in 77.2% and without incentives in 52.3%.
Figure 20: Forced vital capacity when spirometry was performed with and without computerised visual incentives first (p=0.06).

**Conclusion**

In children with neuromuscular weakness, pulmonary function testing is an important component of respiratory risk assessment, and forms an integral part of management decisions. Guidelines for management decisions frequently use predicted values of pulmonary function tests, but inaccuracies in predicting normal values exist in this group of children, as height frequently cannot be precisely measured, and there are important limitations in the accuracy of arm span measurements.14,34,35,105 Junior medical staff, surgeons or anaesthetists frequently interpret pulmonary function tests, but may not be aware of these limitations. Similar problems of pulmonary function prediction exist throughout the country, and are likely to occur in other countries practicing evidence-based medicine.

A series of anthropometric measurements that are accessible in wheel-chair bound children, and have readily identified landmarks were investigated for the
reproducibility of the measurement, and their precision in predicting height and pulmonary function. All were found to be highly reproducible and precise in predicting height and pulmonary function. Distinct racial differences were found in the Asian sub-population. Assessment of the use of the anthropometric measurements in children with Duchenne muscular dystrophy was then undertaken, and the ulna was found to be superior to the other measurements in ease of performance, positioning and identification of landmarks in this group of children. A comparison was made between the height predicted from arm span, and that predicted from ulna length, which showed poor correlation between the two in children with Duchenne muscular dystrophy. Pulmonary function test results may be affected by intelligence, particularly performance intelligence quotients, but not to behaviour in children with Duchenne muscular dystrophy.
Discussion

Pulmonary function tests form an important part of respiratory assessment in childhood neuromuscular weakness. Using height or arm span to predict pulmonary function tests has inherent inaccuracies. There is not a uniform approach in the method of height estimation or in interpretation of pulmonary function tests in neuromuscular weakness throughout Australia, and inaccuracies are well recognised. The technique and prediction equations for using ulna length to predict height and pulmonary function were developed, and are precise. Ulna length is readily measured in neuromuscular weakness, the measurements are reproducible and it is not prone to the inaccuracies of arm span measurement. Using ulna length to predict pulmonary function should facilitate respiratory assessment in childhood neuromuscular weakness.

Respiratory Assessments in Common Use

Pulmonary function tests are the main respiratory assessment tool used to guide management decisions in children with neuromuscular weakness. In children with neuromuscular weakness undergoing corrective spinal surgery, 87.2% had pulmonary function tests in the pre-operative period, and other respiratory investigations were infrequently and inconsistently used. Interpretation of pulmonary function tests were generally by medical officers who were not respiratory physicians, and only 3.8% had documented respiratory physician involvement. Forced vital capacity (FVC) % predicted was the most common pulmonary function test value documented in medical notes when management decisions were being made. There was insufficient documentation of alteration of management plans as a result of the investigations performed to draw conclusions, and the search used would have missed any children
cancelled as a result of their pre-operative investigations. Practices at the Royal Children’s Hospital in Melbourne are now undergoing extensive change, so that referral to respiratory physicians first occurs at 10 years of age, and they are involved in pre-operative respiratory risk assessment.

Although transcutaneous oximetry was not widely available prior to 1985, its use in the later part of the study period remains sporadic. Blood gas analysis was rarely undertaken despite its availability, and good evidence to support its value in assessment of respiratory compromise. POLYSOMNOGRAPHY, assessments of respiratory muscle strength (maximal inspiratory and expiratory pressures or sniff inspiratory pressures) and peak cough flows were not undertaken in any children. No child, even those at the highest respiratory risk was taught the newer techniques of assisted cough, non-invasive ventilation use or air stacking in the pre-operative period.

The incidence of peri-operative complications found in this series is comparable to those found by others. 33,37,38,77,145,155 Haemodynamic complications are common, and a requirement for blood products is the norm. The most common complications seen in the peri-operative period was respiratory in nature with 11.5% of children requiring ventilatory support and 80.8% requiring oxygen therapy. The only post-operative death was due to respiratory failure. The reasons for oxygen use and its withdrawal were not clear from the documentation in the medical histories, and carbon dioxide levels were seldom measured. Many of these children may have benefited from non-invasive ventilation. A non-significant trend was found for the association between pre-operative pulmonary function tests and peri-operative need for ventilatory support (p=0.05). The reason why this did not reach significance may relate to the small numbers of children receiving support (n=9).

In children with neuromuscular weakness, corrective spinal surgery leads to an acute fall in pulmonary function. The mean fall in FVC % predicted is 11.14% in the overall group, 6.09% in Duchenne muscular dystrophy and 15.74% in Spinal muscular atrophy. The fall in FVC % predicted is persistent in pulmonary function tests taken more than a month post-operatively.
With any anaesthetic, there is an acute fall in vital capacity.\textsuperscript{148} The magnitude of the fall and rate of recovery vary with the type of surgery. Procedures distant to the chest are associated with a smaller fall in vital capacity and faster recovery times than those close to the chest or diaphragm.\textsuperscript{218} Procedures involving the thoracic cavity (such as an anterior release) have the greatest impact of all.\textsuperscript{148}

In children with pectus excavatum, the Ravitch surgical repair frequently involves fixation with a metal fixator. Pulmonary restriction is often seen post-operatively and is persistent.\textsuperscript{219,220} It may be due to abnormal chest wall mechanics secondary to the sternal surgery.\textsuperscript{221,222} Spinal fixation might be expected to have a similar effect on chest wall mechanics, particularly if the chest cavity is breeched. The study has found a peri-operative fall in FVC % predicted. Children with neuromuscular weakness involving the respiratory muscles have a reduced ability to cope with the acute fall in vital capacity.

The study has demonstrated that the expected progressive decline in pulmonary function is slowed following corrective spinal surgery from a mean of 5.14\% per year (6.17\% in Duchenne muscular dystrophy and 2.33\% in Spinal muscular atrophy) pre-operatively to 0.99\% per year (3.35\% in Duchenne muscular dystrophy and 0.20\% in Spinal muscular atrophy) post-operatively. This is significant in the overall group (\textit{p}<0.01), and in children with Duchenne muscular dystrophy (\textit{p}=0.02) but is not in Spinal muscular atrophy (\textit{p}=0.27).

In neuromuscular weakness, the decline in respiratory function is due to a combination of progressive weakness of the respiratory muscles, and progression of the spinal deformity, leading to pulmonary restriction.\textsuperscript{3} In Duchenne muscular dystrophy, progression of muscle weakness is generally quicker than that seen in Spinal muscular atrophy type II and III.\textsuperscript{1,3,7,8,11,52} It follows that muscle weakness is the most important factor in respiratory decline in Duchenne muscular dystrophy, whereas spinal deformity may be more important in Spinal muscular atrophy. It would be expected that arresting progression of the spinal deformity might ameliorate the decline in respiratory function more markedly in Spinal muscular atrophy than in Duchenne muscular dystrophy. Indeed the rate of decay of respiratory function is markedly reduced to 0.20\% per year post-operatively in Spinal muscular atrophy
compared to 3.35% in Duchenne muscular dystrophy. The reason why a significant difference in the rates of decline was not found in Spinal muscular atrophy may relate to the small sample size in the post-operative group (n=5), and to the relatively slower rate of decline that was seen pre-operatively in this group compared to the Duchenne muscular dystrophy group.

The influence of corrective spinal surgery on the rate of decline of pulmonary function in neuromuscular weakness has been debated in the literature without consensus.\textsuperscript{2,3,4,223-226} The studies investigating this have generally been limited by small sample size (n=8-32),\textsuperscript{2,3,4,223-226} and relatively short (10-74 months)\textsuperscript{224,225} or incomplete follow up.\textsuperscript{223} Most have compared surgical and non-surgical groups of children\textsuperscript{3,4,223-225} rather than monitoring pulmonary function pre- and post-operatively, and there is frequently no comparison between the groups of children studied\textsuperscript{3,4,224} or the groups characteristics are quite different.\textsuperscript{225} Kennedy, \textit{et al}\textsuperscript{2} has examined the rates of decline in pulmonary function in the pre- and post-operative periods in the same children and compared these to the rate of decline in a non-surgical group, but this study has used a minimum of three pulmonary function tests for inclusion. This necessitates using a common pulmonary function test in the pre- and post-operative analysis, which precludes finding an acute peri-operative fall in pulmonary function, and may influence the calculated rate of post-operative decline. The various methodological limitations of these studies have led to the variability in conclusions and necessitated further study.

The current study has a larger group than previous reports. There was, however, fewer pulmonary function tests performed in the post-operative than the pre-operative periods, and not all children in the pre-operative analysis (n=64) are included in the post-operative analysis (n=26). The postoperative group in the current study is, however larger than the entire operative study group in most other studies of this issue (n=8-32).\textsuperscript{2,3,4,223-226} There is no statistical difference between the children included in both analyses and those only included in the pre-operative analysis, with respect to age at surgery or pulmonary function. The spectrum of disease severity is comparable. The current study group does not appear to be inherently different to the other groups of children whose rate of pulmonary decline has been evaluated. The pre-operative %FVC was 50.2%; in other reported series it has been 42.8%,\textsuperscript{223} 52%\textsuperscript{223} and 1.3
litres. If a difference did exist, it might be that pre-operative pulmonary compliance may influence the post-operative rate of pulmonary decline, but in the absence of a difference, this seems unlikely. Information about the severity of spinal deformities was not available. Despite the lack of a demonstrable difference between the groups, this remains a confounder. The inaccuracies in height estimation that have been identified are also confounders, but are likely to have been present in all the previous studies of this issue.

In the child who died in the peri-operative period of respiratory failure, there were several indicators of marginal respiratory status present despite the limited evaluation used. This child had Nemaline myopathy that is associated with the early onset of both inspiratory and expiratory muscle weakness. His pulmonary function was amongst the lowest in the series. Low resting oxygen saturations in the context of recurrent chest infections are likely to indicate underlying lung disease. The long anaesthetic time represented a significant respiratory insult and he would be expected to have a fall in FVC in the peri-operative period. A more thorough pre-operative respiratory assessment that included blood gas analysis, quantitation of respiratory muscle strength and peak cough flow may have added further information about the magnitude of his respiratory compromise, and may have led to cancellation of his procedure, or to teaching assisted cough, non-invasive ventilation and air stacking prior to his procedure.

This study principally examines the rate of decline in pulmonary function, rather than absolute values of pulmonary function. To determine the rates of decline for individuals, a minimum of two time points are required to give the slope of the curve. It is not necessary that the time points for each individual are the same, as the slope or rate of decline will be independent of the time points used. The overall rates of decline were determined from repeat measures on individual patients using the generalized estimating equations method. When determining the acute post-operative fall in pulmonary function, both pre-operative and post-operative time points must be examined. The pre-operative time-point considered in this study was within 30 days before surgery, and the post-operative time point was 30-90 days post-operatively. This allows for a period of immediate post-operative recovery, that all children undergoing corrective spinal surgery would be expected to undergo.
Predicted values rather than observed were used in this research as the children undergoing corrective spinal surgery were of varying ages, and some were continuing to undergo lung growth, while others had reached their peak or were declining. Observed values would have less meaning. The use of predicted values takes expected lung growth and age into account. It is recognised that there is some error in the calculation of predicted values of pulmonary function from arm span measurements that may be inaccurate, particularly when joint and spinal deformities exist.\textsuperscript{214}

This study is retrospective and covers a long time period. It is likely that referral patterns have changed throughout this 26 year period, and that involvement of a respiratory physician is likely to be more common today than it was many years ago. Practices in orthopaedic surgery, anaesthetics, neurology and respiratory medicine have changed within this time period, but the effect of corrective spinal surgery on the declining respiratory system are likely to remain similar. Deficiencies in documentation, and lack of control of investigations performed have lead to incomplete information.

The natural progression of spinal deformity can be predicted from a relatively early stage in Duchenne muscular dystrophy, and probably can be inferred in many other neuromuscular disorders.\textsuperscript{12} Oda, \textit{et al}\textsuperscript{12} has studied the natural history of spinal deformities in Duchenne muscular dystrophy. Three types of spinal deformity have been identified. Type 1 deformities reach a Cobb angle of 30 degrees before the age of 15 years, and follow an unremitting progressive pattern. Type 2 transition from kyphosis to lordosis before the age of 15 years; those that then develop double curves do not tend to become progressive, those that form long thoracolumbar curves become gradually progressive, and those that form lumbar curves may gradually or suddenly progress. The later two generally require fixation. Type 3 have less severe spinal deformity (<30 degrees) and do not generally require fixation. If the progression to requirement for surgery can be predicted early as this paper suggests, and an acute fall in pulmonary function is expected peri-operatively then the operation should be performed early in those who will require it, to minimise surgical risk and reduce the pre-operative period of faster respiratory decline.
The guidelines that currently exist for the level of pulmonary function at which corrective spinal surgery may be safely undertaken require revision. Padman, et al\textsuperscript{35} found that pre-operative vital capacity (VC) is related to post-operative pulmonary complications, and need for post-operative ventilatory assistance in neuromuscular weakness. Jenkins, et al\textsuperscript{34} found that pre-operative VC is the best predictor of the post-operative clinical course in patients with Duchenne muscular dystrophy. No patient with a pre-operative VC >45% predicted required post-operative ventilation, all those with a pre-operative VC <35% predicted required post-operative ventilatory support, and 2/3 of those with a pre-operative VC <30% predicted had serious post-operative pulmonary complications. Cambridge, et al\textsuperscript{14} and Jenkins, et al\textsuperscript{34} have suggested that the VC % predicted must be greater than 35% to undertake surgical intervention for spinal deformity in Duchenne muscular dystrophy. Corrective spinal surgery has been performed at much lower VC; fifteen children (19.2%) in this series had a pre-operative FVC <35% predicted. Soudon, et al\textsuperscript{50} has found success in a child with Spinal muscular atrophy with a VC of 640 millilitres, without complication. In the current series, success was found in a child with Spinal muscular atrophy who had an FVC of 610 millilitres (19.8% predicted) but continuous positive airway pressure was required for three hours in the post-operative period. The current study has not found a significant association between pre-operative pulmonary function and post-operative respiratory complications, and does not support these guidelines. The more recent use of non-invasive ventilation in the peri-operative period may further alter surgical respiratory risk.

