Accuracy of portable devices in measuring peak cough flow

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Title (57 characters with spaces):

Accuracy of Portable Devices in Measuring Peak Cough Flow

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Short title/running head (57 characters with spaces)

Accuracy of Portable Devices in Measuring Peak Cough Flow

Abstract (196 words):

Peak cough flow (PCF) measurements can be used as indicators of cough effectiveness. Portable peak flow meters and spirometers have been used to measure PCF, but little is known about their accuracy compared to laboratory based pneumotachograph systems. We compared the accuracy of four portable devices (Mini-Wright and Assess peak flow meters, SpiroUSB and Microlab spirometers) in measuring PCF with a calibrated laboratory based pneumotachograph system. Twenty healthy volunteers (mean (SD) age 45 (16)) coughed through a pneumotachograph connected in series with each portable device in turn, and the difference in PCF readings was analysed. In addition, mechanically generated flow waves of constant peak flow were delivered through each device both independently and when connected in series with the pneumotachograph. Agreement between PCF readings obtained with the pneumotachograph and the portable devices was poor. Peak flow readings were lower when measured using the portable devices, for both volitional coughs and mechanically

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generated flow waves; 95% limits of agreement spanned approximately 150 L/min. Of the four portable devices examined none were sufficiently accurate for the measurement of PCF. Depending on the measurement method used, absolute values of PCF reported in the literature may not be directly comparable.

Key words: Peak cough flow; accuracy; peak flow meter; spirometer; pneumotachograph

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1. Introduction

Cough flow testing is useful as an outcome measure in research and a monitoring or diagnostic tool in clinical practice. Peak cough flow (PCF) is commonly used as an indicator of the strength or effectiveness of cough, particularly in clinical populations with neuromuscular impairment (Jones *et al* 2012). Cough can be accurately quantified using laboratory pneumotachograph based systems as described by Singh *et al* (1994), but these can often consist of several components, can be expensive, not easily transportable, and require significant knowledge by the user for correct operation. Practical devices, which can conveniently be applied in clinical settings, patients' homes or other community locations, may be of use to clinicians and researchers. In several clinical studies, standard peak flow meters and hand-held spirometers have been used to measure PCF (Table 1) (LoMauro *et al* 2014, Silverman *et al* 2010, Brito *et al* 2009, Fiore *et al* 2008, Daftary *et al* 2007, Sancho *et al* 2007, Bach *et al* 2006, Dohna-Schwake *et al* 2006, Kang *et al* 2006, Gauld and Boynton 2005, Sancho *et al* 2004, Suarez *et al* 2002, Bach *et al* 1997, Bach and Saporito 1996, Bach 1995, Leiner *et al* 1966, Wright and McKerrow 1959). These devices are designed to measure peak flow during a forced expiratory manoeuvre, and their accuracy in measuring peak flow during cough is uncertain.

In the present study we examined the accuracy of two commonly used peak flow meters and two hand-held spirometers when measuring PCF compared with a laboratory pneumotachograph based measurement system.

2. Materials and Methods

2.1. Study subjects

Healthy volunteers with no medical history of respiratory disease or conditions affecting the anatomy and function of the upper airway who were comfortable coughing repeatedly over a short period of time were recruited. The study had ethical approval from the Psychiatry, Nursing and Midwifery

Research Ethics Committee at King's College London, United Kingdom (study reference PNM/12/13-143). All participants gave written informed consent.

2.2. Study design

Four hand-held devices were compared to a laboratory pneumotachograph based flow measurement system: the Mini-Wright Standard peak flow meter (European Union (EU) Scale, range 60-800 L/min, accuracy $\pm 10\%$ or 10 L/min according to manufacturer, Clement Clarke International, Harlow, England); Assess peak flow meter (range 60-880 L/min, accuracy $\pm 10\%$ or 20 L/min according to manufacturer, Philips Respironics, Pittsburgh, Pennsylvania); SpiroUSB turbine spirometer, (range 12-900 L/min, accuracy $\pm 3\%$ according to manufacturer, CareFusion, San Diego, California); and the Microlab turbine spirometer, (range 12-900 L/min, accuracy $\pm 3\%$ according to manufacturer, CareFusion, San Diego, California). These four devices were selected as they are produced by leading manufacturers and frequently used in clinical practice.

