

## The Value of Multiple Tests of Respiratory Muscle Strength

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## ABSTRACT

**Background:** Respiratory muscle weakness is an important clinical problem. Tests of varying complexity and invasiveness are available to assess respiratory muscle strength. The relative precision of different tests in the detection of weakness is less clear, as is the value of multiple tests.

**Methods & Patients:** We analysed the respiratory muscle function tests of clinical referrals who had multiple tests assessed in our laboratories over a 6 year period. Thresholds for weakness for each test were determined from published and in-house laboratory data. The patients were divided into three groups; those who had all relevant measurements of global inspiratory muscle strength (group A, n=182), those with full assessment of diaphragm strength (group B, n=264), and those for whom expiratory muscle strength was fully evaluated (group C, n=60). We studied the diagnostic outcome of each inspiratory, diaphragm and expiratory muscle test, both singly and in combination, and calculated the impact of using more than one test to detect weakness.

**Results:** The clinical referrals were primarily for the evaluation of neuromuscular diseases and dyspnoea of unknown cause. A low maximal inspiratory mouth pressure (P<sub>I</sub>max) was recorded in 40.1% of referrals in group A, while a low sniff nasal pressure (Sniff P<sub>nasal</sub>) was recorded in 41.8% and a low sniff oesophageal pressure (Sniff P<sub>oes</sub>) in 37.9%. When assessing inspiratory strength with the combination of all three tests 29.6% of patients had weakness. Using the two non-invasive tests, P<sub>I</sub>max and Sniff P<sub>nasal</sub>, in combination we obtained a similar result (low in 32.4%).

Combining Sniff P<sub>di</sub> (low in 68.2%) and Twitch P<sub>di</sub> (low in 67.4%) reduced the diagnoses of patients with diaphragm weakness to 55.3% in group B.

38.3% of the patients in group C had expiratory muscle weakness as measured by P<sub>E</sub>max, compared to 36.7% when weakness was diagnosed by cough P<sub>gas</sub>, and 28.3% when assessed by Twitch T<sub>10</sub>. Combining all three expiratory muscle tests reduced the number of patients diagnosed as having expiratory muscle weakness to 16.7%.

**Conclusion:** The use of single tests, such as P<sub>I</sub>max, P<sub>E</sub>max and other available individual tests of inspiratory, diaphragm and expiratory muscle strength, tend to overdiagnose weakness. Combinations of tests increase diagnostic precision, and in the population studied they reduced the diagnosis of inspiratory, specific diaphragm, and expiratory muscle weakness by 19 – 56%. Measuring both P<sub>I</sub>max and Sniff P<sub>nasal</sub> resulted in a relative reduction of 19.2% of patients falsely diagnosed with inspiratory muscle weakness. The addition of Twitch P<sub>di</sub> to Sniff P<sub>di</sub> increased diagnostic precision by a smaller amount, 18.9%. Having multiple tests of respiratory muscle function available both increases diagnostic precision, and makes assessment possible in a range of clinical circumstances.

## INTRODUCTION

Measurement of respiratory muscle strength is clinically useful in the assessment of selected patients, most commonly those with neuromuscular diseases or unexplained breathlessness.[1, 2]

Maximum inspiratory (P<sub>I</sub>max) and expiratory (P<sub>E</sub>max) pressures are most frequently measured. P<sub>I</sub>max and P<sub>E</sub>max are simple and quick tests and high values exclude clinically significant weakness. However, low values are common and may reflect poor technique or effort, rather than muscle weakness.[3]

Additional tests are available which are likely to improve diagnostic precision but are more complex and invasive.[4-8] We have reviewed our test results, in patients referred for assessment of respiratory muscle strength, to determine the value of multiple respiratory muscle tests. We hypothesized that multiple tests might reduce the number of patients erroneously diagnosed as having weakness.

## PATIENTS AND METHODS

Test results of clinical referrals made to the respiratory muscle laboratories of King's College and Brompton Hospitals between 2000-2006 were analysed. Tests were undertaken according to established methods, as described in the ATS/ERS joint statement.[3] The tests were:

### 1) P<sub>I</sub>max

Maximum inspiratory pressures were measured from functional residual capacity in the standard way,[3, 9] with the patient seated, wearing a nose-clip and using a flanged mouthpiece (P.K. Morgan Ltd<sup>®</sup>, Rainham, UK). Repeated efforts were made, until consistent results were achieved, and the numerically largest pressure noted. The average of the pressure was measured over one second.[3]

Several publications report normal values using a flanged mouthpiece.[9-12] Weakness was defined as the mean normal value minus 1.96 standard deviations based on the study by Wilson et al (Table 1).[9] This number reflects the 100%-line in the figures in the results section.