Corrective spinal surgery represents a significant respiratory risk to children with neuromuscular weakness, but slows the inevitable respiratory decline in the longer term. This has the potential to prolong respiratory independence, and increase longevity. It adds weight to the benefit of corrective spinal surgery, and may significantly alter the risk-benefit ratio. This research highlights the importance of regular monitoring of pulmonary function and spinal deformity in children with neuromuscular weakness, to identify the ideal timing of corrective spinal surgery. Using non-invasive ventilation may improve short-term respiratory risk, and enhance recovery from surgery. The current study has identified alterations in pulmonary function at the time of corrective spinal surgery, that differs from that found in other studies, and requires further investigation in the form of a large prospective study.
Inaccuracy in Predicting Pulmonary Function

In the current series, at least 9.4% of pulmonary function tests have inaccuracies in height estimation. The actual proportion of inaccurate height measurements is likely to be significantly higher, as only those that reduced despite advancing age were identified and no other way of identifying inaccuracies was readily apparent.

Snyder, et al\textsuperscript{227} has obtained anthropometric measurements in a large group of normal United States children. This normative data has been used to develop prediction equations for height from arm span measurements.\textsuperscript{201,228} Miller, et al\textsuperscript{201} used the prediction equations in normal children and those with Duchenne muscular dystrophy. In those with scoliosis, height was estimated by radiographic spine reconstruction. In normal children, the arm span to height correlation coefficient to height is 0.9707, but in children with Duchenne muscular dystrophy it is only 0.4748. This group recommends that arm span not be used to predict height in children with Duchenne muscular dystrophy. Inaccuracies in height estimation impede precise calculation of predicted values of pulmonary function tests and this needs to be realised when interpreting results. When inexperienced staff review the results, errors may occur.

Nationwide Pulmonary Function Test Prediction

The national survey of tertiary paediatric respiratory laboratories revealed that there is not uniformity between laboratories in the method used to estimate height for prediction of normal values of pulmonary function tests in either neuromuscular weakness or scoliosis, and that there is not consistency within the same laboratory for the methods used for both neuromuscular weakness and scoliosis. Several methods of determination of arm span have been adopted in an effort to overcome the difficulties in obtaining accurate measurements. Mostly tape measures are used and run over the skin surface and around corners when joint deformities exist. This reduces the accuracy of the measurements obtained.\textsuperscript{201} Inaccuracies in arm span measurement are recognised by 75% of respiratory laboratory managers. All methods of height estimation used throughout Australia have some degree of inaccuracy, as positioning, weakness or joint deformity can hinder the accuracy of the methods adopted.
The interpretation of pulmonary function tests in children with neuromuscular weakness or scoliosis is also variable. Some rely on observed values only, which does not consider the normal lung growth of childhood or provide reference to the normal population. Others use only predicted values, despite the inaccuracies of determining these, while still others use a combination of the two.

The inconsistencies found mean that the results obtained by various laboratories around Australia are not comparable. All the techniques used have the same potential problems as those faced by the Royal Children’s Hospital, Melbourne. This can lead to errors in interpreting the results. Better methods of height estimation and prediction of pulmonary function tests for children with neuromuscular weakness or spinal deformity are required.

**Modified Method of Prediction of Height and Pulmonary Function**

The major problems with measurement of height or arm span in neuromuscular weakness are:

1) Children are often too weak to stand to have their height measured
2) Spinal deformities are commonly present and lead to a falsely lowered height measurement
3) Positioning for arm span measurements is often impossible because weakness impedes active extension of the arms and maintenance of the position while being measured
4) Those in whom spinal deformity is present are unable to position their back adequately against a wall due to the alteration in the relationship between their shoulders and the lower back
5) The measuring device used for arm span measurement crosses over several joint spaces that may be affected by joint deformities, such as contractures.

A new method of determining height and predicting pulmonary function in those with neuromuscular weakness is needed. The measurement to be used needs to:
1) Be accessible in those with immobility
2) Be reproducible by the same and different observers
3) Not cross over joint spaces that may become immobilised by contractures or deformity
4) Not require posturing that is difficult to adopt or relies on strength
5) Be an accurate predictor of pulmonary function test parameters.

Each of the distal limb anthropometric measurements investigated is a precise predictor of height and pulmonary function and each has similar precision. The measurements have readily identifiable landmarks that facilitate their measurement. The measurement of each is accurate and reproducible, as highlighted by the small individual standard deviation for repeat measurements (Table 10 in the Results chapter). The accuracy of height prediction from ulna length ($R^2$ 0.96 for males and 0.94 for females) is comparable to that from arm span ($R^2$ 0.97 for males and 0.91 for females) and to the accuracy of height estimation from arm span measurements found in other series ($R^2$ 0.87-0.97); but it avoids the difficulties in arm span measurement. The measurements provide an accurate alternative to height for prediction of pulmonary function.

Prediction equations for pulmonary function using ulna length and age have similar precision ($R^2$) to those using height in this study. The degree of precision in prediction of forced expiratory volume in one second (FEV$_1$) ($R^2$ 0.84-0.86) and FVC ($R^2$ 0.83-0.86) is comparable to Zapletal, et al. (200) ($R^2$ 0.86-0.92) and Hibbert, et al. (209) (a study of Australian children: $R^2$ 0.85-0.92) who used height to predict pulmonary function. It is superior to Knudsen, et al. (39) ($R^2$ 0.53-0.80) and the NHanes study (229) ($R^2$ 0.61-0.80). Using ulna length and the prediction equation should facilitate height and pulmonary function estimation when accurate height measurement is not possible.

In children, change in pulmonary function over time provides a sensitive measure to monitor the progress of respiratory disease. Predicted values of pulmonary function, rather than observed values are used to compensate for the expected increase in pulmonary function associated with growth. Accurate measurement of predictor variables is essential. Although the correlation between pulmonary function and height measurements is high, undergoing two calculations (to height and then to
pulmonary function) to obtain a predicted value would compound any inaccuracies. Hence, prediction equations were developed for both height and pulmonary function to obtain the greatest precision.

Pulmonary function test reference ranges have been derived to include 95% of the normally distributed sample. Paediatric reference ranges are seldom reported in the literature. This may be because many other studies have a smaller sample size, and a large number of subjects are required to develop reference ranges. It has been previously shown that flow and volume measurements track at a constant deviation from the mean over time, and it would be expected that longitudinal analysis would not alter the reference range of the current study.

Ulna growth charts provide the normal range and centiles for ulna length compared to age. This allows comparison of an individual’s measurement to the normal population. It would be expected that children would follow along the same centile with advancing age, although a longitudinal study should be performed to confirm this. The growth charts could then be used to monitor growth, in a similar way to monitoring growth in height. Their use may negate the need to perform the cumbersome calculation of height when monitoring growth.

The ulna is accessible in those confined to a wheelchair, and its measurement is unaffected by weakness, joint or spinal deformity. Positioning for the measurement requires only flexion of the elbow so that the proximal end of the bone may be identified. The ulna styloid remains readily identifiable when wrist contractures are present. No strength is required as the forearm may rest on a surface, such as the tray of a wheelchair. The measurement does not cross over joint spaces, and is not limited by joint deformity. When the measurement was performed on children with weakness and joint contractures, positioning and identification of bony landmarks were not problematic. Arm span measurement could be affected by weakness, joint or spinal deformity. Forearm and lower leg measurements cross joints and could be affected by joint deformity such as contracture. Tibia length is readily measured and unaffected by weakness, but palpating the distal end of the medial malleolus became particularly challenging when severe equinovarus deformities of the ankle existed, obscuring the
tip of the medial malleolus. Forearm, lower leg and tibia measurements may be useful in the absence of joint deformity.

Ulna length measurement with a Harpenden anthropometer is simple, requiring only superficial palpation. The technique can be taught to new staff in minutes. Spender, et al.\textsuperscript{228} compared measurements of upper arm length obtained using steel and plastic tape measures to those using an anthropometer. The measurements obtained were on average $1.03 \pm 0.20\text{cm}$ and $1.10 \pm 0.25$ centimetres longer than the anthropometer measurement, respectively, and the intraobserver variability was greater ($p=0.002$). A similar degree of inaccuracy would be expected when measuring the ulna with a tape measure, and is not recommended. Vernier callipers that measure to 0.2cm, are readily available from precision engineering suppliers, and may be used as an alternative to a Harpenden anthropometer. Measurements were only performed on one side of the body, as symmetry has previously been demonstrated.\textsuperscript{43,201}

Several authors have previously documented the relationship between height and various body segments in their own population.\textsuperscript{42,43,201,206,207} Particular attention has been paid to the arm span\textsuperscript{44,198,205}, upper limb,\textsuperscript{45,201,205} and knee height.\textsuperscript{203,204}

Snyder, et al.\textsuperscript{227} has obtained anthropometric measurements of a large group of normal United States children. This normative data has been used to develop prediction equations for height from upper arm, forearm, ulna, lower leg and arm span measurements.\textsuperscript{201,228} Miller, et al.\textsuperscript{201} used the prediction equations for height from forearm, ulna and arm span in three groups of children: normal, idiopathic scoliosis and Duchenne muscular dystrophy. In those with scoliosis, height was estimated by radiographic spine reconstruction. In children who are normal, and those who have idiopathic scoliosis or Duchenne muscular dystrophy without wrist contractures, estimation of height from forearm measurements has a correlation coefficient of $0.96.\textsuperscript{201}$ In children with Duchenne muscular dystrophy and wrist contractures, the ulna length to height correlation coefficient was 0.91. Arm span was far less accurate, with a correlation to height coefficient of only 0.4748. Miller, et al.\textsuperscript{201} recommends that forearm is used if no wrist contractures exist, and ulna length is used if wrist contractures do exist. They recommend arm span not be used in Duchenne muscular dystrophy. Arm span is currently being used in many centres to predict height for use
in nutritional assessment and for calculation of drug doses. It is also being used by
most respiratory laboratories to predict pulmonary function in childhood
neuromuscular weakness and spinal deformity due to the lack of a better alternative.
In the current study, little difference was found between the precisions of forearm or
ulna measurements in predicting height, but the accuracy of forearm measurements
may be limited by wrist contractures.

Spender, et al.\textsuperscript{228} used prediction equations for height from upper arm and lower leg
lengths developed from Snyder, et al.'s data.\textsuperscript{227} Growth in cerebral palsy was assessed.
In the 47 children with spastic quadriplegia, height or recumbent length could only be
measured in 17, upper arm length in 43 and lower leg length in 46 children. Although
the same measurements were not used in the current study, similar difficulties were
found in measuring the forearm, tibia and lower leg length in the group of children
with Duchenne Muscular Dystrophy. Both upper arm (correlation coefficients: 0.7-
0.86) and lower leg (correlation coefficients: 0.67-0.86) were found to be good
predictors of height in the 6-19 year age group.\textsuperscript{228} Height was reduced in spastic
quadriplegia, but maintained in the normal range in children with diplegia and
hemiplegia. There is evidence that limb growth may be impaired in upper motor
neuron lesions, but no evidence exists within the available literature, that body
proportions are altered in those with neuromuscular weakness or spinal deformity.

Prediction equations for height from knee height have been developed from normative
data. These prediction equations have been used to compare the patient's recumbent
length to the knee height predicted stature in children with cerebral palsy involving
the lower limb. Johnson and Ferrara\textsuperscript{204} found that the prediction was not accurate in
males aged 12-18 years with lower limb cerebral palsy ($R^2$ 0.54), but was accurate in
females ($R^2$ 0.95). Hogan\textsuperscript{203} was unable to obtain the knee height measurement in 34
of 56 children due to the severity of the lower limb involvement with cerebral palsy.
In those in whom the measurement was obtained, knee height was a reliable predictor
of recumbent length ($R^2$ 0.78). In the current study, both the tibia and lower leg length
measurement were impeded by equinovarus deformities of the ankle. It is not
surprising that the ease of measurement and the accuracy of knee height prediction are
also reduced when lower limb cerebral palsy is present.
Influence of Racial Background

The racial backgrounds of children in this series are representative of the Australian population. Schools approached for this study consisted of public, private, religious and independent primary and secondary schools. They were randomly selected from all metropolitan Melbourne schools to ensure adequate representation of socio-economic and ethnic groups. The Australian society is multicultural, with a large proportion being Caucasian (77% in the current series). The prediction equations developed are applicable to the Australian Caucasian population. Thirteen per cent of children have an Asian background, consisting mainly of children from Southeast Asia, with small numbers from India and the remainder of Asia. Not surprisingly, this subgroup was found to be anthropometrically distinct, leading to the development of separate prediction equations for this group. If arm span, tibia or forearm length were to be used to predict height in this group, the prediction equations developed for the Asian subgroup should be used. There was not a significant difference in the prediction of height from ulna length in this subgroup, and the prediction equations for the entire group may be used. In the Asian subgroup, both FEV₁ and FVC predictions from all the upper limb measurements, including ulna length are significantly different, to the overall prediction equations. This suggests that pulmonary function is smaller in proportion to the upper limbs in the Asian subgroup than the overall group. When predicting pulmonary function in the Asian sub-population the specific prediction equations developed for this population should be used. If the racial background is not known, or is mixed, then the overall prediction equations more closely predict both height and pulmonary function.