The devices under test were attached individually to a Fleisch-type pneumotachograph (ID 4.4 cm, length 6.0 cm, PK Morgan Ltd, Rainham, England). Differential pressure was measured using a Validyne differential pressure transducer (MP45, range $\pm 2 \text{ cmH}_2\text{O}$, Validyne Engineering, Northridge, California) and the signal amplified (CD15, Validyne Engineering, Northridge, California) and acquired on a laptop running LabChart software (LabChart Pro, version 7.2.2, ADInstruments Ltd, Oxford, England) with analog-to-digital sampling of 2 kHz (PowerLab/16SP, ADInstruments Ltd, Oxford, England). The pneumotachograph system was linear in the flow range 0-700 L/min (R² = 0.999845) and had a frequency response of 50 Hz. A two-point calibration was performed at the beginning of each testing session, using a rotameter (InFlux OF1"S, 60-600 L/min flow, Techniquip Ltd, Taunton, England).

2.3. Methods

A bacterial filter (Spiroguard Standard, Air Safety Medical, Morecambe, England), the pneumotachograph and one portable device were connected in series. Participants were instructed to

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cough through the filter so that the peak flow of each cough was measured by the pneumotachograph system and the portable device. The portable devices were tested in a random order and were always connected downstream from the pneumotachograph. The calibration of the SpiroUSB and the Microlab turbine spirometers was verified with a 3 litre calibration syringe at the beginning of each testing session as per manufacturer's recommendation. For each device, volunteers were instructed to produce five strong coughs (from total lung capacity), five weak coughs (from residual volume) and five coughs of subjectively moderate strength (between strong and weak cough efforts). Participants were seated during testing. Altogether, 300 coughs were measured per portable device. Volunteers also performed spirometric forced expiratory manoeuvres through the pneumotachograph with each portable device connected in series in random order. One hundred maximal and 100

subjectively submaximal forced expiratory manoeuvres were measured per portable device, giving a

range of expiratory flows during forced expiration without glottic closure.

In order to control for any systematic effect on cough flow measurements caused by the in-series connection of pneumotachograph and alternative device, flow waves of consistent peak flow were mechanically generated using a 50 L pressure vessel (Medical Engineering Department, Royal Brompton Hospital, London, England) connected to a balloon occlusion valve (Medical Engineering Department, Royal Brompton Hospital, London, England). The barrel was pressurised with compressed air to a predetermined pressure, monitored with a digital manometer (C9553 Pressure Meter, Comark, Norwich, England), at which point the occlusion valve was opened and a burst of short duration airflow released. The consistency of peak flow for these flow bursts was confirmed with five consecutive measurements with the pneumotachograph system. Vessel pressures of 5, 10, 15, 20, 30 and 40 cmH₂O were used, resulting in bursts of airflow with mean (SD) peak flows of 138 (0.4), 250 (1.3), 343 (0.8), 422 (0.8), 559 (1.6) and 684 (2.9) L/min, respectively. Using the mechanically produced airflows, the agreement of peak flow measurements between systems was determined with the pneumotachograph and alternative devices connected in series (identical setup as used for volunteers, including bacterial filter); and with pneumotachograph and alternative devices connected in isolation (including bacterial filter). Five measurements were made at each flow level for each portable device connected in series and in isolation.

2.4. Analysis

Data were analysed using statistical software (Stata version 12.1, StataCorp LP, College Station, Texas). Bland-Altman analysis was used to compare peak flow measurements obtained from the pneumotachograph and each device for both measurements of volitional PCF, peak flow obtained from forced expiratory manoeuvres and the mechanically generated flow waves with devices used in series and in isolation.