Test	Sex	Calculation	Cutoff [cmH <sub>2</sub> O]	Rounded [cmH <sub>2</sub> O]
<b>P<sub>I</sub>max</b>	Cutoff <sub>male</sub>	10.4 kPa - 1.96 * 3.0 kPa	44.8	45
	Cutoff <sub>female</sub>	7.2 kPa - 1.96 * 2.1 kPa	31.6	30
<b>Sniff Poes</b>	Cutoff <sub>male</sub>	105 cmH <sub>2</sub> O - 1.96 * 26 cmH <sub>2</sub> O	54.0	55
	Cutoff <sub>female</sub>	92 cmH <sub>2</sub> O - 1.96 * 22 cmH <sub>2</sub> O	48.9	50
<b>Sniff Pnasal</b>	Cutoff <sub>male</sub>	0.91 * 55 cmH <sub>2</sub> O	50.1	50
	Cutoff <sub>female</sub>	0.91 * 50 cmH <sub>2</sub> O	45.5	45
<b>Sniff Pdi</b>	Cutoff <sub>male</sub>	148 cmH <sub>2</sub> O - 1.96 * 24 cmH <sub>2</sub> O	101.0	100
	Cutoff <sub>female</sub>	121 cmH <sub>2</sub> O - 1.96 * 25 cmH <sub>2</sub> O	72.0	70
<b>Twitch Pdi</b>	Cutoff <sub>male</sub> +	28 cmH <sub>2</sub> O - 1.96 * 5 cmH <sub>2</sub> O	18.2	18
	Cutoff <sub>female</sub>			
<b>PEmax</b>	Cutoff <sub>male</sub>	14.4 kPa - 1.96 * 3.3 kPa	80.5	80
	Cutoff <sub>female</sub>	9.1 kPa - 1.96 * 1.6 kPa	61.1	60
<b>Cough Pgas</b>	Cutoff <sub>male</sub>	214.4 cmH <sub>2</sub> O - 1.96 * 42.2 cmH <sub>2</sub> O	131.7	130
	Cutoff <sub>female</sub>	165.1 cmH <sub>2</sub> O - 1.96 * 34.8 cmH <sub>2</sub> O	96.9	95
<b>Twitch T10</b>	Cutoff <sub>male</sub> +	x = 1.6 - 1.96 * 0.20	16.1	16
	Cutoff <sub>female</sub>	re-transformation: y = 10 <sup>x</sup>		

**Table 1:** Cutoffs for the diagnosis of weakness for each respiratory muscle test.**2) Sniff manoeuvres**

Balloon catheters for the measurement of pressure (Cooper Surgical<sup>®</sup>, CT/USA) lubricated with lignocaine (2%) gel, were introduced via one nostril into the oesophagus and stomach as described by Baydur et al.[13] The distal balloon (filled with 2ml of air) measured the gastric pressure (Pgas); the proximal balloon (filled with 0.5ml of air) the oesophageal pressure (Poes). Transdiaphragmatic pressure (Pdi) was derived by calculating the difference between Poes and Pgas. Differential pressure transducers were connected to amplifiers (Validyne<sup>®</sup>, Northridge, CA, USA) that transmitted the signal to a computer (Apple iMac<sup>®</sup> Computers, Cupertino, CA, USA). LabVIEW4.1<sup>®</sup> was used for recording and analysis of data (National Instruments<sup>®</sup>, Austin, TX, USA). Later referrals were analysed using 16-Channel Powerlab<sup>®</sup> with CHART V<sup>®</sup> software (ADInstruments<sup>®</sup>, Colorado Springs, CO, USA).

**2a) Sniff oesophageal pressure (Sniff Poes)**

Sniff manoeuvres were performed with the patient seated and the balloon catheters in place as described above.[3] At least 5-10 maximal sniffs were measured; the largest numerical pressure was noted. Data of Laroche et al were used to calculate the normal cutoff values (Table 1).[5]

**2b) Sniff nasal pressure (Sniff Pnasal)**

A plug, used to obstruct one nostril, incorporated the distal 2-3cm of a 30 cm polyethylene catheter with a 2 mm internal diameter (Intersurgical Scientific Instruments<sup>®</sup>, Oxford, UK). The proximal end of the catheter was attached to a pressure transducer (Validyne<sup>®</sup>, Northridge, CA, USA). At least 5-10 maximal sniffs were performed until a consistent value of sniff pressure was reached; the highest numerical pressure was taken. Heritier et al (1994) described a close relationship between Sniff Pnasal and Sniff Poes ( $r=0.99$ ) in normal subjects without nasal obstruction.[4] The ratio of Sniff Pnasal to Sniff Poes was 0.91. Lower limit of normal cutoffs were derived using the values from the Sniff Poes test<sup>5</sup> multiplied by the 0.91, the ratio of Sniff Pnasal / Sniff Poes (Table 1).[4]