Limitations

The response rate was lower than anticipated. This may in part be due to the request by many schools to give students the responsibility for the questionnaire. When schools were agreeable, a recruitment package was sent directly to the parent or guardian, who returned the completed questionnaire and consent form to the chief investigator in a reply-paid envelope. In developing prediction equations and normal reference ranges, all children with potential illnesses that may lead to them falling outside the normal reference range were excluded. This was clearly explained on the
information sheet. Despite asking all to return the form, even if this was the case, it may have led to a reduced return rate. The incidence of both asthma\textsuperscript{231} and attention deficit hyperactivity disorder\textsuperscript{232} is far greater in our community than our responses suggest. We believe participation bias to have little impact on the results, as this is not a prevalence study and only normal subjects were sought.

In this study pulmonary function measurements were performed in the standing position. In those with neuromuscular weakness, it is likely that these measurements will be performed in the sitting position. Townsend, et al\textsuperscript{233} and Laloo, et al\textsuperscript{234} have both examined pulmonary function values obtained in the standing and sitting positions in adults. Laloo, et al\textsuperscript{234} has found the FEV\textsubscript{1} in the standing position is approximately 5\% larger than in the sitting position in women but less than 5\% in men. Townsend, et al\textsuperscript{233} found the FEV\textsubscript{1} and FVC to be 7\% and 6\% larger, respectively in the standing position in men. The American Thoracic Society indicates that the vital capacity is larger in the standing than the sitting position in childhood, but this has not been quantitated.\textsuperscript{208} It is recommended that the same posture be adopted for each test. Normal pulmonary function tests span a large range, and monitoring of progress is best achieved by comparing an individual’s test to their previous results, so that progress may be monitored.

**Other Clinical Uses**

Height estimation from ulna length would be appropriate in any situation where accurate and precise height measurement is not possible such as in those with weakness, spasticity or in those with spinal deformity, which impacts on the accuracy of both height and arm span measurements. This includes children with neuromuscular weakness and cerebral palsy. In those with hemiplegia, the ulna of the non-affected side should be used. Although arm span measurements have equal accuracy in predicting height, ulna length may also be used in those with pathology confined to the lower limbs, such as spina bifida and spastic diplegia, as it has equal precision to arm span measurement in predicting height.
Height estimation is of particular importance in assessment of nutritional status, where weight for height ratios are more meaningful than weights alone.\textsuperscript{235} Medication doses in children often need to be proportional to size so that over dosage in small children does not occur. In most instances, the dose is calculated from weight, but when accuracy of dosages is of extreme importance, such as with chemotherapy, body surface area is used, and this requires a height measurement.\textsuperscript{236-238}

Children with cerebral palsy commonly have growth impairment. It has been postulated that impairment in linear growth may be due to nutritional deficiencies, the underlying neurological abnormality or other factors. Several authors have investigated the contribution of malnutrition.\textsuperscript{239-241} Malnutrition can be identified by reduced triceps skin fold thickness by two years of age.\textsuperscript{239} Gastrostomy feeding has been found to normalise the weight to length ratio in 11 of 19 children.\textsuperscript{240} Why growth enhancement did not occur in the remainder of children is unclear. Stallings, \textit{et al}.\textsuperscript{239} found that impairment of linear growth in spastic quadriplegia is related to pubertal stage and oro-motor score, which may contribute to malnutrition. Impairment in linear growth worsens with advancing age.\textsuperscript{239,241} It seems unlikely that the sole aetiology of growth restriction is the underlying static neurological abnormality, but the contribution of nutritional and other factors to growth impairment is still being deciphered. Spender, \textit{et al}.\textsuperscript{228} found growth restriction was present in those with spastic quadriplegia, but not in those with diplegia or hemiplegia. There was no predilection for upper or lower limb growth restriction in any of the types of cerebral palsy. An accurate predictor of height, such as ulna length may be used to monitor growth and nutrition over time, and to better define the aetiology of growth restriction.

Body surface area can be estimated from height and weight. It can be used to calculate medication doses, renal function, cardiac output and oxygen consumption.\textsuperscript{242,243} Using ulna length to precisely predict height should assist in the estimation of body surface area in disabled children.


**Relationship Between Height Predicted from Ulna Length and Arm Span**

In boys with Duchenne muscular dystrophy, the height predicted from arm span and that predicted from ulna length do not correlate well. The heights tend to correlate reasonably well in smaller children, who are likely to be younger and still mobile. As the size of the children increase, there is a tendency for age to increase, and weakness to become more marked. In these children mobility is generally reduced and joint deformities are common. The correlation between the predicted heights in larger children is poor. The reason why arm span measurements may become inaccurate in larger children is that when weakness begins, the arms can no longer be held actively in full lateral extension and the elbows tend to flex while the measurement is being taken. In children with joint deformities, performing the measurement requires running a tape measure over the skin, and around joints that are immobilised by contractures, limiting the accuracy of the measurement. In these children, there is a tendency to over-estimate the height predicted from arm span measurements.

**Effect of Intelligence and Behaviour on Performance of Pulmonary Function Tests**

Boys with Duchenne muscular dystrophy are able to achieve a pulmonary function test technique that produces adequate and reproducible results. The results of pulmonary function testing in Duchenne muscular dystrophy are related to measures of intelligence, particularly performance intelligence quotients (IQ), but are not related to measures of oppositional behaviour. The use of computerised visual incentives led to a trend towards a greater FVC, but this was not statistically significant (p=0.06). Learning the technique required to perform pulmonary function tests was reported to be easier with computerised visual incentives in 88.6% of boys, and one child was unable to master the technique required without the use of computerised visual incentives.
Intellectual impairment is not universal in Duchenne muscular dystrophy. The mean full-scale and verbal IQ is 80 (1 standard deviation below the population mean), but values are normally distributed around the mean. Some subsets of children with Duchenne muscular dystrophy are likely to be more impaired than others and this may relate to the position of the genetic deletion. Teaching the technique required to perform pulmonary function tests requires verbal commands. Children with Duchenne muscular dystrophy and lower verbal IQ may have particular deficits in understanding verbal commands, and so other methods of teaching (such as demonstrating and using computerised visual incentives) should also be employed.

Pulmonary function test results are closely associated with performance IQ as expected, since pulmonary function testing is a task children need to perform and master. The mean performance IQ is less impaired (85) than full-scale and verbal IQ in Duchenne muscular dystrophy, but may worsen with worsening disease severity, as weakness limits the child’s ability to perform tasks. The effect of this was minimised by performing intelligence testing at a younger age (6-14 years), in the early phases of disease progression. Pulmonary function tends to decline as weakness worsens, and had the performance IQ not been measured in the younger age groups, this may have led to an accentuation of the association between performance IQ and pulmonary function.

The relationship between pulmonary function and intelligence in Duchenne muscular dystrophy may be due to difficulties in understanding or learning to perform the technique required for pulmonary function testing. It is unlikely that disease severity is causal in this association, as previous research has consistently demonstrated no relationship between intelligence and disease severity or functional ability. No measures of disease severity were included in this research.

The boys found the pulmonary function test technique easier to master with the use of computerised visual incentives and there was a trend towards an improved FVC when incentives were used with the first pulmonary function test attempt. The reason this did not reach statistical significance may relate to the small size of the difference in results with and without computerised visual incentives. Computerised visual incentives provide another method that can be used to teach the pulmonary function
test technique that does not rely on verbal commands and may be comprehended more easily by some.

In children with Duchenne muscular dystrophy, the muscles may tire more quickly, so the number of pulmonary function tests attempts should be minimised to limit the effect of muscle tiredness. Time was taken between attempts with and without computerised visual incentives to allow recovery of tired muscles, and no first test effect could be demonstrated. In clinical practice, when time-constraints exist, computerised visual incentives should be used initially due to their potential small benefit in helping to teach the pulmonary function test technique required.

Intelligence is unlikely to change over time, and the Wechsler test-retest data remain stable. 293 Assessment of intelligence at a time distant to spirometry testing is not likely to have a significant impact on the results obtained. Ratings of oppositional behaviour have been recorded in the 12 months prior to performance of pulmonary function tests in this study. The behaviour of children, and the scores that would be recorded may change over time, although the changes would not be expected to be great in the absence of any intervention. The timing of the behavioural assessment is a confounder that could not be eliminated due to time constraints at the pulmonary function test visit. Its effect is likely to be small.

This study has a cross-sectional design and does not examine the compounding effect of repeat testing on several separate occasions. Further investigation is required to discern if the relationship between intelligence and pulmonary function changes after children have had the opportunity to perform pulmonary function tests with computerised visual incentives on several occasions.
Conclusions

The current clinical practices of using pulmonary function tests in pre-operative risk assessment prior to corrective spinal surgery and the impact of corrective spinal surgery on the respiratory system in childhood neuromuscular weakness have been evaluated. Imprecision in the method of height estimation and pulmonary function prediction has been highlighted and a new precise method of pulmonary function prediction has been developed for children with neuromuscular weakness. Limitation in the ability of children with Duchenne muscular dystrophy to master the technique required to perform pulmonary function testing have been identified and techniques to augment testing have been identified.

Pulmonary function tests are the main assessment tool used in pre-operative respiratory risk assessment in children with neuromuscular weakness undergoing corrective spinal surgery. Corrective spinal surgery carries significant respiratory risk and requires post-operative oxygen therapy in 80.8% and ventilatory support in 11.5%. It may cause respiratory failure and death. It leads to an acute fall in pulmonary function of 11.14% (6.09% in Duchenne muscular dystrophy and 15.74% in Spinal muscular atrophy) in the peri-operative period. Following corrective spinal surgery the rate of decline in pulmonary function is reduced from a pre-operative rate of 5.14 to 0.99 %/year overall (p=0.01), 6.17 to 3.15%/year in Duchenne muscular dystrophy (p=0.02) and 2.33 to 0.20%/year in Spinal muscular atrophy (p=0.27). The long-term benefit of an altered rate of decline of pulmonary function may alter the risk-benefit ratio of corrective spinal surgery in neuromuscular weakness.

Imprecision in height measurements that are used to predict pulmonary function tests exist in at least 9.4% of children with neuromuscular weakness undergoing corrective spinal surgery. Throughout Australia there is not consistency in the method of height
estimation used in neuromuscular weakness or spinal deformity, nor in the value of pulmonary function tests that are used in interpretation. The results obtained in different centres are not readily comparable due to the inconsistencies in the methods used.

The ulna is readily accessible in children with neuromuscular weakness and its bony landmarks are well preserved in those with weakness and joint deformities. Its measurement with a Harpenden anthropometer is highly reproducible (inter-observer variability standard deviation 0.61% of the mean) and it is an accurate predictor of both height ($R^2$ 0.96 in males and 0.94 in females) and pulmonary function ($R^2$ for forced vital capacity: 0.86 in males and 0.83 in females). Using ulna length to predict height and pulmonary function in children with neuromuscular weakness minimizes the inaccuracies introduced when measuring height or arm span. Ulna growth charts allow easy comparison to the normal population. Children from Asia are anthropometrically distinct, and separate prediction equations for pulmonary function from ulna length are required for the female Asian subgroup. Prediction of height from ulna length is not altered in this subgroup. Ulna length may be used to predict height in children with neuromuscular weakness, spinal deformities, cerebral palsy or other disabilities. Its use should facilitate respiratory assessment, monitoring of growth, and calculation of body surface area.

Performance of pulmonary function tests is effort dependent and the technique required is complex, requiring understanding, concentration and practice. In Duchenne muscular dystrophy, intelligence is reduced by one standard deviation below normal, and behavioural abnormalities are common. Pulmonary function test results are affected by intelligence, particularly performance intelligence quotients, but not behaviour in Duchenne muscular dystrophy. Using computerised visual incentives tends ($p=0.06$) to augment pulmonary function testing in this group. Teaching children with Duchenne muscular dystrophy to perform pulmonary function tests should include verbal commands, demonstrating the technique required and using computerised visual incentives.