3. Results

Twenty volunteers, mean (SD) age 45 (16), were studied, with at least one female and one male participant per age decade. The mean differences and 95% limits of agreement for volunteers' PCF obtained with the pneumotachograph system and the four portable devices are summarised in Table 2. Bland-Altman analysis indicated that measurements of PCF were lower with the devices tested compared with the pneumotachograph system (Figure 1). Measurements of PCF were markedly lower using the Mini-Wright peak flow meter (mean (95% limits of agreement) bias 56 L/min (-26 to 138 L/min)) (Figure 1a), with the difference increasing with increasing PCF (Spearman's rank correlation coefficient $r_s = 0.38$, p <0.0001). Despite a small overall mean (95% limits of agreement) bias of 3 L/min (-76 to 82 L/min) across the range (Figure 1b), PCFs measured using the Assess device were lower than the pneumotachograph system at low PCF and higher at high PCF ($r_s = -0.46$, p <0.0001). Both the SpiroUSB (mean (95% limits of agreement) bias 50 L/min (-26 to 125 L/min)) (Figure 1c) and the Microlab spirometers (mean (95% limits of agreement) bias 55 L/min (-23 to 132 L/min)) (Figure 1d) returned PCF readings that were consistently lower than those measured using the pneumotachograph system.

Some coughs with low peak flows were not registered by the portable devices and were excluded from the Bland Altman analysis. The Mini-Wright and Assess peak flow meters did not register 15 coughs with PCF between 60 L/min (lowest mark on the devices' scale) and 118 L/min, as measured by the pneumotachograph. Thirty-four coughs with PCF from 89 to 207 L/min were not registered by

the SpiroUSB spirometer. Twenty-five coughs with PCF from 58 to 237 L/min were not registered by the Microlab spirometer.

The results for the mechanically generated flow waves are presented in Tables 3 and 4 and in Figure 2. Example traces of mechanically generated flow waves in comparison with human cough flow waves are given in Figure 3. All portable devices recorded lower peak flow compared to the pneumotachograph system regardless of whether measurements were made when connected in series (Table 3) or in isolation (Table 4). The differences in measured peak flow between the pneumotachograph and alternative devices were smaller when the instruments were connected in series; and larger when the instruments were used in isolation. When instruments were connected in series, the pneumotachograph and portable devices all gave lower peak flow readings compared to when instruments were used in isolation; whereby measurements were always reduced to a greater extent for the pneumotachograph (mean (SD) difference 79 (38) L/min) than for the portable devices (mean (SD) difference 9 (6) L/min).

Correlation analysis to examine the relationship between cough rise time (time from initiation of positive flow to peak flow) and the degree of inaccuracy indicated statistically significant weak inverse correlations for the Mini-Wright ($r_s = -0.29$, p<0.0001) and the Assess peak flow meter ($r_s = -0.28$, p<0.0001); and statistically significant moderate inverse correlations for the SpiroUSB ($r_s = -0.68$, p<0.0001) and the Microlab spirometer ($r_s = -0.55$, p<0.0001) (Figure 4).

Bland-Altman analysis of peak flow measurements during spirometric forced expiratory manoeuvres performed with each device connected in series with the pneumotachograph demonstrated a smaller bias and narrower limits of agreement compared to those for PCF (Table 5, Figure 5). Similar weak and moderate correlations between time to peak flow and the degree of inaccuracy were observed: $r_s =$ -0.34 (p<0.0001) Mini-Wright peak flow meter, $r_s = 0.16$ (p=0.021) Assess peak flow meter, $r_s = -0.56$ (p<0.0001) SpiroUSB spirometer, $r_s = -0.66$ (p<0.0001) Microlab spirometer (Figure 6).

4. Discussion

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The results of this study indicate that when compared to a laboratory pneumotachograph based measurement system, four portable clinical flow measurement devices were inaccurate when measuring cough peak flows and returned lower PCF readings. These differences are clinically relevant when compared with the magnitude of PCF measurements in clinical populations. In addition, some low flow coughs were not registered by these devices, which impacts on their utility in very weak or severely obstructed patient populations.

The advantage of a compact, portable and practical clinical flow measurement device over a complex pneumotachograph system for the purpose of clinical practice and research is self-evident. This is particularly true for clinical populations with neuromuscular conditions, where mobility and transportation can be problematic. However, it should not be assumed that portable peak flow meters and hand-held spirometers are accurate when used for PCF measurement, as these devices are designed to measure peak flow during a forced expiratory manoeuvre. In our measurements of mechanically generated flow waves, the portable devices under test showed good instrument repeatability, with small standard deviations at each level of flow. It could be argued that good instrument repeatability justifies the use of these devices in studies with repeated measures designs. However, the accuracy of PCF measurements becomes particularly problematic when patients are assessed against absolute thresholds. Clinical guidelines cite PCF thresholds of 160 L/min and 270 L/min to direct clinical care of patients with neuromuscular conditions (Bott et al 2009, American Thoracic Society 2004). A scenario can be envisaged whereby the PCF measured for a patient could lie on either side of these threshold values, depending on the measurement device used. Our data highlights the importance of considering which measurement device was used to measure PCF when interpreting values.