**2c) Sniff transdiaphragmatic pressure (Sniff Pdi)**

Pressure catheters were placed and maximal sniff manoeuvres performed as described above. The highest numerical pressure of 5-10 consistent sniffs was taken. Normal cutoffs refer to the data of Miller et al who described normal values for the sniff Pdi test (Table 1).[8]

**3) Twitch transdiaphragmatic pressure (Twitch Pdi)**

Twitch transdiaphragmatic pressure was measured following magnetic stimulation of the phrenic nerves, via a bilateral anterolateral approach at functional residual capacity.[6, 14, 15] The patient was seated, wore a nose-clip, and the mouth was closed. For magnetic stimulation a Magstim 200<sup>®</sup> (Magstim Company Ltd.<sup>®</sup>, Whitland, UK) with a 43-mm double coil (P/N9784-00; Magstim Company Ltd.<sup>®</sup>, Whitland, UK) was used. After achieving a supramaximal stimulus, at least five consistent twitches were recorded and the average Twitch Pdi calculated.

Luo et al investigated twitch Pdi in normal subjects and found it to be 28 (5) cmH<sub>2</sub>O (Table 1).[6] No distinction was made for normal values between the sexes because the available literature on gender differences is insufficient.

**4) PEmax**

Maximum expiratory pressures were measured from total lung capacity in the standard way, with the patient seated, wearing a nose-clip and using a flanged mouthpiece (P.K.

Morgan Ltd<sup>®</sup>, Rainham, UK).[3, 9] Repeated efforts were made, until consistent results were achieved; the numerically largest pressure averaged over one second was measured.[3] Several studies have reported normal values, using a flanged mouthpiece.[9-12] Normal value cutoffs refer to the study of Wilson et al (Table 1).[9]

### 5) Cough gastric pressure (Cough Pgas)

Pressure balloons were positioned as described in section 2. The cough manoeuvre was performed as previously reported, breathing in deeply first, with the patient seated, wearing a nose-clip.[3] Coughs were repeated at least 5-10 times, until consistent measurements were achieved. The numerically highest value was taken, measuring from relaxed end-expiratory baseline gastric pressure to peak pressure during the cough. Man et al described cough gastric pressures in 99 healthy volunteers, enabling normal cutoffs to be calculated (Table 1).[7]

### 6) Twitch T10 gastric pressure (Twitch T10)

Gastric pressure was measured as described in section 2 and magnetic stimulation of the thoracic nerve roots was performed with a 90mm circular coil (P/N9784-00; MAGSTIM Company Ltd.<sup>®</sup>, Whitland, UK) placed with its centre over the 10<sup>th</sup> thoracic vertebra in the mid-line.[16] The manoeuvre was undertaken at functional residual capacity, with the patient seated, wearing a nose-clip, and the mouth closed. Twitches were repeated at least 5-10 times, until consistent measurements were obtained, and an average Twitch T10 was calculated. There are few normal data reported for this test. Our laboratory data is from 65 normal subjects (41 males, 24 females, mean age 51 (16) years, BMI 25.6 (3.6) kg/m<sup>2</sup>). The results are not normal-distributed; being positively skewed. The median was 39.4 cmH<sub>2</sub>O (interquartile range 26.6 cmH<sub>2</sub>O). The cutoff for weakness was calculated after transformation of the data into a log-normal distribution (mean 1.6 (0.20)). The mean minus 1.96 standard deviations was calculated and the parameter retransformed ( $y=10^x$ ) to give the cutoff in Table 1. As for Twitch Pdi, no distinction was made between sexes due to the relatively limited data.

The outcome of the respiratory muscle tests, in diagnosing weakness was studied, singly and in combination. Cross-tabulation identified the diagnosis of weakness for each test, and the added value of using more than one test in detecting respiratory muscle weakness was determined.

For the purposes of analysis, patients` data were used for comparison only if all of the global inspiratory, specific diaphragm, or expiratory muscle tests were performed. For inspiratory muscle tests (PImax, Sniff Pnasal and Sniff Poes) this was 182 of the referrals (Group A), for diaphragm specific tests (Sniff Pdi and Twitch Pdi) 264 (Group B), and for expiratory muscle tests (PEmax, Cough Pgas and Twitch T10) 60 (Group C). Individual test results were judged relative to the diagnosis achieved by combining all relevant tests.