In childhood neuromuscular weakness, pulmonary function testing is an integral component of respiratory assessment that is used for monitoring progress, pre-
operative risk assessment, guiding investigations for sleep-disordered breathing and prognostication. The currently used methods of pulmonary function test performance and prediction pose some problems that are particular to this group of children. This research has highlighted ways to overcome many of the inaccuracies in current practice. In children with Duchenne muscular dystrophy, teaching the technique required for pulmonary function testing should include careful explanation, demonstration and the use of computerised visual incentives. Ulna length is a precise and reproducible predictor of height and normal values of pulmonary function testing in children with neuromuscular weakness. In considering corrective spinal surgery, pre-operative risk assessment should include pulmonary function testing and consideration of the impact corrective spinal surgery will have on the respiratory system, as this may alter the risk-benefit ratio. A review of the indications for, the timing of, and the contraindications for corrective spinal surgery in children with neuromuscular weakness is needed in the modern era with the availability of techniques to assist with mucociliary clearance and the potential to provide peri-operative non-invasive ventilatory support.
References


Appendix 1

Questionnaire used for national survey of height and pulmonary function test prediction in neuromuscular weakness or scoliosis.
Respiratory Laboratory Managers Questionnaire

1. Hospital: ____________________________________________

2. Manager’s Name: ____________________________________

3. Approximate number of PFTs performed on children with neuromuscular weakness per year: __________________________________________

4. Usual method of height estimation in children with neuromuscular weakness:
   (Please circle the single most appropriate)
   a) Sitting height
   b) Arms extended laterally and span measured against a wall
   c) Tape measure run over posterior skin surface from one middle finger to the other
   d) Tape measure run over anterior skin surface from one middle finger to the other
   e) Tape measure run over skin from one middle finger to midline and measurement doubled
   f) Other method
      Please specify __________________________________________

5. Interpretation of PFT’s in neuromuscular weakness:
   (Please circle the single most appropriate)
   a) Mainly predicted values used
   b) Mainly observed values used
   c) Combination of predicted and observed values used

6. Approximate number of PFTs performed on children with scoliosis per year: __________________________________________

7. Usual method of height estimation in children with scoliosis:
   (Please circle the single most appropriate)
   a) Sitting height
   b) Arms extended laterally and span measured against a wall
   c) Tape measure run over posterior skin surface from one middle finger to the other
   d) Tape measure run over anterior skin surface from one middle finger to the other
   e) Tape measure run over skin from 1 middle finger to midline and measurement doubled
   f) Other method
      Please specify __________________________________________

8. Interpretation of PFT’s in scoliosis:
   (Please circle the single most appropriate)
   a) Mainly predicted values used
   b) Mainly observed values used
   c) Combination of predicted and observed values used

9. List any perceived problems with the method(s) of prediction of PFT you use: __________________________________________

                  Please return by email to: gauldl@cryptic.rch.unimelb.edu.au
                  Thank you for your time.
Appendix 2

Subject information sheet, questionnaire and consent form used for investigating a modified method of prediction of height and pulmonary function.
I would like to invite you and your child to participate in important research which is being conducted by the Royal Children's Hospital.

Research at the Royal Children’s Hospital helps improve the health of children in Victoria. The Department of Respiratory Medicine looks after children with lung diseases such as asthma and cystic fibrosis. Here is an opportunity for you to help us improve the management of children with lung diseases.

Enclosed is information about the study to read, a brief questionnaire and a consent form for you to sign.

Instructions for Parents or Guardians

1. Read the "Information Statement" carefully.

2. Fill in the "Questionnaire"

3. If you understand the "Parent/Guardian Information Statement" and want your child to participate, sign the "Consent form".

4. Tear off and return the "Questionnaire" and "Consent Form" to the school.

5. If you have any questions, you can contact:
   Dr Leanne Gauld
   Royal Children's Hospital
   (03) 9345 4811.

A Member of Women's & Children's Health
Flemington Road Parkville Victoria 3052 Australia
Telephone (03) 9345 5522 Facsimile (03) 9345 5789
INFORMATION STATEMENT

Title of Project
Using Simple Measurements to Predict Height and Breathing Tests.

Thank you for taking the time to read this Information Statement.

Your child is invited to participate in a Research Project that is explained below.

What is the Research Project about?
Breathing tests are what we use to measure how air moves when you breathe. We use height to predict how strong your child should blow. Some children have significant lung problems, but cannot stand to measure their height. This study is trying to find other measurements that we can use to predict height and breathing tests.

Who are the Researchers?
Dr Leanne Gauld

Why am I and my child being asked to be in this research project?
Your child is healthy and old enough to perform breathing tests.

What does my child need to do to be in this research project? Your child needs to agree to participate, and sign a consent form. You need to fill in the questionnaire and consent form. I then come to your child’s school to measure your child’s height, arm span, length of forearms and lower legs. He/she blows into a breathing machine 3 times.

Is there likely to be a benefit to my child?
This study is unlikely to benefit your child directly, but may help someone you know.

Is there likely to be a benefit to other children in the future?
This study may help children with lung problems who cannot stand to be measured.

What are the possible risks and/or side effects for my child? There should be no risks or side effects.

What are the possible discomforts and/or inconveniences for me or my child? The study takes approximately 30 minutes of your child’s time.

What will be done to make sure the information is confidential? Your child’s name will be kept confidential. Measurements obtained will not be released to anyone without your written consent.

Will I be informed of the results when the research project is finished? When the study is completed, a copy of the results will be sent to your child’s school for the newsletter.

You can decide whether or not you give permission for your child to take part in this research project. You do not have to decide whether or not you would like to withdraw your child from this research project at any time. No explanation is needed.

You may like to discuss your participation in this research project with your family and with your doctor. You can ask for further information before deciding if your child will take part.

The name and telephone number of the person to contact for more information or in an emergency is: Dr Leanne Gauld 9345 4811

For parents/guardians who speak languages other than English
If you would also like Information about the research and the Consent Form in your language, please ask for it.

What are my child’s rights as a Participant?
1. I am informed that except where stated above, no information regarding my child’s medical history will be released. This is subject to legal requirements.
2. I am informed that the results of any tests involving my child will not be published so as to reveal my child’s identity. This is subject to legal requirements.
3. The detail of the procedure proposed has also been explained to me. This includes how long it will take, how often the procedure will be performed and whether any discomfort will result.
4. It has also been explained that my child’s involvement in the research may not be of any benefit to him or her. I understand that the purpose of this research project is to improve the quality of medical care in the future.
5. I have been asked if I would like to have a family member or a friend with me while the project is explained to me.
6. I understand that this project follows the guidelines of the National Statement on Ethical Conduct in Research Involving Humans (1999).
7. I understand that this research project has been approved by the Royal Children’s Hospital Ethics in Human Research Committee on behalf of Women’s and Children’s Health Board.
8. I have received a copy of this document.

If you have any questions about patient rights contact
The RCH Patient Representative, RCH Hospital Support Unit, Phone 9345 5676
QUESTIONNAIRE

1. Child’s Name: ____________________________
   Surname: ____________________________ First Name: ____________________________

2. Date of Birth: ____________________________ (day/mth/yr) Gender: M / F

3. Does your child suffer from curvature of the spine or spinal abnormality? Y / N
   If yes, please explain __________________________________________________________

4. Does your child have muscle weakness? Y / N
   If yes, please explain __________________________________________________________

5. Does your child have any lung problems? Y / N
   If yes, please explain _________________________________________________________

6. Does your child have any hormone or growth problems? Y / N
   If yes, please explain _________________________________________________________

7. Was your child born 5 weeks or more early? Y / N
   If yes, please explain _________________________________________________________

8. Has your child got any other illnesses? Y / N
   If yes, please explain _________________________________________________________

9. List any regular medications: 1. _____________________________________________
   2. _____________________________________________
   3. _____________________________________________

10. List any other medications taken in the last 4 weeks: 1. _________________________
    (Include: all asthma medications all other medications) 2. _________________________
    3. __________________________________

11. Is there a personal or family history of growth problems? Y / N
    If yes, give details ____________________________________________________________

12. Body proportions vary in different racial groups. We need to know your child’s racial
    background. Please circle one or two of the following:
    Caucasian  Mediterranean  Aboriginal  Pacific Islander  Asian
    Other ________________
CONSENT FORM

Title of Project
Using Simple Measurements to Predict Height and Breathing Tests

Principal Investigator(s)  Dr Leanne Gauld

Brief outline of research project including benefits, possible risks, inconveniences and Discomforts.
Breathing tests are what we use to measure the way air moves when you breathe. We use height to work out How strong you should be able to blow. Some children cannot stand to measure their height. This study is trying to find another measurement we can use to predict height and breathing tests.

What Happens to You?
After filling in the questionnaire and consent forms, I measure your child's height, sitting height, forearms and lower legs. He/she then blows hard into a breathing machine 3 times. The whole visit takes approximately 30 minutes.

Possible Benefits
Your participation may help the medical care of children with lung problems who are unable to stand.

I, ___________________________________________ (Print Name)
voluntarily consent to my child taking part in this research project, which has been explained to my child by Dr Leanne Gauld.

I have received a Participant Information Statement to keep and I believe I understand the purpose, extent and possible effects of my involvement.

I understand that if I refuse to consent, or I withdraw from the study at any time without explanation, this will not affect my access to the best available treatment and care from Women's and Children's Health (The Royal Women's Hospital OR The Royal Children's Hospital).

I understand that I will receive a copy of this consent form.

SIGNATURE ____________________________ Date __________

I have explained the study to the Participant who has signed above, and believe that they understand the purpose, extent and possible effects of their involvement in this study.

RESEARCHER'S SIGNATURE ____________________________ Date __________
Appendix 3

Approval of study of modified method of prediction of height and pulmonary function by Royal Children’s Hospital Ethics in Human Research Committee.
**ETHICS IN HUMAN RESEARCH COMMITTEE**

**APPROVAL**

<table>
<thead>
<tr>
<th>EHRC REF. No:</th>
<th>21008 A</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROJECT TITLE:</td>
<td>Usefulness of Simple Anthropological Measurements in the Prediction of Height and Pulmonary Function Tests</td>
</tr>
<tr>
<td>INVESTIGATOR(S):</td>
<td>L Gauld, C Robertson</td>
</tr>
<tr>
<td>DATE OF APPROVAL:</td>
<td>30 March, 2001</td>
</tr>
<tr>
<td>DURATION:</td>
<td>48 months</td>
</tr>
</tbody>
</table>

**SIGNED:**  

<table>
<thead>
<tr>
<th>COMMITTEE REPRESENTATIVE</th>
<th>3/4/01</th>
</tr>
</thead>
</table>

**CONDITIONS**

**ALL PROJECTS**

1. Any proposed change in protocol and the reasons for that change, together with an indication of ethical implications (if any), must be submitted to the Ethics in Human Research Committee for approval.

2. The Principal Investigator must notify the Secretary of the Ethics in Human Research Committee of:
   - Actual starting date of project.
   - Any adverse effects of the study on participants and steps taken to deal with them.
   - Any unforeseen events.

3. A progress report must be submitted annually and at the conclusion of the project, with special emphasis on ethical matters.

**DRUG TRIALS**

4. The investigators must maintain all records relating to the study for a period of 23 years.

5. The investigator(s) must report to the Sponsor and the Ethics in Human Research Committee within 24 hours of becoming aware of any serious adverse event experienced by any subject during the trial.
Appendix 4

Approval of study of modified method of prediction of height and pulmonary function by the Department of Employment, Education and Training of Victoria.
24 April 2001

Dr Leanne Gauld
Department of Respiratory Medicine
Royal Children’s Hospital
Flemington Road
Parkville 3052

Dear Dr Gauld

Thank you for your application of 30 March 2001 in which you request permission to conduct a research study in government schools titled: *Usefulness of Simple Anthropological Measurements in the Prediction of Height and Pulmonary Function tests in Australian Children.*

I am pleased to advise that on the basis of the information you have provided your research proposal is approved in principle subject to the conditions detailed below.

1. Should your institution’s ethics committee require changes or you decide to make changes, these changes must be submitted to the Department of Education, Employment and Training for its consideration before you proceed.
2. You obtain approval for the research to be conducted in each school directly from the principal. Details of your research, copies of this letter of approval and the letter of approval from the relevant ethics committee are to be provided to the principal. The final decision as to whether or not your research can proceed in a school rests with the principal.

3. No student is to participate in this research study unless they are willing to do so and parental permission is received. Sufficient information must be provided to enable parents to make an informed decision and their consent must be obtained in writing.

4. As a matter of courtesy, you should advise the relevant Regional Director of the schools you intend to approach. An outline of your research and a copy of this letter should be provided to the Regional Director.

5. Any extensions or variations to the research proposal, additional research involving use of the data collected, or publication of the data beyond that normally associated with academic studies will require a further research approval submission.

6. At the conclusion of your study, a copy or summary of the research findings should be forwarded to me at the above address.

I wish you well with your research study. Should you have further enquiries on this matter, please contact Louise Dressing, Senior Research Project Officer, School Community Support Branch, on 9637 2349.

Yours sincerely

[Signature]

JOHN ALLMAN
A/Manager
School & Regional Operations

encl.
Appendix 5

Questionnaire for study of effect of intelligence and behaviour on performance of pulmonary function tests in children with Duchenne muscular dystrophy.
Participant Questionnaire

Visual Incentives Improve Spirometry in Children with Duchenne Muscular Dystrophy

Please Circle

1. When performing spirometry without computer graphics, how hard did you find doing the test?  1 2 3 4 5

2. When performing spirometry with computer graphics, how hard did you find doing the test?  1 2 3 4 5

3. Did you find spirometry easier with or without computer graphics?  WITH WITHOUT

Please note:  1 = Very easy
              2 = Easy
              3 = Neither easy nor hard
              4 = Hard
              5 = Very hard
Appendix 6

Approval of the study of the effect of intelligence and behaviour on performance of pulmonary function tests in Duchenne muscular dystrophy by the South East Health Research Ethics Committee.
23rd April 2003

Dr Leanne Gauld
Respiratory Laboratory
Sydney Childrens Hospital

Dear Dr Gauld

Re: Visual Incentives Improve Spirometry in Children with Duchenne Muscular Dystrophy. 03/078

The Research Ethics Committee at its meeting on 22nd April 2003 considered and approved the above study.

This approval is given subject to the following:

- Changes to the Consent Form. The first paragraph of the Consent Form should provide more information about computer graphics and explain that these are the visual incentives.
- The term lower intelligence should be removed from this paragraph and replaced with words like ‘children who find it more difficult’.

This study has been allocated the reference number 03/078. This reference must be quoted in all correspondence with the Committee.

Please note that any approval relates to the ethical content of the trial, and individual arrangements should be negotiated with the Heads of Departments in those situations where use of their resources is involved.