The Mini-Wright and Assess peak flow meters have been used previously for PCF measurement in clinical studies (Table 1). The Assess peak flow meter (formerly Access Model 710, Health Scan Products Inc, Cedar Grove, New Jersey) was used in the frequently cited clinical studies by Bach and collaborators (Bach *et al* 1997, Bach and Saporito 1996, Bach 1995). To our knowledge, the

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SpiroUSB and Microlab spirometers have not previously been used for PCF measurement in clinical studies, but a similar turbine-based hand-held spirometer (Spirobank, Medical International Research, Rome, Italy) was used in the study by Fiore *et al* (2008).

Sancho *et al* (2004) and Silverman *et al* (2014) have both previously examined the accuracy of different portable devices for cough flow testing using repeated maximal cough efforts. This method, however, presumes that repeated coughs are sufficiently consistent for intra-subject variability to be ignored. Although intra-subject variability may be accounted for by randomising the order of devices, and by obtaining repeated measurements within a certain range, for example three maximal coughs within 5% PCF as in the study by Sancho *et al*, intra-subject variability due to fatigue, discomfort, motivation, or practice effect remains a limitation of this method, especially with increasing number of repetitions. Also, measurements across the mid and lower range of potential values may not be assessed conveniently using maximal efforts. The method applied in our study, connecting two devices in series, eliminated the problem of intra-subject variability, and allowed the direct comparison of coughs across a range of PCF values.

Using mechanically generated flow waves, simulating human expiratory flow waves with consistent peak flows, has been used previously to test spirometers and peak flow meters (Miller *et al* 2005, 2003). Such an approach allows comparison of measurement devices without the influence of intrasubject variability or bias due to in-series connection of instruments. The mechanical testing system employed in the current study produced flow waves with peak flows and rise times within the range observed in human coughs (Sivasothy *et al* 2001) and indicated greater inaccuracy of PCF measurements when using the four devices in isolation. The smaller differences in PCF observed with the in series setup is most likely the result of increased air flow resistance causing greater relative reductions in pneumotachograph PCF measurements. It is likely, therefore, that the differences in PCF measurements between the pneumotachograph and portable devices during coughs in the healthy human subjects were also underestimated. In cough, the time to peak flow (rise time) is shorter than during a forced expiratory manoeuvre (Miller *et al* 2002, Sivasothy *et al* 2001). We theorized that this short rise time may be the critical characteristic causing inaccuracies in measurement, as peak flow meters and hand-held spirometers may not respond adequately to such a rapid change in signal. Thus, increasing inaccuracy could be expected with shorter cough rise time. Our data partly supports this theory. There was a correlation of weak to moderate strength between cough rise time and the inaccuracy in PCF in our human volunteers. Similarly, more consistent agreement could be expected for peak flow measurements during forced expiratory manoeuvres than during cough, since the portable devices were designed for peak flow measurements during forced expiratory manoeuvres. Better agreement was demonstrated for peak flow measurements during forced expiratory manoeuvres, more so for the two spirometers and the Assess peak flow meter than for the Mini-Wright peak flow meter. The 95% limits of agreement were also narrower than for PCF measurements, but still spanned approximately 90 L/min for all four portable devices. Of note, the accuracy of hand-held peak flow meters in measuring peak flow during forced expiratory manoeuvres has been investigated by others, with devices performing variably (Miller et al 2003, Folgering et al 1998). We suggest that rise time is one factor influencing accuracy of peak flow measurements, but that further interactions between characteristics of human cough and properties of measurement devices impact on the performance of instruments. This identifies an interesting area for further investigation.

In order to advance cough flow measurement in clinical research, recommendations based on a consensus statement would be of benefit, similar to those produced for the measurement of cough frequency and reflex cough sensitivity (Morice *et al* 2007). Clearly, there is a demand for technology that enables scientifically accurate, but also practical and convenient measurement of cough flow. Developers of measurement devices should consider the research and clinical conditions such devices are likely to be applied in.