For statistical analysis and graph-plots, we used SPSS<sup>®</sup> Version 13.0 (SPSS<sup>®</sup> Inc., Chicago, IL, USA). Results are given as mean (standard deviation, SD) for all tests except Twitch T10 values, for which results are given as median and interquartile range because of non-normal distribution of the data. Correlation coefficients were calculated for all tests (Pearson`s correlation coefficient), except Twitch T10, for which Spearman`s correlation coefficient was used.

Values for single tests were converted into percentage of cutoff-threshold for males and females as described above. Weakness was defined as a result of <100% of the cutoff

threshold, while normal strength was considered as being  $\geq 100\%$  of this value. To describe and compare the test combinations we calculated the mean of the different populations, the standard error of the mean (SEM), and the 95% confidence interval (CI). Significance was accepted at the level of 95%.

## RESULTS

The most common reason for referral was to investigate neuromuscular diseases and the cause of breathlessness (Tables 2 and 3). For the 3 groups data on age, sex, and lung function are shown in Table 4; results of respiratory muscle tests are shown in Table 5.

Neuromuscular disease	156
Dyspnoea of unknown origin	94
Chronic obstructive pulmonary diseases (COPD)	45
Rheumatological disease	37
Chest wall disease (acquired and congenital)	22
Other restrictive lung diseases	15
Obesity hypoventilation	14
Malignancy	7
Others	23

**Table 2:** Diagnoses of all patients

Groups	FEV1 (%pred)	VC (%pred)	FEV1/FVC (%)
<b>Neuromuscular disease</b>	67.4 (19.0)	65.5 (21.1)	74.4 (13.3)
<b>Dyspnoea of unknown cause</b>	79.2 (18.6)	80.1 (27.3)	78.4 (9.7)
<b>COPD</b>	50.9 (19.7)	65.7 (21.8)	58.8 (15.7)
<b>Rheumatological disease</b>	62.4 (20.5)	65.5 (22.0)	78.5 (12.9)
<b>Chest Wall disease</b>	59.8 (20.5)	59.8 (20.2)	78.8 (9.3)
<b>Other restrictive lung diseases</b>	51.3 (21.4)	54.0 (25.2)	76.6 (8.1)
<b>Obesity hypoventilation</b>	52.3 (18.3)	55.7 (13.1)	78.2 (8.4)

**Table 3:** Baseline spirometry of main diagnostic groups.

	Group A (n=182)	Group B (n=264)	Group C (n=60)
sex [m/f]	109/73	160/104	44/16
Age [years]	52.6 (14.9) (18-84)	52.3 (14.5) (18-85)	51.3 (12.3) (24-73)
FEV1 [%pred]	59.4 (23.5) (16-115)	61.8 (23.5) (16-118)	62.4 (25.2) (21-115)
FEV1/FVC [%]	73.1 (13.1) (33-98)	73.4 (12.8) (33-98)	72.9 (15.4) (21-95)
VC [%pred]	66.1 (23.5) (16-118)	68.0 (23.4) (16-143)	68.9 (23.1) (23-118)
$\Delta$ VC [%] (n=101)	22.1 (16.5) (0-71)	20.1 (14.2) (0-71)	23.8 (14.9) (0-71)

**Table 4:** Descriptive statistics of the patient subgroups (values in mean (SD), minimum – maximum in brackets). The letters A, B, and C refer to the separation into subgroups as shown in table 5 and the methods section. m=male, f=female, FEV1%pred = Forced expiratory volume in one second as percentage of predicted value, VC%pred = Vital capacity as percentage of predicted value, ΔVC = fall of vital capacity when changing position from sitting to supine.

	Group A (n=182)	Group B (n=264)	Group C (n=60)
PImax †	50.5 (27.8; 4-139)		
PImax *	131.0 (72.1; 9-378)		
Sniff P <sub>nasal</sub> †	57.8 (27.4; 8-143)		
Sniff P <sub>nasal</sub> *	120.7 (57.4; 16-286)		
Sniff Poes †	65.1 (27.2; 6-152)		
Sniff Poes *	123.0 (51.2; 11-276)		
Sniff Pdi †		69.6 (35.8; 0-170)	
Sniff Pdi *		81.8 (46.2; 0-243)	
Twitch Pdi †		14.5 (10.3; 0-56)	
Twitch Pdi *		80.7 (57.2; 0-309)	
PEmax †			86.0 (34.8; 19-165)
PEmax *			114.7 (44.9; 32-274)
Cough Pgas †			154.7 (80.8; 12-320)
Cough Pgas *			127.6 (65.4; 13-240)
Twitch T10 †			27.7 (31.8; 0-116)
Twitch T10 *			172.8 (198.9; 0-724)

**Table 5:** Respiratory muscle test results for each group shown as mean (SD; minimum – maximum) for all tests except for Twitch T10 which is reported as median (interquartile range; minimum-maximum).