Yours sincerely

Kim Brehey
Executive Officer
Human Research Ethics Committee - Eastern Section
Appendix 7

Publications from this work to date:

i) Prediction of Childhood Pulmonary Function Using Ulna Length

ii) Height Prediction from Ulna Length
Prediction of Childhood Pulmonary Function Using Ulna Length

Leanne M. Gauld, Johanna Kappers, John B. Carlin, and Colin F. Robertson

Department of Respiratory Medicine, Royal Children’s Hospital, Parkville, Victoria, and Department of Paediatrics, University of Melbourne, Melbourne, Australia

Pulmonary function is important in neuromuscular weakness. In children, height determines normal values. Height measurement is unreliable when neuromuscular weakness or spinal deformity is present. The aim of this study was to accurately predict pulmonary function from a limb segment measurement that is precise and reproducible. Normal males (n = 1,144) and females (n = 1,199), 5.3 to 19.6 years old, were recruited from Melbourne schools. Height, weight, ulna, forearm, tibia, and lower leg lengths were measured using a Harpenden stadiometer and callipers, and electronic scales. Three maximal expiratory maneuvers were performed. Limb measurements were highly reproducible. Linear regression on log-transformed FEV, and FVC was used to develop prediction equations from limb measurements and age. In males FEV₁ = 0.071U + 0.046A + 1.269; r² = 0.86; FVC exp = 0.77U + 0.041A + 1.285; r² = 0.86 and in females FEV₁ = 0.072U + 0.041A + 1.272; r² = 0.84; FVC exp = 0.078U + 0.037A + 1.315; r² = 0.83 (U refers to ulna length and A refers to age). Precision is similar to equations using height. Ulna measurement is accessible in wheelchair-bound children. Using ulna length to predict pulmonary function should facilitate respiratory assessment in children whose height is difficult to measure.

Keywords: pediatrics; anthropometry; respiratory function tests; neuromuscular diseases; scoliosis

The pulmonary consequences of neuromuscular weakness result from impaired function of respiratory muscles and spinal deformity (1, 2). The impact on pulmonary function depends on the pattern of involvement and the rate of progression of the underlying disease (3, 6). Outcome is related to the rate of decline in pulmonary function (16). Monitoring pulmonary function is important in neuromuscular weakness and spinal deformity, where restrictive defects occur and major surgery, such as corrective spinal surgery, is required (7, 10).

Pulmonary function changes throughout childhood and is related to height and age. Height has traditionally been used to predict normal values (11, 14). When spinal deformity, weakness, or immobility is present, height measurement is difficult and inaccurate. Arm span has been used to estimate height, and prediction equations have been developed for healthy children in various populations (15, 19). Precision of arm span measurements is limited by weakness and joint deformity that restrict the ability to actively extend the arms fully. Spinal deformity alters the position adopted during the measurement and reduces accuracy. It is common practice to predict height from a measurement of arm span obtained with a flexible tape measure that is run over the skin and around corners. This practice leads to significant error and has poor reproducibility.

This study aimed to identify a long bone or distal body segment measurement that could be precisely and reproducibly measured and could be used to accurately predict measurements of pulmonary function.

METHODS

Subjects
A total of 27 of 40 approached metropolitan Melbourne schools were recruited using a presentation at a routine school assembly, and students aged 7 to 18 years were invited to participate. Interested students received an information sheet, a questionnaire, and a consent form for their parents or guardian to read and complete. The questionnaire asked for details on gender, date of birth, medical information, growth at birth, medication use, and racial background.

Students were excluded if the questionnaire revealed significant respiratory or systemic illness, spinal deformity, disease known to cause growth disturbance, prematurity (<35 weeks gestation), muscle weakness or abnormal tone, use of medications thought to alter growth, or use of asthma preventer or reliever medication in the preceding 4 weeks.

Measurements
All measurements obtained during the study were made in schools. Anthropometric measurements were obtained with the subjects dressed in light clothing with shoes and socks removed. The same anthropometric and spirometric equipment was used for each student. The same observer obtained all measurements. Weight measurements were in kilograms to the nearest 0.1 kg. All other measurements were in centimeters to the nearest millimeter. Age was calculated in (decimal) years for the day of measurement.

Distal limb measurements were chosen because they are the most accessible in immobilized children. Although the upper arm is also accessible, landmarks are more difficult to delineate, which impairs reproducibility (18). Arm span was included so that comparison could be made with the best currently available method of height estimation in this group. The Harpenden stadiometer and callipers and Wellerburn electronic scales were used because of their high degree of accuracy.

Each student underwent a brief medical examination of the spine for scoliosis. Those in whom scoliosis was thought likely were referred to their local doctor and were excluded from further participation.

Standing height was obtained using a portable Harpenden Stadiometer (Holtain Ltd, Crosswell, UK). Each student placed bis/hers feet on the base plate, together throughout their length. The back was placed firmly against the vertical plate, with the head, shoulders, buttocks, and heels touching this plate. The head was placed in the Frankfurt horizontal plane. The head plate was lowered to sit on the vertex. Gentle vertical traction was applied to the mastoid processes as a deep inspiration was taken to obtain the measurement.

Weight was obtained by standing on zeroed Wellerburn electronic scales (Wellerburn, Southampton, UK). Weight measurement was omitted in the presence of plaster casts and in the case of one student who weighed in excess of the scales ability to measure (150 kg).
Arm span was measured on a wooden arm span stadiometer (17). The frame consisted of two vertical poles and a horizontal beam with measurements marked in millimeters. The frame sits neatly against the wall, and each pole is held stable by three wooden feet. Attached to the horizontal beam is a mobile vertical wooden plate that is positioned 80 to 200 cm above the floor. Students were measured while standing with their back against the wall, with their head, shoulders, buttocks, and heels touching the wall. The feet were vertically below the head, which was in the Frankfurt horizontal plane. The feet were together throughout their length. The arms were extended laterally so that the hands were at the same level from the floor as the shoulders. The palms faced forward. The middle finger of the right hand just touched the protruding right hand pole. The vertical plate was moved medially until it rested against the middle finger of the left hand. If the middle finger had been traumatized or amputated, this measurement was omitted.

Ulma length was obtained in the sitting position with the left forearm resting comfortably on a table. The palm faced downward, and the fingers were extended but together. The elbow was bent at 90° to 110°. The proximal end of the ulna was found by palpating along its length. The tip of the styloid process was felt at the wrist by palpating down the length of the bone distally, until it ends at the styloid process. The tips of the tubercle of the scapula were placed adjacent to both ends of the ulna (see Figure 1).

Forearm measurements were made in the same position as the ulna measurement. The forearm was used to measure from the tip of the left middle finger to the most lateral aspect of the elbow. If the middle finger of the left hand had been traumatized or amputated, the right arm was substituted.

Tibia length was measured in the seated position, using the Harpenden calipers. The right tibial plate was found by palpating along the medial border of the tibia until its proximal aspect was identified. The distal end was found by palpating at the most distal point of the medial malleolus. Lower leg length was measured using the Harpenden portable stadiometer. The subject was seated beside the stadiometer, facing it. The level of the seat was set such that the knee was at a higher level than the hip. The lateral aspect of the lower leg was placed firmly against the stadiometer. The foot was placed directly below the knee. The head plate of the stadiometer was brought down to rest on the upper aspect of the knee.

To determine reproducibility of the measurements, 14 subjects were measured on two separate occasions on the same day by 1 M.G. Both 1 M.G. and an independent observer trained for the measurements, measured another 15 subjects. The first measurement obtained by 1 M.G. was included in the analysis for the production of pulmonary function on all occasions.

Subjects underwent pulmonary function tests (PFT) in the standing position with a nose clip. A Jaeger MasterS cope Spirometer with a heated pneumotach and Version 3.13 Jaeger software (Jaeger, Hoechberg, Germany) was used. Children were asked to make a maximal inspiration followed immediately by a maximal forced expiratory maneuver without a pause in between. A minimum of three maneuvers was performed. Maneuvers were considered acceptable if there was a rapid rise in peak flow and a flat maximally prolonged expiratory curve (29). Computerized visual incentives were often used for encouragement.

To ensure reproducibility, FEV1 and FVC of two maneuvers were required to be within 200 ml of each other. The best maneuver was defined as the one with the greatest sum of FEV1 and FVC and was used for analysis (21). FEV1, FVC, and mean midexpiratory flow (MMEF) were recorded. If acceptable and reproducible PFT could not be obtained after several attempts, PFT were not included in the analysis.

To evaluate the feasibility of performing the limb measurements in children with neuromuscular weakness, each measurement was performed on 20 children with Duchenne Muscular Dystrophy (DMD). A subjective evaluation of the ease of positioning, identification of landmarks, and performance of the measurements was made.

Statistical Analysis

A large sample was used to ensure that variation across the age range could be adequately described and results would have comparable precision to previous studies (21).

Data were double entered into two identical forms of a Microsoft Access database that had built-in validation checks. Stata statistical software was used for analysis (22). Exploratory analysis indicated that linear regression models performed best on logarithmically transformed pulmonary function variables. Linear regression equations were developed including each of the anthropometric measurements and age.

Reference ranges were created by back transforming 95% prediction intervals obtained from the regression models because linear prediction was performed in the log scale. Back transformation automatically produces a range that can be expressed in ratios ("% predicted") relative to the central predicted or normal values.

The white and Asian subgroups were compared with the overall group by using interaction terms in each linear regression analysis to assess whether the pattern of the relationship between the dependent measure (pulmonary function) and the two independent measures of age and anthropometric measurement was similar between the two groups. A two-degree-of-freedom Wald test was used, and separate prediction equations were obtained whenever this test indicated statistical difference at the 0.05 level.

Intra- and interobserver variability was analyzed by calculating the SD of differences between repeated measurements by the same observer (intra) and independent observers (inter) (23). These were used to derive the SD of individual values, which was expressed as a percentage of the mean.

Ethical Approval

The study was approved by the Royal Children's Hospital Ethics in Human Research Committee and by the Department of Employment, Education, and Training of Victoria. Informed consent was obtained from parents and from children over the age of 12 years.

RESULTS

A total of 2,810 students (53% of available students) returned a completed questionnaire and a consent form. The response rate was 71% for primary school students and 33% for high school students. A total of 467 students were excluded on the basis of their questionnaire or sedans or check. The reasons for exclusion are shown in Table 1. The ages of included subjects were distributed equally from 7 to 18 years, with few lying outside this range.

The measurement of each variable was highly reproducible. The SD of intraobserver differences for repeat ulna measurements was 0.13 cm, corresponding to an SD of 0.093 cm for individual values or 0.41% relative to the mean value. Intra- and interobserver variability was calculated similarly for all repeat measurements, and results are shown in Table 2.

Prediction equations for FVC, FEV1, and MMEF were developed using each of the anthropometric measurements as predictor variables and are recorded in Tables E1-E6 in the online supple-

Figure 1. Method of ulna length measurement.
TABLE 1. REASONS FOR EXCLUSION

<table>
<thead>
<tr>
<th>Reason for Exclusion</th>
<th>Males (%)</th>
<th>Females (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>145 (12.7)</td>
<td>102 (8.5)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>55 (4.3)</td>
<td>49 (4.1)</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>15 (1.3)</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td>Medications</td>
<td>23 (2.0)</td>
<td>9 (0.8)</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>4 (0.3)</td>
<td>7 (0.6)</td>
</tr>
<tr>
<td>Maturity</td>
<td>1 (0.1)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Others</td>
<td>14 (2.2%)</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td>Total</td>
<td>252 (22.9)</td>
<td>210 (17.5)</td>
</tr>
</tbody>
</table>

* Percentage of total recruited males (n = 1,144) and females (n = 1,199).

Deformity, and 14 had significant wrist and elbow contractures. The ulna was readily accessible in all children, and the elbow could be placed at 90° or greater, enabling easy identification of the proximal end of the ulna. The ulna styloid process was readily identifiable in all children, and its identification was not limited by wrist contracture. Increasing difficulty was encountered in identifying the distal end of the medial malleolus and in obtaining a tibia length measurement as tibia-equivalenar deformities of the ankle worsened in severity. Adequate positioning for forearm and lower leg length measurements was not possible for any child with wrist or ankle deformities, respectively.

DISCUSSION

In children, change in pulmonary function over time provides a sensitive measure to monitor the progress of respiratory disease. Predicted values of pulmonary function, rather than observed values are used to compensate for the expected increase in pulmonary function associated with growth (24). In an individual, flow and volume measurements track along percentile lines throughout childhood and adolescence (25). Accurate measurement of predictor variables is essential.

Measurement of each of the limb segments is reproducible and provides an accurate alternative to height for prediction of pulmonary function. The precision of prediction equations for each of the anthropometric measurements was similar. Ulna length was chosen because it is readily accessible, even in wheelchair-bound children, and its measurement is unaffected by weakness or by joint or spinal deformity. In children with DMD, the elbow may not permit bending to 90°, nor the wrist full extension, but it was possible to adopt a reasonable position in all cases such that bony landmarks were readily identified and the measurement was unhindered. Forearm and lower leg measurements cross joints and could be affected by joint deformity such as contracture. Arm span measurement could also be affected by weakness or by joint or spinal deformity, and was included only for comparison. Tibia length is readily measured and unaffected by weakness, but palpating the distal end of the medial malleolus becomes particularly challenging in the face of severe equinovarus deformities of the ankle.

In this study, prediction equations for pulmonary function using ulna length and age have similar precision (r²) to those using height. The degree of precision in prediction of FEV₁ and FVC in this study is comparable with that of Ziptel and coworkers (14) (r² = 0.86–0.92) and Hibbert and coworkers (21) (a study of Australian children; r² = 0.85–0.92) who used height to predict pulmonary function. It is superior to that in the study of Knudsen and coworkers (11) (r² = 0.53–0.80) and the Sahnas study (26) (r² = 0.61–0.80).