5. Conclusions

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In conclusion, the four portable flow measurement devices examined in our study did not accurately measure PCF. It is important to recognise that, depending on the measurement instrument, absolute values of PCF reported in the literature may not be directly comparable. Similarly, peak flow meters and hand-held spirometers should be used with caution when measuring PCF in clinical practice, particularly in respect to directing patient management.

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References

- American Thoracic Society 2004 Respiratory care of the patient with Duchenne muscular dystrophy *Am. J. Respir. Crit. Care Med.* **170** 456-65
- Bach J R, Goncalves M R, Paez S, Winck J C, Leitao S and Abreu P 2006 Expiratory flow maneuvers in patients with neuromuscular diseases *Am. J. Phys. Med. Rehabil.* **85** 105-1
- Bach J R, Ishikawa Y and Kim H 1997 Prevention of pulmonary morbidity for patients with Duchenne muscular dystrophy *Chest* **112** 1024-8
- Bach J R and Saporito L R 1996 Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure: A different approach to weaning *Chest* **110** 1566-71
- Bach J R 1995 Amyotrophic lateral sclerosis: Predictors for prolongation of life by noninvasive respiratory aids *Arch. Phys. Med. Rehabil.* **76** 828-32
- Bland J M and Altman D G 1999 Measuring agreement in method comparison studies *Stat. Methods Med. Res.* **8** 135-60
- Bott J, Blumenthal S, Buxton M, Ellum S, Falconer C, Garrod R, Harvey A, Hughes T, Lincoln M, Mikelsons C, Potter C, Pryor J, Rimington L, Sinfield F, Thompson C, Vaughn P and White J 2009 Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient *Thorax* 64 i1-i52

- Brito M F, Moreira G A, Pradella-Hallinan M and Tufik S 2009 Air stacking and chest compression increase peak cough flow in patients with Duchenne musclular dysptrophy *J. Bras. Pneumol.* **35** 973-9
- Cardoso F, de Abreu L, Raimundo R, Faustino N, Araujo S, Valenti V, Sato M, Martins S and Torquato J 2012 Evaluation of peak cough flow in Brazilian healthy adults *Int. Arch. Med.* **5** 25
- Cleary S, Misiaszek J E, Kalra S, Wheeler S and Johnston W 2013 The effects of lung volume recruitment on coughing and pulmonary function in patients with ALS *Amyotroph. Lateral Scler. Frontotemporal Degener.* **14** 111-5
- Daftary A S, Crisanti M, Kalra M, Wong B and Amin R 2007 Effect of long-term steroids on cough efficiency and respiratory muscle strength in patients with Duchenne muscular dystrophy *Pediatrics* **119** e320-4
- Dohna-Schwake C, Ragette R, Teschler H, Voit T and Mellies U 2006 IPPB-assisted coughing in neuromuscular disorders *Pediatr. Pulmonol.* **41** 551-7
- Fiore J F, Chiavegato L D, Denehy L, Paisani D M and Faresin S M 2008 Do directed cough maneuvers improve cough effectiveness in the early period after open heart surgery? Effect of thoracic support and maximal inspiration on cough peak expiratory flow, cough expiratory volume, and thoracic pain *Respir. care* 53 1027-34
- Folgering H, v d Brink W, v Heeswijk O and v Herwaarden C 1998 Eleven peak flow meters: a clinical evaluation *Eur. Respir. J.* **11** 188-93
- Freitas F S, Ibiapina C C, Alvim C G, Britto R R and Parreira V F 2010 Relationship between cough strength and functional level in elderly *Braz. J. Phys. Ther.* **14** 470-6
- Gauld L M and Boynton A 2005 Relationship between peak cough flow and spirometry in Duchenne muscular dystrophy *Pediatr. Pulmonol.* **39** 457-60
- Jones U, Enright S and Busse M 2012 Management of respiratory problems in people with neurodegenreative conditions: A narrative review *Physiotherapy* **98** 1-12
- Kang S W, Shin J C, Park C I, Moon J H, Rha D W and Cho D 2006 Relationship between inspiratory muscle strength and cough capacity in cervical spinal cord injured patients *Spinal Cord* 44 242-8
- Kimura Y, Takahashi M, Wada F and Hachisuka K 2013 Differences in the peak cough flow among stroke patients with and without dysphagia *J. UOEH* **35** 9-16
- Lee S C, Kang S, Kim M T, Kim Y K, Chang W H and Im S H 2013 Correlation between voluntary cough and laryngeal cough reflex flows in patients with traumatic brain injury *Arch. Phys. Med. Rehabil.* **94** 1580-3
- Leiner G C, Abramowitz S, Small M J and Stenby V B 1966 Cough peak flow rate *Am. J. Med. Sci.* **251** 211-4
- LoMauro A, Romei M, D'Angelo M G and Aliverti A 2014 Determinants of cough efficiency in Duchenne muscular dystrophy *Pediatr. Pulmonol.* **49** 357-65
- Miller M R, Atkins P R and Pedersen O F 2003 Inadequate peak expiratory flow meter characteristics detected by a computerised explosive decompression device *Thorax* **58** 411-6