† = [cmH<sub>2</sub>O]

\* = [% of cutoff]

### Global Inspiratory Muscle Tests (Group A)

182 patients completed all inspiratory muscle tests (PImax, Sniff P<sub>nasal</sub>, and Sniff Poes (Figures 1). PImax was low in 40.1%, Sniff P<sub>nasal</sub> in 41.8%, and Sniff Poes in 37.9%. Correlation between PImax and Sniff P<sub>nasal</sub> was  $r=0.74$  ( $p<0.01$ ; Figure 1), between PImax and Sniff Poes was  $r=0.73$  ( $p<0.01$ ; Figure 1), and Sniff P<sub>nasal</sub> vs Sniff Poes was  $r=0.90$  ( $p<0.01$ ; Figure 1). The cross-tabulation (Table 6) shows the numbers of the patients having low or normal results in all of the tests. Combining the results for the three tests of global inspiratory muscle strength demonstrated a diagnosis of weakness in 29.1% (Table 7). This is a relative reduction of 27.4% compared to PImax alone. Using two non-invasive tests, PImax and Sniff P<sub>nasal</sub>, in combination obtained a similar result (low in 32.4%).

**Cross-tabulation for Group A: Inspiratory Muscle Tests**

		<b>Sniff Pnasal</b>		<b>total</b>
		normal	low	
<b>PImax</b>	Normal	92	17	109
	Low	14	59	73
<b>total</b>		106	76	182
		<b>Sniff Poes</b>		<b>total</b>
		normal	low	
<b>PImax</b>	Normal	94	15	109
	Low	19	54	73
<b>total</b>		113	69	182
		<b>Sniff Poes</b>		<b>total</b>
		normal	low	
<b>Sniff Pnasal</b>	Normal	101	5	106
	Low	12	64	76
<b>total</b>		113	69	182

**Cross-tabulation for Group B: Diaphragm Tests**

		<b>Twitch Pdi</b>		<b>total</b>
		normal	low	
<b>Sniff Pdi</b>	Normal	52	32	84
	Low	34	146	180
<b>total</b>		86	178	264

**Cross-tabulation for Group C: Expiratory Muscle Tests**

		<b>PEmax</b>		<b>total</b>
		normal	low	
<b>Cough Pgas</b>	Normal	31	7	38
	Low	6	16	22
<b>total</b>		37	23	60
		<b>Twitch T10</b>		<b>total</b>
		normal	low	
<b>PEmax</b>	Normal	30	7	37
	Low	13	10	23
<b>total</b>		43	17	60
		<b>Twitch T10</b>		<b>total</b>
		normal	low	
<b>Cough Pgas</b>	Normal	36	2	38
	Low	7	15	22
<b>total</b>		43	17	60

**Table 6:** Cross-tabulation of each test measuring global inspiratory, diaphragm and expiratory strength. The letters refer to the groups defined in the methods section.

Inspiratory Muscle Weakness			
	diagnosed as weak	SEM	95% CI
1) P <sub>lmax</sub>	40.1% (73/182)	3.64	32.9-47.3
2) Sniff P <sub>nasal</sub>	41.8% (76/182)	3.67	34.5-41.8
3) Sniff P <sub>oes</sub>	37.9% (69/182)	3.61	30.8-45.0
4) P <sub>lmax</sub> + Sniff P <sub>nasal</sub>	32.4% (59/182)	3.48	25.6-39.3
5) P <sub>lmax</sub> + Sniff P <sub>oes</sub>	29.7% (54/182)	3.40	23.0-36.4
6) P <sub>lmax</sub> + Sniff P <sub>nasal</sub> + Sniff P <sub>oes</sub>	29.1% (53/182)	3.38	22.5-35.8

**Table 7:** SEM = Standard Error of the Mean, CI = Confidence Interval. Combination of P<sub>lmax</sub>, Sniff P<sub>nasal</sub>, and Sniff P<sub>oes</sub> results reduces diagnosis of global inspiratory weakness to 29.1%. This is a relative reduction of 27.4% compared to P<sub>lmax</sub> alone, 30.4% reduction compared to Sniff P<sub>nasal</sub> alone, and 23.2% reduction compared to Sniff P<sub>oes</sub> alone. A combination of two tests (4 and 5) reduces the rate to 32.4% and 29.7%, respectively. There was no significant difference between the single tests. Performing all three tests achieved the highest precision.