Spender and coworkers (27) compared measurements of upper arm length obtained using steel and plastic tape measures with those obtained using an anthropometer. The measurements obtained were on average 1.03 ± 0.20 cm and 1.10 ± 0.25 cm longer than the anthropometer measurement, respectively, and the intraobserver variability was greater (p = 0.002). A similar degree of inaccuracy would be expected when measuring the ulna with a tape measure and is not recommended. Ulna length measurement with a Harpenden caliper is simple, requiring only superficial palpation. The technique can be taught to new staff in minutes. Vernier calipers, that measure to 0.2 cm, are available from precision engineering stores for $500 (Australian dollars) and may be used. Measurements were only performed on one side of the body as symmetry has previously been demonstrated (16, 28). The small values of the SD for individual values demonstrates the precision and reproducibility of the measurement.

Several authors have previously documented the relationship

| TABLE 2. STANDARD DEVIATIONS OF INTRAOBSERVER AND INTEROBSERVER VARIABILITIES |
|----------------------------------|-----------------|----------------|
|                                  | Individual SD   | Individual SD |
|                                  |                  | % of Mean     |
| Intraobserver variability        |                  |               |
| Ulna length                      | 0.08             | 0.08           |
| Height                           | 0.13             | 0.13           |
| Age                              | 0.08             | 0.08           |
| Sex                              | 0.10             | 0.10           |
| forearm                          | 0.09             | 0.09           |
| interobserver variability        |                  |               |
| Ulna length                      | 0.13             | 0.13           |
| Height                           | 0.12             | 0.12           |
| Age                              | 0.13             | 0.13           |
| Sex                              | 0.10             | 0.10           |

TABLE 3. PREDICTION EQUATIONS FOR PULMONARY FUNCTION TEST VALUES USING ULNA LENGTH AND AGE

<table>
<thead>
<tr>
<th>Prediction Equation</th>
<th>r²</th>
<th>RMSE (Log Scale)</th>
<th>95% Reference Range (% Predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n = 1,144</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ = exp (0.027 - 0.046 - A) - 1.269</td>
<td>0.86</td>
<td>0.149</td>
<td>75-134</td>
</tr>
<tr>
<td>FVC = exp (0.072 - 0.041 - A) - 1.285</td>
<td>0.86</td>
<td>0.154</td>
<td>74-135</td>
</tr>
<tr>
<td>MMEF = exp (0.060 - 0.054 - 0.1011)</td>
<td>0.67</td>
<td>0.253</td>
<td>63-158</td>
</tr>
<tr>
<td>Females, n = 1,199</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ = exp (0.027 - 0.041 - A) - 1.272</td>
<td>0.84</td>
<td>0.127</td>
<td>78-128</td>
</tr>
<tr>
<td>FVC = exp (0.076 - 0.045 - A) - 1.113</td>
<td>0.81</td>
<td>0.155</td>
<td>78-128</td>
</tr>
<tr>
<td>MMEF = exp (0.053 - 0.054 - A) - 0.806</td>
<td>0.61</td>
<td>0.234</td>
<td>63-158</td>
</tr>
</tbody>
</table>

Definition of abbreviations: A = age; MMEF = mean mid-expiratory flow; RMSE = root mean square error; U = ulna length.

between height and various body segments in their study populations (15, 16, 28-30). Particular attention has been paid to the upper limb (18, 28, 31) and arm span (17, 19, 31). In normal children, height prediction from upper limb measurements has high correlation coefficients (18). Arm span measurement is difficult and inaccurate in the presence of weakness or of joint or spinal deformity. It is currently being used by most respiratory laboratories to predict PFT in childhood neuromuscular weakness and spinal deformity due to the lack of a better alternative. Snyder and coworkers (32) have obtained anthropometric measurements of a large group of normal children in the United States. This normative data has been used to develop prediction equations for height from upper arm, forearm, ulna, lower leg, and arm span measurements (27, 28). Miller and Koreska (26) used the prediction equations for height from forearm, ulna, and arm span in three groups of children: normal children, children with idiopathic scoliosis, and children with DMD. In those with scoliosis, height was estimated by radiographic spine reconstruction. In children who are normal, have idiopathic scoliosis, or have DMD without wrist contractures, estimation of height from forearm measurements has a correlation coefficient of 0.96 (27). In children with DMD and wrist contractures, the ulna length to height correlation coefficient was 0.91. Interestingly, the arm span to height correlation coefficient is only 0.74 (8). Miller and Koreska (26) recommend that forearm is used if no wrist contractures exist, and ulna length is used if wrist contractures do exist. They recommend arm span not be used in children with DMD. In the current study, little difference was found between the precision of forearm or ulna measurements in predicting pulmonary function.

Spender and coworkers (27) used prediction equations for height from upper arm and lower leg developed from Snyder and coworkers (32) data. Growth in cerebral palsy was assessed. It was found that height was reduced in children with spastic quadriplegia but was maintained in the normal range in children with diplegia and hemiplegia. There is evidence that limb growth may be impaired in upper motor neuron lesions, but the authors were unable to find evidence within the available literature that body proportions are altered in those with neuromuscular weakness or spinal deformity.

Schools approached for this study consisted of public, private, religious, and independent primary and secondary schools. They were randomly selected from all metropolitan Melbourne schools to ensure adequate representation of socioeconomic and ethnic groups. Because of the multicultural nature of the Australian society (as represented by this sample), the prediction equations developed can be applicable in other multicultural societies with similar racial distribution.

The response rate was lower than anticipated. This may be due, in part, to the request by many schools to give the students the responsibility for the questionnaire. When schools were agreeable, a recruitment package was sent directly to the parent or guardian, who returned the completed questionnaire and the consent form to the chief investigator in a reply-paid envelope. In developing prediction equations and normal reference ranges, all children with potential illnesses that may lead to them falling outside the normal reference range were excluded. This was clearly explained on the information sheet. Despite asking all children to return the form, even if this was the case, it may have led to a reduced return rate. The incidence of both asthma (33) and attention deficit hyperactivity disorder (34) is far greater in our community than suggested by the responses in this study.

We believe participation bias to have little impact on the results, as this is not a prevalence study and only normal subjects were sought.
In this study, pulmonary function measurements were performed with children in the standing position. In those with neuromuscular weakness, it is likely that these measurements will be performed in the sitting position. Both Townsend (35) and Lalor and coworkers (36) have examined pulmonary function values obtained in the standing and sitting positions in adults. Lalor and coworkers (36) have found the FEV, in the standing position to be approximately 5% greater than that in the sitting position in women but less than 5% in men. Townsend (35) found the FEV, and FVC to be 7 and 6% greater, respectively, in the standing position in men. The American Thoracic Society indicates that the VC is larger in the standing than in the sitting position in childhood, but this has not been quantitated (20). It is recommended that the same posture be adopted for each test. Normal PFTs span a large range, and monitoring of progress is best achieved by comparing an individual's test with their previous results so that progress may be monitored.

Height measurement is inaccurate in the presence of spinal deformity and when immobility is present. Spinal deformity causes restrictive pulmonary defects (37, 39). Measurement of pulmonary function is particularly important in monitoring progress and in preoperative pulmonary risk assessment. Arm span measurements may be performed, but positioning for the measurement is often limited by the deformity of the spine, which may lead to an inequality of the level of the shoulders. This makes the measurement and the PFT predicted from it less accurate.

In children with neuromuscular weakness, immobility is common particularly in the later phases of the disease when the declining respiratory status is gaining importance. In DM1, the FVC rises in early childhood, plateaus in mid-childhood, and then declines (30, 40). The age of acquisition and the magnitude of the plateau have prognostic implications (3). Children with neuromuscular weakness commonly have progressive spinal deformities that warrant the restrictive pulmonary defect and make manual corrective spinal surgery necessary (1, 2, 4, 43). Accurate predicted pulmonary function is important for monitoring disease progression, preoperative pulmonary risk assessment, enabling investigative pathways for sleep disordered breathing, and instigation of respiratory supportive techniques such as noninvasive ventilation and teaching techniques to assist mucus clearance (41, 44, 45).

Conclusions
Measurement of pulmonary function is an important component of respiratory assessment in those with neuromuscular weakness or spinal deformity. Pulmonary function changes throughout childhood so that absolute values are not easily interpreted. Prediction equations have used a combination of height and age, and arm span has been used to predict height, but neither height nor arm span is easily and accurately measured in those with weakness or joint or spinal deformity. Using ulnar length to predict pulmonary function minimizes the inaccuracies introduced when measuring height or arm span. Its use will lead to more accurate prediction of pulmonary function in childhood neuromuscular weakness or spinal deformity.

Conflict of Interest Statement: L.G.M. has no declared conflict of interest; J.K. has no declared conflict of interest; J.B.C. has no declared conflict of interest; C.P.B. has no declared conflict of interest.

Acknowledgement: The authors would like to acknowledge Ms. A. Stewart and Ms. K. Briggs for performing pulmonary function tests, Ms. Suzanne Vidmar for statistical computer assistance, and the students and staff of the participating schools.

References
16. Cheng JC, Leung SS, Chu BS, Tie PW, Lee CW, Chan AK, Xia G.
Online Data Supplement

Title: Prediction of Childhood Pulmonary Function Using Ulna Length

Authors: Leanne M. Gauld,¹
Johanna Kappers,¹
John, B. Carlin,²
Colin F. Robertson¹
Table E1: Prediction equations for pulmonary function test values using height and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>Males (n=1144)</th>
<th>Females (n=1199)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FEV₁ = exp (0.016 x H* + 0.021 x A↑ - 1.768)</td>
<td>FEV₁ = exp (0.016 x H* + 0.020 x A↑ - 1.728)</td>
</tr>
<tr>
<td></td>
<td>FVC = exp (0.017 x H* + 0.017 x A↑ -1.798)</td>
<td>FVC = exp (0.017 x H* + 0.016 x A↑ - 1.831)</td>
</tr>
<tr>
<td></td>
<td>MMEF = exp (0.014 x H* + 0.032 x A↑ - 1.451)</td>
<td>MMEF = exp (0.012 x H* + 0.039 x A↑ - 1.164)</td>
</tr>
<tr>
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<td>R²</td>
<td>RMSE (log scale)</td>
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<tr>
<td>Males (n=1144)</td>
<td>0.89</td>
<td>0.132</td>
</tr>
<tr>
<td></td>
<td>0.89</td>
<td>0.137</td>
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<td></td>
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<td>0.245</td>
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<td>Females (n=1199)</td>
<td>0.88</td>
<td>0.133</td>
</tr>
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<td></td>
<td>0.86</td>
<td>0.121</td>
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<tr>
<td></td>
<td>0.62</td>
<td>0.231</td>
</tr>
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</table>

*height, †age
Table E2: Prediction equations for PFT values using arm span and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1135)</strong></td>
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<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.014 \times AS^* + 0.032 \times \text{A}^\dagger - 1.512)$</td>
<td>0.88</td>
<td>0.140</td>
<td>76 - 132</td>
</tr>
<tr>
<td>$FVC = \exp (0.015 \times AS^* + 0.027 \times \text{A}^\dagger - 1.543)$</td>
<td>0.88</td>
<td>0.144</td>
<td>75 - 133</td>
</tr>
<tr>
<td>$MMEF = \exp (0.011 \times AS^* + 0.042 \times \text{A}^\dagger - 1.216)$</td>
<td>0.68</td>
<td>0.249</td>
<td>61 - 163</td>
</tr>
<tr>
<td><strong>Females (n=1198)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.010 \times AS^* + 0.047 \times \text{A}^\dagger - 1.148)$</td>
<td>0.83</td>
<td>0.135</td>
<td>77 - 130</td>
</tr>
<tr>
<td>$FVC = \exp (0.010 \times AS^* + 0.043 \times \text{A}^\dagger - 1.182)$</td>
<td>0.81</td>
<td>0.143</td>
<td>76 - 132</td>
</tr>
<tr>
<td>$MMEF = \exp (0.067 \times AS^* + 0.059 \times \text{A}^\dagger - 0.697)$</td>
<td>0.60</td>
<td>0.237</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

*arm span, †age
Table E3: Prediction equations for PFT values using ulna length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.071 \times U^* + 0.046 \times A \dagger - 1.269)$</td>
<td>0.86</td>
<td>0.149</td>
<td>75 - 134</td>
</tr>
<tr>
<td>$FVC = \exp(0.077 \times U^* + 0.041 \times A \dagger - 1.285)$</td>
<td>0.86</td>
<td>0.154</td>
<td>74 - 135</td>
</tr>
<tr>
<td>$MMEF = \exp(0.060 \times U^* + 0.053 \times A \dagger - 1.013)$</td>
<td>0.67</td>
<td>0.253</td>
<td>63 - 158</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp(0.072 \times U^* + 0.041 \times A \dagger - 1.272)$</td>
<td>0.84</td>
<td>0.127</td>
<td>78 - 128</td>
</tr>
<tr>
<td>$FVC = \exp(0.078 \times U^* + 0.037 \times A \dagger - 1.315)$</td>
<td>0.83</td>
<td>0.135</td>
<td>78 - 128</td>
</tr>
<tr>
<td>$MMEF = \exp(0.053 \times U^* + 0.054 \times A \dagger - 0.806)$</td>
<td>0.61</td>
<td>0.234</td>
<td>63 - 158</td>
</tr>
</tbody>
</table>