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- Miller M R, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten C P M, Gustafsson P, Jensen R, Johnson D C, MacIntyre N, McKay R, Navajas D, Pedersen O F, Pellegrino R, Viegi G and Wanger J 2005 Standardisation of spirometry *Eur. Respir. J.* 26 319-38
- Miller M R, Lloyd J and Bright P 2002 Recording flow in the first second of a maximal forced expiratory manoeuvre: influence of frequency content *Eur. Respir. J.* **19** 530-3
- Morice A H, Fontana G A, Belvisi M G, Birring S S, Chung K F, Dicpinigaitis P V, Kastelik J A, McGarvey L P, Smith J A, Tatar M and Widdicombe J 2007 ERS guidelines on the assessment of cough *Eur. Respir. J.* **29** 1256-76
- Sancho J, Servera E, Diaz J and Marin J 2004 Comparison of peak cough flows measured by pneumotachograph and a portable peak flow meter *Am. J. Phys. Med. Rehabil.* **83** 608-12
- Sancho J, Servera E, Diaz J and Marin J 2007 Predictors of ineffective cough during a chest infection in patients with stable amyotrophic lateral sclerosis *Am. J. Respir. Crit. Care Med.* **175** 1266-71
- Silverman E P, Carnaby-Mann G, Pitts T, Davenport P, Okun M S and Sapienza C 2014 Concordance and discriminatory power of cough measurement devices for individuals with Parkinson disease *Chest* 145 1089-96
- Singh P, Murty G E, Mahajan R P, Knights D and Aitkenhead A R 1994 The tussometer: accuracy and reproducibility *Br. J. Anaesth.* **73** 145-8
- Sivasothy P, Brown L, Smith I E and Shneerson J M 2001 Effect of manually assisted cough and mechanical insufflation on cough flow of normal subjects, patients with chronic obstructive pulmonary disease (COPD), and patients with respiratory muscle weakness *Thorax* **56** 438-44
- Suarez A A, Pessolano F A, Monteiro S G, Ferreyra G P, Capria M E, Mesa L, Dubrovsky A and De Vito E L 2002 Peak flow and peak cough flow in the evaluation of expiratory muscle weakness and bulbar impairment in patients with neuromuscular disease *Am. J. Phys. Med. Rehabil.* 81 506-11
- Wright B M and McKerrow C B 1959 Maximum forced expiratory flow rate as a measure of ventilatory capacity *BMJ* **2** 1041-7

Table 1. Portable peak flow meters and spirometers used for the measurement of peak cough flow in clinical research.

Device	Study	Study population
Peak flow meters		
AsmaPLAN (Vitalograph, Ennis,	LoMauro <i>et al,</i>	Duchenne muscular dystrophy
Ireland)	2014	
	Sancho et al,	Neuromuscular disease, healthy
	2004	subjects
Assess (Philips Respironics,	Cleary et al, 2013	Amyotrophic lateral sclerosis
Pittsburgh, Pennsylvania) ^a	Bach et al, 2006	Restrictive pulmonary syndrome due
		to neuromuscular disease
	Kang <i>et al</i> , 2006	Cervical spinal cord injury
	Bach et al 1997	Duchenne muscular dystrophy
	Bach and Saporito	Spinal cord injury, progressive
	1996	neuromuscular disease
	Bach 1995	Amyotrophic lateral sclerosis
Astech (Astech, New York, New	Daftary <i>et al</i> ,	Duchenne muscular dystrophy
York)	2007	
MicroPeak (Micro Medical Ltd,	Lee <i>et al</i> , 2013	Traumatic brain injury, healthy
Rochester, England)		subjects
Mini-Wright (Clement Clarke	Silverman et al,	Healthy subjects, Parkinson's disease
International, Harlow, England)	2014	
	Cardoso et al,	Healthy subjects
	2012	
	Freitas et al, 2010	Healthy elderly subjects
	Brito et al, 2009	Duchenne muscular dystrophy
Mini-Wright DIGITAL	Silver man et al,	Healthy subjects, Parkinson's disease