### Diaphragm Strength Tests (Group B)

For tests of diaphragm function the 264 clinical referrals who had both Sniff P<sub>di</sub> and Twitch P<sub>di</sub> measurements were analysed (Table 5). 68.2% had weakness when assessed by Sniff P<sub>di</sub>, and 67.4% when Twitch P<sub>di</sub> was measured. Correlation between Sniff P<sub>di</sub> and Twitch P<sub>di</sub> was  $r=0.57$  ( $p<0.01$ ; Figure 2). Combining both tests reduced the number of patients considered to have diaphragm weakness to 55.3% (Tables 6 and 8), a relative reduction of 18.9% compared to Sniff P<sub>di</sub> alone.

Diaphragm Weakness			
	diagnosed as weak	SEM	95% CI
1) Sniff P <sub>di</sub>	68.2% (180/264)	2.87	62.5-73.8
2) Twitch P <sub>di</sub>	67.4% (178/264)	2.89	61.7-73.1
3) Sniff P <sub>di</sub> + Twitch P <sub>di</sub>	55.3% (146/264)	3.07	49.3-61.3

**Table 8:** SEM = Standard Error of the Mean, CI = Confidence Interval. The combination of Sniff P<sub>di</sub> and Twitch P<sub>di</sub> diagnosed 55.3% of patients as having diaphragm weakness. The two tests combined reduced the diagnosis of diaphragm weakness by 18.9% compared to Sniff P<sub>di</sub> alone, and 18.0% compared to Twitch P<sub>di</sub> alone, respectively .

### Expiratory Muscle Tests (Group C)

For expiratory muscle strength tests, data of 60 patients who completed measurement of cough Pgas, Twitch T10 as well as PEmax were analysed. 38.3% of the patients had expiratory muscle weakness when assessed by PEmax. When assessed by cough Pgas 36.7% of the patients had low values, and with Twitch T10, 28.3% of the patients were considered to be weak. The correlation between PEmax and cough Pgas was  $r=0.61$  ( $p<0.01$ ; Figure 3), between PEmax and Twitch T10  $r=0.28$  ( $p=0.03$ ; Figure 3), and between cough Pgas and Twitch T10  $r=0.63$  ( $p<0.01$ ; Figure 3). The combination of all three tests of expiratory muscle strength yielded a diagnosis of weakness in 16.7% (Table 6 and 9), a relative reduction of 56.4% compared to PEmax alone.

Expiratory Muscle Weakness			
	diagnosed as weak	SEM	95% CI
1) PEmax	38.3% (23/60)	6.33	25.7-51.0
2) Cough Pgas	36.7% (22/60)	6.27	24.1-49.2
3) Twitch T10	28.3% (17/60)	5.87	16.6-40.1
4) PEmax + Cough Pgas	26.7% (16/60)	5.76	15.1-38.2
5) PEmax + Cough Pgas + Twitch T10	16.7% (10/60)	4.85	8.0-26.4

**Table 9:** SEM = Standard Error of the Mean, CI = Confidence Interval. The combination of PEmax, cough Pgas and Twitch T10 diagnosed 16.7% of the patients to have expiratory muscle weakness, and reduced the number of falsely positive diagnoses compared to PEmax and Cough Pgas. The relative reduction of false diagnosis was 56.4% compared to PEmax, and 54.5% compared to cough Pgas.

### DISCUSSION

PImax and PEmax are widely used, easily applied and non-invasive bedside tests. In our study PImax and PEmax diagnosed weakness in 40.1% and 38.2% respectively. However, the tests require maximal effort, coordination and cooperation and low values are common and difficult to interpret with confidence.[3, 4] Sniff Pnasal achieves similar results as PImax and Sniff Poes, whilst more precise, is invasive. Sniff Poes, compared to Sniff Pnasal, reduces the diagnosis of weakness by about 10%. The combination of the two non-invasive tests, PImax and Sniff Pnasal, reduces the diagnosis of weakness by about 20% compared to Sniff Pnasal or PImax alone. It is of interest that by performing all three tests the increase in diagnostic precision is around 30% compared to PImax or Sniff Pnasal alone, but they are not significantly better than the combination of PImax and Sniff Pnasal. Thus, for patients who are able to sniff, and in whom there is likely to be good transmission of intrathoracic pressures (there being no nasal obstruction or airways obstruction) the combination of the non-invasive tests PImax and Sniff Pnasal is almost as precise as when the invasive Sniff Poes test is added to the assessment.