*ulna length, †age
Table E4: Prediction equations for PFT values using forearm length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>( R^2 )</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{FEV}_1 = \exp (0.046 \times F^{*} + 0.042 \times A^{\dagger} - 1.419) )</td>
<td>0.87</td>
<td>0.145</td>
<td>75 - 133</td>
</tr>
<tr>
<td>( \text{FVC} = \exp (0.050 \times F^{*} + 0.038 \times A^{\dagger} - 1.433) )</td>
<td>0.87</td>
<td>0.150</td>
<td>75 - 134</td>
</tr>
<tr>
<td>( \text{MMEF} = \exp (0.067 \times F^{*} - 1.659) )</td>
<td>0.66</td>
<td>0.251</td>
<td>60 - 167</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{FEV}_1 = \exp (0.046 \times F^{*} + 0.039 \times A^{\dagger} - 1.426) )</td>
<td>0.85</td>
<td>0.125</td>
<td>78 - 128</td>
</tr>
<tr>
<td>( \text{FVC} = \exp (0.050 \times F^{*} + 0.035 \times A^{\dagger} - 1.470) )</td>
<td>0.84</td>
<td>0.133</td>
<td>77 - 130</td>
</tr>
<tr>
<td>( \text{MMEF} = \exp (0.035 \times F^{*} + 0.052 \times A^{\dagger} + 0.934) )</td>
<td>0.61</td>
<td>0.233</td>
<td>63 - 158</td>
</tr>
</tbody>
</table>

*forearm, †age
Table E5: Prediction equations for PFT values using tibia length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>$R^2$</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.039 \times T^* + 0.056 \times A^\dagger - 1.085)$</td>
<td>0.85</td>
<td>0.153</td>
<td>74 - 135</td>
</tr>
<tr>
<td>$FVC = \exp (0.043 \times T^* + 0.053 \times A^\dagger - 1.084)$</td>
<td>0.85</td>
<td>0.159</td>
<td>73 - 137</td>
</tr>
<tr>
<td>$MMEF = \exp (0.034 \times T^* + 0.062 \times A^\dagger - 0.855)$</td>
<td>0.67</td>
<td>0.255</td>
<td>61 - 165</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FEV_1 = \exp (0.042 \times T^* + 0.046 \times A^\dagger - 1.108)$</td>
<td>0.85</td>
<td>0.130</td>
<td>78 - 128</td>
</tr>
<tr>
<td>$FVC = \exp (0.046 \times T^* + 0.042 \times A^\dagger - 1.148)$</td>
<td>0.83</td>
<td>0.137</td>
<td>76 - 131</td>
</tr>
<tr>
<td>$MMEF = \exp (0.028 \times T^* + 0.060 \times A^\dagger - 0.630)$</td>
<td>0.60</td>
<td>0.237</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

*tibia length, †age
**Table E.6**: Prediction equations for PFT values using lower leg length and age.

<table>
<thead>
<tr>
<th>Prediction equation</th>
<th>( R^2 )</th>
<th>RMSE (log scale)</th>
<th>95% reference range (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n=1144)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( FEV_1 = \exp(0.036 \times L^* + 0.048 \times \text{A}^\dagger - 1.326) )</td>
<td>0.86</td>
<td>0.148</td>
<td>75 - 134</td>
</tr>
<tr>
<td>( FVC = \exp(0.039 \times L^* + 0.045 \times \text{A}^\dagger - 1.345) )</td>
<td>0.86</td>
<td>0.152</td>
<td>74 - 135</td>
</tr>
<tr>
<td>( MMEF = \exp(0.030 \times L^* + 0.056 \times \text{A}^\dagger - 1.059) )</td>
<td>0.68</td>
<td>0.252</td>
<td>61 - 164</td>
</tr>
<tr>
<td><strong>Females (n=1199)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( FEV_1 = \exp(0.038 \times L^* + 0.041 \times \text{A}^\dagger - 1.391) )</td>
<td>0.85</td>
<td>0.124</td>
<td>78 - 128</td>
</tr>
<tr>
<td>( FVC = \exp(0.042 \times L^* + 0.036 \times \text{A}^\dagger - 1.455) )</td>
<td>0.84</td>
<td>0.130</td>
<td>78 - 129</td>
</tr>
<tr>
<td>( MMEF = \exp(0.025 \times L^* + 0.057 \times \text{A}^\dagger - 0.805) )</td>
<td>0.60</td>
<td>0.236</td>
<td>63 - 159</td>
</tr>
</tbody>
</table>

*lower leg length, \(^\dagger\)age*
\[ FVC = \exp (0.078 \times U^* + 0.037 \times A^* - 1.315) \quad \text{RMSE} = 0.135 \]

<table>
<thead>
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<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
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<tbody>
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<td>16</td>
<td>1.21</td>
<td>1.26</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>17</td>
<td>1.31</td>
<td>1.36</td>
<td>1.41</td>
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</tr>
<tr>
<td>18</td>
<td>1.42</td>
<td>1.47</td>
<td>1.53</td>
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<tr>
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</tr>
</tbody>
</table>

Per year of age, multiply by: 1.0378
Per cm of ulna length, multiply by: 1.0812

Reference ranges: Multiply or divide by:
- 50% 1.095
- 75% 1.168
- 80% 1.189
- 90% 1.248
- 95% 1.302

*ulna length, †age

Figure E1

E1: Method of prediction of "normal" FVC for females.
Height prediction from ulna length

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Height is fundamental to assessing growth and nutrition, calculating body surface area, and predicting pulmonary function in childhood. Its measurement is hindered by muscle weakness, joint, or spinal deformity. Arm span has been used as a substitute, but is inaccurate. The objective of the study was to identify a limb measurement that precisely and reproducibly predicts height in childhood. Males (n=1144) and females (n=1199), aged 5 years 4 months to 19 years 7 months, without disability were recruited from Melbourne schools. Height, arm span, ulna, forearm, tibia, and lower leg lengths were measured with a Harpenden stadiometer and anthropometer. Prediction equations for height based on ulna length (U) and age in years (A) were developed using linear regression. Ulna centile charts were developed by the LMS method. For males, height (cm) = 140.6055 + 1.32184 * A + 28.003 * U^2 (R^2=0.96); for females, height (cm) = 4.4550 + 1.33154 * A + 31.455 * U^2 (R^2=0.84). Intra- and inter-observer variability was 0.41% and 0.61% relative to the mean, respectively. Height prediction equations from tibia, forearm, and lower leg length were calculated. We show that ulna measurement is reproducible and precisely predicts height in school-age children. It appears to be superior to arm span measurement when neuromuscular weakness, joint, or spinal deformity exists. Ulna growth charts should facilitate growth assessment.

Height measurement is important for monitoring growth and nutrition (Scud and Kopil 1991, Walker et al. 1996, Pegal et al. 2002), calculation of medication dose (Bailey and Briars 1996), glomerular filtration (Wang et al. 1992, Bailey and Briars 1996), and predicting normal ranges of pulmonary function tests (Zapletal et al. 1969, Knudsen et al. 1983, Schwartz et al. 1988). Inability to measure height accurately limits medical assessment. Children whose height is difficult to measure include those who only use wheelchairs as a result of cerebral palsy (CP) or neuromuscular weakness, those with spinal deformity, and those with lower limb amputation or deformity. Arm span has generally been substituted for height measurement, and good prediction equation exists (Janz et al. 1988; Jarzem and Gedhill 1993; Cheng et al. 1996, 1998; Parker et al. 1996).

Accurate arm span measurement relies on consistent and precise positioning. To achieve this, the back is placed against a wall, and active and full extension of the arms held at right angles to the trunk is necessary. This outstretched position must be maintained until correct positioning is confirmed and a measurement can be taken (Miller and Koreska 1992, Jarzem and Gedhill 1993, Cheng et al. 1996). Forming and holding this position becomes impossible where significant neuromuscular weakness, joint deformity or abnormal muscle tone exists. In these situations arm span measurement becomes imprecise, in spinal deformity, simple height measurement with a stadiometer leads to an inaccurate representation of stature. Arm span measurement in this group is also inaccurate owing to the effect of spinal deformity on positioning for the measurement. Rotational, kyphotic, and lordotic deformities limit the ability to place the back firmly against a vertical wall. Shoulder imbalance leads to disparity in the level of the arms from the floor, which reduces accuracy (Bago et al. 1996).

Despite limitations in the precision of arm span measurements in children with disability and in those with deformity, this method is still being used extensively to predict height. Upper limb (Janderholm and Lindgren 1978, Miller and Koreska 1992, Jarzem and Gedhill 1993) and knee height (Johnson and Ferranti 1991, Hogan 1995) measurements have been used but their use is not widespread. This study sought to determine whether an accessible distal limb measurement could be reliably and reproducibly measured in children for the accurate prediction of height, and to develop prediction equations for height from the anthropometric measurement.

**Methods**

**PARTICIPANTS AND PROCEDURE**

Detailed methods of this study have already been described (Gauld et al. 2005). Students aged 5 to 19 years were recruited from metropolitan Melbourne schools. Study sample range was 5 years 4 months to 19 years 7 months. A screening questionnaire was completed in order to exclude the following: individuals with asthma who had required medication in the preceding 4 weeks; those who were born preterm (gestation of less than 35 weeks); those with spinal deformity; those using medication thought to alter growth; those with neuromuscular weakness or abnormal tone; and those with any other major medical illnesses or growth disturbance. Parents or guardians were asked to provide information about their child’s racial background to allow racial subgroup analysis. A paediatric respiratory physician conducted a brief examination of the spine to exclude those with spinal deformity.

Recruited children had their height, weight, arm span, ulna, forearm, tibia, and lower leg length measured with a Harpenden Portable Stadiometer (Holtain Ltd, Crosswell, UK), Seidell electronic scales (Wedderburn, Southampton, UK), an arm span stadiometer (Hibbert et al. 1988) and a Harpenden anthropometer (Holtain Ltd, Crosswell, UK). All measurements were performed in light clothing with shoes and socks removed. Weight measurements were in kilograms to the nearest 100g. All other measurements were in centimetres to the nearest millimetre. Age was calculated in (decimal) years from the day of the measurement. All measurements were taken by a paediatric respiratory physician or a registered nurse.

Ulna length was obtained in the sitting position with the left forearm resting comfortably on a table. The palm faced downwards and the fingers were extended but together. The elbow was bent at 90 to 110°. The proximal end of the ulna was found by palpating along its length. The tip of the styloid process was felt at the wrist by palpating down the length of the bone distally, until its end was felt. The tips of the Harpenden anthropometer were placed adjacent to both end points (Fig. 1). A detailed description of the other measurements is provided in Gauld et al. (2005).

To determine reproducibility of the measurements, 14 participants were measured on two separate occasions on the same day by a paediatric respiratory physician. Both the paediatric respiratory physician and an independent observer, trained in making the measurements, measured another 15 participants.

Each limb measurement was recorded for a small group of children with neuromuscular weakness and joint deformities in order to subjectively evaluate the ease of positioning, identification of landmarks, and performance of the measurements in the target group.

**Statistical analysis**

A large sample was used to ensure that variation across the age range could be adequately described and so that results would have a precision comparable to that of previous studies (Hibbert et al. 1989). Data were double-entered into two identical forms of a Microsoft Access database that had built-in validation checks. Stata statistical software was used for analysis.

Intraobserver and interobserver variability were analyzed by calculating the standard deviation (SD) of differences between repeat measurements by the same observer (intraobserver) and independent observers (interobserver; Chinn 1991). These were used to derive the SD of individual values, which was expressed as a percentage of the mean. Linear regression equations were developed, and these included each of the anthropometric measurements and age. Reference ranges were calculated to include 95% (2SD) of children without disability. Growth charts showing change in ulna length with age were developed using the LMS method (Cole 1990, Cole and Green 1992). This method uses the median (M), coefficient of variation (S), and skewness (E) to fit smooth centile curves to reference data.

The Asian subgroup was compared to all other groups by using interaction terms in each linear regression analysis. This was in order to assess whether the pattern of the relationship between height and the anthropometric measurements was similar between the two groups. A two-degree-of-freedom Wald test was used, and separate prediction equations were obtained for the Asian group whenever this test indicated statistical difference at p=0.05.

**Ethical approval**

The study was approved by the Royal Children's Hospital Ethics in Human Research Committee, Sydney, and the Department of Employment, Education and Training of Victoria, Melbourne, Australia. Written informed consent was obtained from parents and from children over the age of 12 years.

**Results**

A total of 2810 students (53% of those approached) returned a completed questionnaire and consent form; 467 children were excluded on the basis of their questionnaire responses or scoliosis examination. The age distribution was consistent from 7 to 18 years, with few outliers.

Each anthropometric measurement was highly reproducible. The SD of intra-observer differences for repeat ulna

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SD of differences (n=14)</th>
<th>Individual SD of differences (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>0.08</td>
<td>0.07</td>
</tr>
<tr>
<td>Height</td>
<td>0.23</td>
<td>0.19</td>
</tr>
<tr>
<td>Arm span</td>
<td>0.57</td>
<td>0.35</td>
</tr>
<tr>
<td>Ulna</td>
<td>0.13</td>
<td>0.12</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.17</td>
<td>0.15</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.16</td>
<td>0.11</td>
</tr>
<tr>
<td>Lower leg</td>
<td>0.10</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**Table I: Standard deviations (SDs) of repeat measurements in children without disability**
measurements was 0.13 cm, corresponding to a SD of 0.09 cm for individual values or 0.11% relative to the mean value. Inter-observer and inter-observer variability were calculated similarly for all repeat measurements and are shown in Table I.