(www.miniwrightpeakflowmeter.com)	2014	
Wright (Wright and McKerrow 1959)	Gauld and	Duchenne muscular dystrophy
	Boynton, 2005	
	Leiner et al, 1966	Obstructive and/or restrictive
		pulmonary disease, healthy subjects
Personal Best (Philips Respironics,	Suarez et al, 2002	Duchenne muscular dystrophy,
Pittsburgh, Pennsylvania)		amyotrophic lateral sclerosis
Pocketpeak (Ferraris Medical Ltd,	Dohna-Schwake	Muscular dystrophies
Enfield, England)	et al, 2006	
Enfield, England) Spirometers	et al, 2006	
Enfield, England) Spirometers Autospiro AS-505 (Minato Medical	<i>et al</i> , 2006 Kimura <i>et al</i> ,	Stroke
Enfield, England) Spirometers Autospiro AS-505 (Minato Medical Science, Osaka, Japan)	<i>et al</i> , 2006 Kimura <i>et al</i> , 2013	Stroke
Enfield, England) Spirometers Autospiro AS-505 (Minato Medical Science, Osaka, Japan) Micro-S 2000 (C. Schatzman, Madrid,	<i>et al</i> , 2006 Kimura <i>et al</i> , 2013 Sancho <i>et al</i> ,	Stroke Amyotrophic lateral sclerosis
Enfield, England) Spirometers Autospiro AS-505 (Minato Medical Science, Osaka, Japan) Micro-S 2000 (C. Schatzman, Madrid, Spain)	<i>et al</i> , 2006 Kimura <i>et al</i> , 2013 Sancho <i>et al</i> , 2007	Stroke Amyotrophic lateral sclerosis
Enfield, England) Spirometers Autospiro AS-505 (Minato Medical Science, Osaka, Japan) Micro-S 2000 (C. Schatzman, Madrid, Spain) Spirobank (Medical International	<i>et al</i> , 2006 Kimura <i>et al</i> , 2013 Sancho <i>et al</i> , 2007 Fiore <i>et al</i> , 2008	Stroke Amyotrophic lateral sclerosis Cardiac surgery

^a Formerly manufactured as Access Model 710 peak flow meter (Health Scan Products Inc, Cedar Grove, New

Jersey, USA)

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Table 2. Coughs from healthy volunteers: Agreement between peak cough flow measurements

 (Bland-Altman method of analysis) comparing four clinical flow measurement devices with the

 pneumotachograph measurement system.

Measurement device	n ^a	Mean difference from	95% limits of agreement
		pneumotachograph (bias) ^b	L/min
		L/min	
Mini-Wright peak flow	291	56	-26 to 138
meter			
Assess peak flow meter	284	3	-76 to 82
SpiroUSB spirometer	266	50	-26 to 125
Microlab spirometer	275	55	-23 to 132

^a Number of measurements contributing to analysis, which excludes measurements where the alternative device

did not return a reading (see text)

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Table 3. Mechanically generated flow waves: Agreement between peak flow measurements (Bland-

Altman method of analysis) with four portable devices connected in series with the

pneumotachograph measurement system.

n ^a	Mean difference from	95% limits of agreement
	pneumotachograph (bias) ^b	L/min
	L/min	
30	80	0 to 160
30	25	4 to 46
30	58	-2 to 118
30	54	-5 to 113
	n ^a 30 30 30 30	n ^a Mean difference from pneumotachograph (bias) ^b L/min 30 80 30 25 30 58 30 54

^a Number of measurements contributing to analysis

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Table 4. Mechanically generated flow waves: Agreement between peak flow measurements (Bland

 Altman method of analysis) recorded from four portable devices and the pneumotachograph

 measurement system in isolation (not connected in series).