In this study cough Pgas and PEmax resulted in similar diagnostic outcomes, but the combination of these two volitional tests reduced the diagnosis of expiratory muscle weakness

by around 30% compared to PEmax. The combination of all three expiratory tests reduced the diagnosis of weakness by approximately 55% and was the only combination that reached statistical significance in comparison to the single tests PEmax and cough Pgas.

For the diaphragm specific tests, 68.2% of the referrals were weak when assessed by Sniff Pdi and 67.4% by Twitch Pdi. Tests of diaphragm function are complex and relatively invasive. For patients able to perform maximum sniff efforts the Sniff Pdi test is as precise as Twitch Pdi, and less costly. However, there will be clinical situations in which Twitch Pdi is more appropriate, as when assessing patients in ICU, and the Twitch technique also allows the separate evaluation of each hemidiaphragm. Furthermore, the combination of Sniff Pdi and Twitch Pdi is more precise than either test alone, reducing the relative risk of a false diagnosis of weakness by almost 20%.

The validity of cut-off values is important. Tests of respiratory muscle strength can either show normal or low results. A low test result means that the patient is weak as judged by this single test. The different cut-off points for each test were taken from the appropriate literature. We compared the published data most appropriate to the methods used at King's College Hospital and Royal Brompton Hospital. The cut-off for a normally distributed population was taken for all tests (except the non-normally distributed Twitch T10) by subtracting 1.96xStandard Deviation from the mean for a normal population. This definition is widely accepted for creating cut-offs and defining "abnormality". We adopted a similar approach for all tests, except Twitch T10 for which the only data are our own laboratory values. The number of normal subjects, for each test, reported in the literature is substantial, and reproducibility well described, although we acknowledge that future studies of Twitch T10, to supplement our own results from 65 normal subjects, will be useful.

A limitation of the study is a lack of sufficient normal data on the nonvolitional tests that were used to assess diaphragm strength (Twitch Pdi) and expiratory muscle strength (Twitch T10), which does not allow a distinction between reference values for different sexes. More data, from future studies, are needed for Twitch Pdi and Twitch T10 to establish normal values for males and females. Inevitably, combining male and female data must reduce the sensitivity of the tests for diagnosing weakness. The relative paucity of Twitch T10 data reduces but does not negate the considerable value of Twitch T10 as an expiratory muscle test.

Combining Twitch T10 results with other, voluntary, tests is helpful in so much as some patients are less good at voluntary tests, but will reduce sensitivity in so much as the Twitch T10 test has inherent variability, including that due to gender. Despite the fact that lack of gender specific data for Twitch T10 must reduce the sensitivity of the test it is of note that the test diagnoses weakness in a slightly higher percentage of cases than the PEmax + Cough Pgas combination.

In summary, the outcome of any one test of inspiratory, specific diaphragm, or expiratory muscle strength is broadly similar to any other test. However, combination of tests can substantially increase diagnostic precision.

In many patients it is the assessment of inspiratory muscle strength that is most clinically relevant and the good diagnostic performance of the non-invasive PImax – Sniff Pnasal combination is important.

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#### LEGENDS

**Figure 1a:** Correlation P<sub>I</sub>max vs Sniff P<sub>nasal</sub>; vertical and horizontal bars are added at the cutoff for normal values (=100%) as a marker for normal inspiratory muscle strength (thresholds as described in the method section).

**Figure 1b:** Correlation PImax vs Sniff Poes; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal inspiratory muscle strength (thresholds as described in the method section).

**Figure 1c:** Correlation Sniff Pnasal vs Sniff Poes; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal inspiratory muscle strength (thresholds as described in the method section).

**Figure 2:** Correlation Sniff Pdi vs Twitch Pdi; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal diaphragm muscle strength (thresholds as described in the method section).

**Figure 3a:** Correlation PEmax vs Cough Pgas; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal expiratory muscle strength (thresholds as described in the method section).

**Figure 3b:** Correlation PEmax vs Twitch T10; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal expiratory muscle strength (thresholds as described in the method section).

**Figure 3c:** Correlation cough Pgas vs Twitch T10; vertical and horizontal bars are added at the lower threshold of normal (referred in the tests as 100% normal) as a marker for normal expiratory muscle strength (thresholds as described in the method section).