Prediction equations for height from each of the anthropometric measurements have been developed from linear regression analysis. Age was included to improve the accuracy of prediction; however, weight did not significantly improve accuracy and was therefore not included. The prediction equations and 95% reference ranges are shown in Table II. The relationship between height and ulna length is graphically represented in Figure 2, and the linear regression (excluding

### Table II: Prediction equations for height estimation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prediction equation for height</th>
<th>R²</th>
<th>RMSE</th>
<th>95% reference range (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n = 1144)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm span</td>
<td>( H = 0.829 AS + 0.214 A + 16.258 )</td>
<td>0.97</td>
<td>5.214</td>
<td>6.30</td>
</tr>
<tr>
<td>Ulna</td>
<td>( H = 0.605 M + 1.5084 + 28.003 )</td>
<td>0.96</td>
<td>5.896</td>
<td>7.64</td>
</tr>
<tr>
<td>Forearm</td>
<td>( H = 2.394 F + 1.1934 + 20.432 )</td>
<td>0.97</td>
<td>3.556</td>
<td>7.00</td>
</tr>
<tr>
<td>Tibia</td>
<td>( H = 2.758 T + 1.717A + 56.909 )</td>
<td>0.96</td>
<td>5.791</td>
<td>7.45</td>
</tr>
<tr>
<td>Lower leg</td>
<td>( H = 2.125 L + 1.527A + 21.818 )</td>
<td>0.98</td>
<td>5.062</td>
<td>6.00</td>
</tr>
<tr>
<td><strong>Females (n = 1199)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm span</td>
<td>( H = 0.493 AS + 1.595A + 56.976 )</td>
<td>0.91</td>
<td>4.484</td>
<td>8.79</td>
</tr>
<tr>
<td>Ulna</td>
<td>( H = 0.349 M + 1.5154 + 51.485 )</td>
<td>0.94</td>
<td>3.785</td>
<td>7.42</td>
</tr>
<tr>
<td>Forearm</td>
<td>( H = 2.908 F + 1.171A + 21.167 )</td>
<td>0.95</td>
<td>3.344</td>
<td>6.55</td>
</tr>
<tr>
<td>Tibia</td>
<td>( H = 2.771 T + 1.457A + 57.748 )</td>
<td>0.95</td>
<td>5.385</td>
<td>6.63</td>
</tr>
<tr>
<td>Lower leg</td>
<td>( H = 2.475 L + 1.185A + 21.151 )</td>
<td>0.97</td>
<td>2.717</td>
<td>5.33</td>
</tr>
</tbody>
</table>

RMSE, root mean square of the error; \( H \), height; AS, arm span; A, age; \( M \), ulna length; \( F \), forearm length; \( T \), tibia length; \( L \), lower leg length.

**Figure 2:** Relationship between height and ulna length for males and females with prediction equation, third and 97th centiles.

**Figure 3:** Growth charts for ulna length change with age for males and females.

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age) and reference range are overlaid. The prediction equation depicted had $R^2=0.95$ for males and $R^2=0.92$ for females, compared to $R^2=0.96$ for males and $R^2=0.94$ for females when age was included. Growth charts for change in ulna length with age for males and females are shown in Figure 5.

Table III summarizes the racial mix of included students. Most of the children were Caucasian ($n=1801$) or Asian ($n=307$). The prediction equations developed are precise for the Caucasian subpopulation. The most anthropometrically distinct subpopulation was the group from Asia. Prediction equations for height in the male and female Asian subpopulation were significantly different ($p<0.05$) when using arm span, forearm, or tibia length as independent predictors. There was no significant difference in the prediction equations when ulna length was used. The prediction equations for the Asian subpopulation are summarized in Table IV, along with $R^2$, root mean square of the error, and $p$ value for the difference.

**Performance of Measurements in Disabled Children**

Twenty children with Duchenne muscular dystrophy underwent the limb measurements. Mean age was 12 years 1 month (range: 7 years 2 months to 18 years 6 months). Seventeen children required a wheelchair. All children had significant fixed ankle deformity, and 14 had significant wrist and elbow contractures. The ulna was readily accessible in all children, and the elbow could be placed at 90° or greater, enabling easy identification of the proximal end of the ulna. The ulna styloid process was readily identifiable in all children, and its identification was not limited by wrist contracture (Fig. 4). Identifying the distal end of the medial malleolus, and obtaining a tibia length measurement was found to be increasingly difficult as equinovalvus deformities of the ankle worsened in severity. Adequate positioning for forearm and lower leg length measurements was not possible for any child with wrist or ankle deformities.

**Discussion**

Each of the distal limb anthropometric measurements investigated is a precise predictor of height in children with disability. The accuracy of height prediction from ulna length (males $R^2=0.96$, females $R^2=0.94$) is comparable to that from arm span (males $R^2=0.97$, females $R^2=0.91$). The measurements have readily identifiable landmarks that facilitate their measurement (Jazem and Gledhill 1993). They are accurate and reproducible, as highlighted by the small individual SD for repeat measurements (Table I). Using ulna length and the prediction equation should facilitate height estimation when its accurate measurement is not possible. Ulna growth charts provide the normal range and centiles for ulna length compared with age. This permits the comparison of an individual's measurement with that in the population of those without disability.

Ulna length measurement with a Harpenden anthropometer is simple, requiring only superficial palpation. The technique can be taught quickly to clinical staff. Spender et al. (1989) compared measurements of upper arm length obtained by using steel and plastic tape measures with those obtained by using an anthropometer; values obtained were on average 1.03 cm (SD 0.2 cm) and 1.1 cm (SD 0.25 cm) greater than the anthropometer values respectively, and the intraobserver variability was greater ($p=0.002$). A similar degree of inaccuracy would be expected when measuring the ulna with a tape measure, and is not recommended. Vernier callipers are readily

### Table III: Racial backgrounds of participants without disability

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n$</td>
<td>%</td>
<td>$n$</td>
<td>%</td>
</tr>
<tr>
<td>Anglo-Saxon</td>
<td>728</td>
<td>65.6</td>
<td>792</td>
<td>66.1</td>
</tr>
<tr>
<td>Asian</td>
<td>173</td>
<td>15.1</td>
<td>134</td>
<td>11.2</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>109</td>
<td>9</td>
<td>147</td>
<td>12.3</td>
</tr>
<tr>
<td>South American</td>
<td>13</td>
<td>1.1</td>
<td>18</td>
<td>1.5</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>7</td>
<td>0.6</td>
<td>5</td>
<td>0.4</td>
</tr>
<tr>
<td>African</td>
<td>5</td>
<td>0.3</td>
<td>4</td>
<td>0.3</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Mixed</td>
<td>109</td>
<td>9.5</td>
<td>86</td>
<td>7.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
<td>0.7</td>
<td>11</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>1114</td>
<td>100</td>
<td>1195</td>
<td>100</td>
</tr>
</tbody>
</table>

*Defined within Caucasian category. *No subdivisions recorded.

### Table IV: Prediction equations for height estimation in the Asian subgroup, using anthropometric measurements and $p$ value for difference between prediction in this subgroup and overall group

<table>
<thead>
<tr>
<th>Prediction equation for height</th>
<th>$R^2$</th>
<th>RMSE</th>
<th>95% reference range (cm)</th>
<th>$p^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males ($n = 159$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$H = 0.785A + 0.890A + 21.644$</td>
<td>0.97</td>
<td>5.120</td>
<td>6.12</td>
<td>0.03</td>
</tr>
<tr>
<td>$H = 1.171f + 1.591A + 33.650$</td>
<td>0.95</td>
<td>4.367</td>
<td>8.56</td>
<td>0.00b</td>
</tr>
<tr>
<td>$H = 2.421f + 1.574 + 23.615$</td>
<td>0.96</td>
<td>5.817</td>
<td>7.48</td>
<td>0.10b</td>
</tr>
<tr>
<td>$H = 2.297 + 2.129 + 12.941$</td>
<td>0.95</td>
<td>4.153</td>
<td>8.14</td>
<td>0.02</td>
</tr>
<tr>
<td>$H = 2.625 + 1.704 + 15.290$</td>
<td>0.97</td>
<td>2.996</td>
<td>5.87</td>
<td>0.00b</td>
</tr>
<tr>
<td>Females ($n = 15$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$H = 0.752A + 0.841A + 25.060$</td>
<td>0.96</td>
<td>2.724</td>
<td>5.34</td>
<td>0.001</td>
</tr>
<tr>
<td>$H = 1.605f + 1.079A + 29.115$</td>
<td>0.95</td>
<td>4.294</td>
<td>8.42</td>
<td>0.22b</td>
</tr>
<tr>
<td>$H = 2.711f + 1.554A + 26.476$</td>
<td>0.95</td>
<td>5.131</td>
<td>6.14</td>
<td>0.002</td>
</tr>
<tr>
<td>$H = 2.782f + 1.445A + 37.559$</td>
<td>0.95</td>
<td>3.094</td>
<td>6.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$H = 2.445 + 1.574A + 21.213$</td>
<td>0.97</td>
<td>2.526</td>
<td>6.39</td>
<td>0.35b</td>
</tr>
</tbody>
</table>

*Difference between the Asian and overall group. *Not significant. RMSE, root mean square of the error; H, height; A, arm span; f, age; U, ulna length; F, forearm length; T, tibia length; L, lower leg length.

available from Holtain Ltd (Crosswell, UK) and can be used as an alternative to a Harpenden anthropometer. Measurements were performed on only one side of the body, because symmetry has previously been demonstrated (Miller and Koreska 1992, Cheng et al. 1998). In those with hemiplegia, the ulna of the non-affected side should be measured.

Snyder et al. (1977) have obtained anthropometric measurements of a large group of children without disability in the United States. These normative data have been used to develop prediction equations for height from measurements of the upper arm, forearm, ulna, lower leg, and arm span (Spender et al. 1989, Miller and Koreska 1992). Miller and Koreska (1992) evaluated the prediction equations for height from forearm, ulna, and arm span in three groups: children without wrist contractures, children with idiopathic scoliosis, and children with Duchenne muscular dystrophy. In those with scoliosis, height was estimated by radiographic spine reconstruction. In children without wrist contractures, and those who have idiopathic scoliosis or Duchenne muscular dystrophy without wrist contractures, estimation of height from forearm or ulna measurements have correlation coefficients of 0.96 and 0.91, respectively (Miller and Koreska 1992). In children with Duchenne muscular dystrophy and wrist contractures, forearm measurements could not be obtained and arm span did not correlate well with height (r=0.475). Ulna length remained a good predictor of height (r=0.91). The current study has developed different prediction equations that include age, in addition to the anthropometric measurement, leading to greater precision than in the prediction equations developed by Snyder et al. (1977).

Spender et al. (1989) evaluated the prediction equations for height from upper arm and lower leg lengths developed from the data of Snyder et al. (1977). Growth in CP was assessed. In the 47 children with spastic quadriplegia, height or recumbent length could be measured in only 17 children, upper arm length in only 4 children, and lower leg length in only 40. Both upper arm (males r=0.77, females r=0.86) and lower leg (males r=0.67, females r=0.86) were found to be good predictors of height in the 6- to 19-year age group, suggesting that long bone growth remains proportional to height in children with spastic quadriplegia (Spender et al. 1989).

Prediction equations for height from knee height have been developed from normative data. These prediction equations have been used to compare the patient's recumbent length to knee height and, hence, predicted stature in children with CP which affects the lower limb. Johnson and Ferrara (1991) found that the prediction was not accurate in males aged 12 to 18 years with lower limb CP (R<sup>2</sup>=0.54) but was accurate in females (R<sup>2</sup>=0.95). Hogan (1999) was unable to obtain the knee height measurement in 34 of 56 children because of the severity of the lower limb involvement with CP. In those for whom measurement was obtained, knee height was a reliable predictor of recumbent length (R<sup>2</sup>=0.78). In the current study, both the ulna and lower leg height measurement were impeded by equinovarus deformities of the ankle. Ulna length measurement is not impeded by joint deformity, and its accuracy should not be impaired.

An accurate predictor of height, such as ulna length, could be used to aid in monitoring of growth and nutrition. Body surface area can be estimated from height and weight, and can be used to calculate medication doses, renal function, cardiac output, and oxygen consumption (Wang et al. 1992, Bailey and Briars 1996). Predicted values of pulmonary function tests rely on accurate height measurement and, therefore, using ulna length to predict height could facilitate this (Zapletal et al. 1969, Knudsen et al. 1985, Quanjer et al. 1989).

Conclusion
Measurement of ulna length with a Harpenden anthropometer is accurate and reproducible, and provides a precise predictor of height in children without disability. The ulna is accessible in those with severe disabilities, and its landmarks are readily identified in those with muscle weakness and joint deformities. Ulna growth charts allow easy comparison with the normal population. Children from Asia are anthropometrically distinct, but prediction of height from ulna length is not altered in this subgroup. Using ulna length to predict height in children with CP, neuromuscular weakness, spinal deformities, or other disabilities should facilitate the assessment of growth, the calculation of body surface area, and the prediction of normal values of pulmonary function tests.

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References

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SSBP 8th International Symposium
Gran Via Hotel, Barcelona, Spain 11th & 12th November 2004

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Professor Jean-Pierre Fryns, Belgium: "The Fragile X syndrome and X-linked mental retardation: 25 years later"
Professor Paul Hagerman, USA: "Fragile X: Molecular insights into clinical involvement"
Dr Isabel Tejada, Spain: "Genetic cause of mental retardation: the state of the Art"
Professor Anita Thapar, UK: "Advances in the genetics of Attention Deficit Hyperactivity Disorder"
Dr Jeremy Turk, UK: "Fragile X syndrome: a longitudinal developmental perspective"

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