Measurement device	n ^a	Mean difference from	95% limits of agreement
		pneumotachograph (bias) ^b	L/min
		L/min	
Mini-Wright peak flow	30	175	54 to 296
meter			
Assess peak flow meter	30	95	37 to 152
SpiroUSB spirometer	30	115	-8 to 239
Microlab spirometer	30	112	-8 to 233

^a Number of measurements contributing to analysis

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Table 5. Forced expiratory manoeuvres from healthy volunteers: Agreement between peak flow

 measurements (Bland-Altman method of analysis) comparing four clinical flow measurement devices

 with the pneumotachograph measurement system.

Measurement device	n ^a	Mean difference from	95% limits of agreement
		pneumotachograph (bias) ^b	L/min
		L/min	
Mini-Wright peak flow	200	41	-6 to 89
meter			
Assess peak flow meter	200	24	-22 to 70
SpiroUSB spirometer	200	14	-29 to 58
Microlab spirometer	200	12	-44 to 69

^a Number of measurements contributing to analysis



Figure 1. Coughs by healthy volunteers: Bland-Altman graphs of the agreement in measuring peak cough flow (L/min) between the pneumotachograph measurement system and (a) the Mini-Wright peak flow meter, (b) the Assess peak flow meter, (c) the SpiroUSB spirometer and (d) the Microlab spirometer. The difference between two measurements (pneumotachograph – alternative device) is plotted against the mean of two measurements. Solid lines indicate the lines of equality (no difference between measurements). Three dashed lines indicate the mean difference between measurements (bias) and the upper and lower 95% limits of agreement (bias \pm 1.96SD).



Figure 2. Mechanically generated flow waves: Agreement in measuring peak flow (L/min) between pneumotachograph and (a) Mini-Wright peak flow meter, (b) Assess peak flow meter, (c) SpiroUSB spirometer and (d) Microlab spirometer. The difference between two measurements (pneumotachograph – alternative device) is plotted against the mean of two measurements. Shown are the differences with pneumotachograph and alternative device connected in series (square markers); and measurements made with the instruments in isolation (triangular markers).



Figure 3. Examples of flow-time plots showing human coughs and mechanically generated flow waves of corresponding peak flow. (a) Maximally effortful voluntary cough from a healthy volunteer (peak cough flow = 666 L/min, rise time = 0.05 sec, volume expelled = 3.5 L). (b) Mechanically generated flow burst (peak flow = 680 L/min, rise time = 0.03 sec, volume expelled = 1.6 L). (c) Maximally effortful voluntary cough from a subject with severely weakened cough following stroke (peak flow = 120 L/min, rise time = 0.14 sec, volume expelled = 0.4 L). (d) Mechanically generated flow burst (peak flow = 138 L/min, rise time = 0.04 sec, volume expelled = 0.2 L).



Figure 4. Coughs by healthy volunteers: The difference (pneumotachograph – alternative device) in measured peak cough flow (L/min) between pneumotachograph and (a) Mini-Wright peak flow meter, (b) Assess peak flow meter, (c) SpiroUSB spirometer and (d) Microlab spirometer is plotted against cough rise time (sec). Solid lines indicate the lines of equality (no difference between measurements).



Figure 5. Forced expiratory manoeuvres by healthy volunteers: Bland-Altman graphs of the agreement in measuring peak flow (L/min) between the pneumotachograph measurement system and (a) the Mini-Wright peak flow meter, (b) the Assess peak flow meter, (c) the SpiroUSB spirometer and (d) the Microlab spirometer. The difference between two measurements (pneumotachograph – alternative device) is plotted against the mean of two measurements. Solid lines indicate the lines of equality (no difference between measurements). Three dashed lines indicate the mean difference between measurements (bias) and the upper and lower 95% limits of agreement (bias \pm 1.96SD).



Figure 6. Forced expiratory manoeuvres by healthy volunteers: The difference (pneumotachograph – alternative device) in measured peak flow (L/min) between pneumotachograph and (a) Mini-Wright peak flow meter, (b) Assess peak flow meter, (c) SpiroUSB spirometer and (d) Microlab spirometer is plotted against rise time (sec). Solid lines indicate the lines of equality (no difference between measurements).