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Figure 1

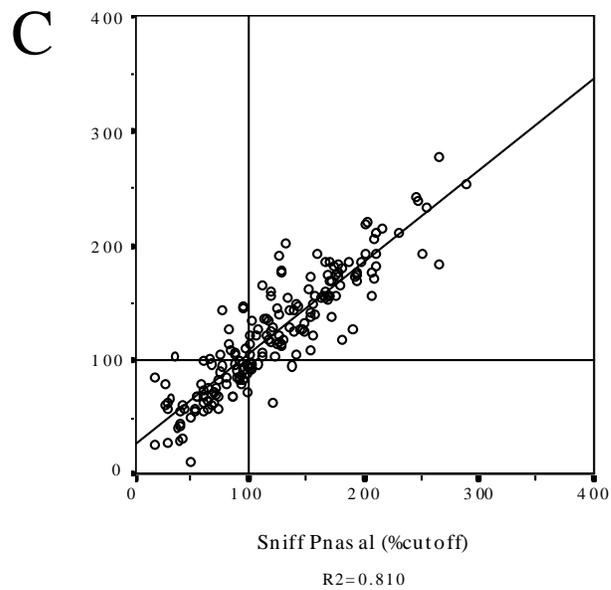
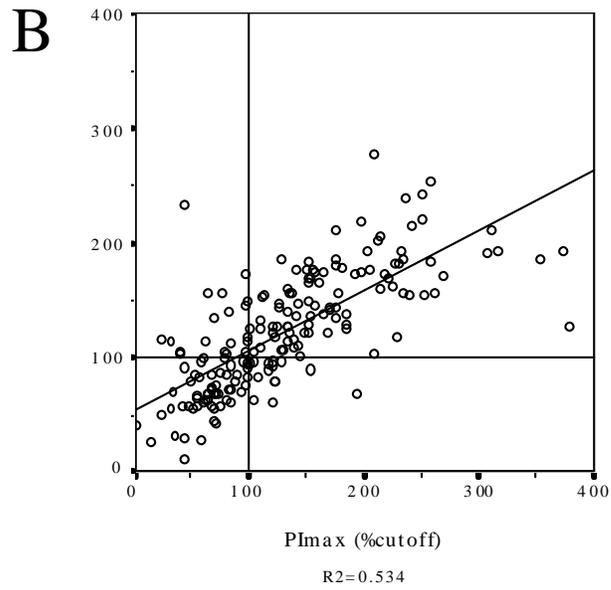
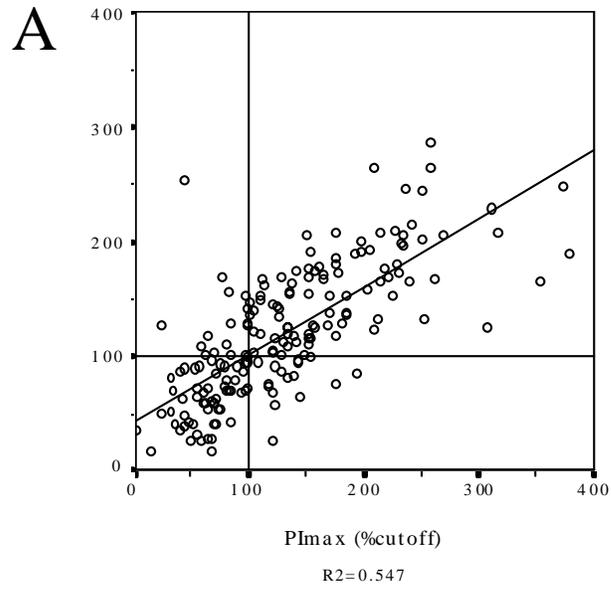


Figure 2

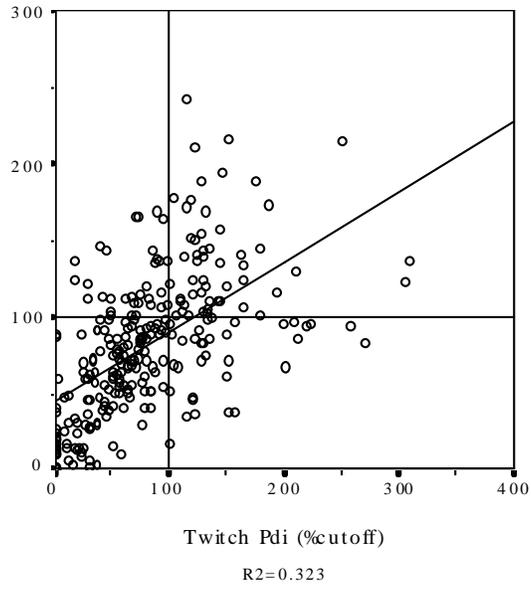


Figure 3

