

HOW TO QUANTIFY COUGHING? CORRELATIONS WITH QUALITY OF LIFE IN CHRONIC COUGH

Angela Kelsall^{1,2} BSc, Samantha Decalmer¹ MB ChB MRCP, Deborah Webster¹ MA MPhil, Nailah Brown¹ BSc, Kevin McGuinness^{1,2} BSc, Ashley Woodcock^{1,2} MD FRCP, Jaclyn Smith¹ PhD MRCP

¹Respiratory Research Group, University of Manchester, Manchester, UK and ²North West Lung Centre, University Hospital of South Manchester NHS Foundation Trust, Manchester, UK

Correspondence:

Ms Angela Kelsall,

North West Lung Research Centre,

Wythenshawe Hospital, Southmoor Rd,

Wythenshawe, Manchester M23 9LT,

United Kingdom

Telephone +44 161 291 5034

Fax +44 161 291 5057

Email: Angela.Kelsall@manchester.ac.uk

Financial Support: Moulton Charitable Trust.

No financial or other potential conflicts of interest exist for any of the authors.

Manuscript Word count: 1457

Abstract: (word count 199)

Different methods are used for quantifying coughing in sound recordings, but as yet no method has been shown to be more valid than any other. We have examined the relationships between three different units of cough and evaluated their ability to predict subjective ratings of cough and cough related quality of life.

70 subjects (mean age 55yrs (SD±11.7yrs), 73% female) with chronic unexplained cough (median duration 4.8yrs (IQR 2.5-10.1 yrs), performed fully ambulatory 24-hour sound recordings, manually counted by trained observers and quantified in (1) explosive phases, (2) cough seconds and (3) cough epochs. Subjects also completed cough visual analogue scales (VAS) and the Leicester cough questionnaire (LCQ).

All units of cough were strongly correlated; explosive phases and cough seconds correlated slightly more strongly than cough seconds with cough epochs or explosive phases with cough epochs ($r=0.99$ $p<0.001$, $r=0.92$, $p<0.001$ and $r=0.90$, $p<0.001$, respectively). LCQ scores correlated moderately with explosive phases and seconds ($r=-0.53$, $p<0.001$ and $r=-0.53$, $p<0.001$); epochs correlated slightly less well ($r=-0.46$, $p<0.001$). Cough VAS scores showed a similar pattern.

Explosive phases and seconds are interchangeable units of cough, moderately related to subjective measures and cough related quality of life; epochs are a less satisfactory alternative.

Key words:

Ambulatory cough monitoring

Chronic cough

Cough epochs

Cough seconds

Explosive phases

Introduction

The assessment of cough, both in clinical practice and in clinical research, has been impeded by a lack of valid tools. In recent years, cough assessment has been improved by the development of objective cough monitoring systems(1-4) and cough specific quality of life questionnaires(5, 6). Ambulatory sound recording systems are increasingly used to objectively measure coughing, but there is no agreement about the best method for quantifying the recorded events. Indeed, many studies to date have failed to describe how cough is defined or quantified(7). The European guidelines for the assessment of cough state ‘there is little to commend any particular method of quantifying cough over any other’(8). Acoustic cough waveforms are generally described as comprising of three phases(9) an ‘explosive’ phase, produced by sudden opening of the glottis, an ‘intermediate’ phase as the cough sound decays and sometimes an additional ‘glottal’ or ‘voiced’ phase, produced by a partial closure of the vocal cords (Figure 1). In contrast, sound recordings of spontaneous coughing find a much wider variety of patterns. In disease, prolonged series of explosive phases tend to occur (Figure 2), either after a single breath or with several breaths interspersed; these are often referred to as cough ‘epochs’, (‘peals’, ‘bouts’ or attacks(7)). Consequently coughing is commonly quantified by counting either the number of explosive phases or epochs. We have described a novel method for quantifying coughing, ‘cough seconds’(10-13). The numbers of seconds containing at least one explosive phase are counted, giving an estimate of the amount of time spent coughing.

Depending on the unit of cough, very different results can be obtained from the same sound recording. In Figure 2, a series of cough waveforms can be quantified as either as 4 explosive phases, 2 cough seconds, or a single cough epoch. In small groups of patients with cystic fibrosis, chronic obstructive pulmonary disease, asthma, chronic cough and interstitial lung disease, there is a linear relationship between cough seconds and explosive phases(14). The

relationships between all the different units of cough in use have not been defined but their understanding would facilitate comparison of studies where the units differ.

The aim of this study was to compare different methods for quantifying coughing in subjects with chronic cough. Furthermore we have tested the validity of these different cough units by examining correlations with the patients' perception of cough measured by cough visual analogue scale (VAS) and cough specific quality of life.

Methods and Materials

Subjects

Patients with chronic unexplained cough (> 8 weeks duration) were recruited from a tertiary referral clinic. Current or ex-smokers of less than six months were excluded from the study. Local Research Ethical approval was granted and written consent obtained.

Cough Recordings

Fully ambulatory 24 hour sound recordings were made, using a lapel microphone with either a modified MP3 player (IAudio, Cowon Systems Inc, Seoul, Korea, n=31) or a validated custom-built recording device (Vitalograph Ltd, Buckingham, UK, n=39). Participants were encouraged to continue their normal daily routine over the monitoring period. Recordings were downloaded to a PC and cough waveforms were quantified by a trained observer, using an audiovisual display (CoolEdit2000™, Syntrillium Software Corporation, Arizona, US). Excellent inter and intra subject agreement has been found for quantification in cough seconds, explosive phases and cough epochs(15-18).

For each recording coughs were quantified by three different methods, see Figure 2 and online sound file for Figure 2.

1. Explosive phases – the explosive phase is the characteristic sound we recognise as a cough; the irregular, noise-like waveform is readily differentiated from voiced phases which are audibly voice-like and have a regular (periodic) waveform (see Figure 1).
2. Cough seconds – the number of seconds containing at least one explosive phase were counted.
3. Cough epochs – the number of periods of continuous coughing without 2 second pauses were counted. The audiovisual display of the sound recordings shows the waveforms plotted against time, allowing measurement of pauses. Cough epochs defined as breaths

containing at least one explosive phase could not be examined using this system as it is not validated for detecting breath sounds.

Subjective Measures of Cough

After each 24hr recording, subjects completed a cough VAS for both day and night time i.e. a 100mm linear scale, where the extremes were marked 'no cough' and 'worst cough ever'.

Cough related quality of life was measured using the Leicester Cough Questionnaires (LCQ); a validated questionnaire, comprising 19 questions(5). Scores range from 3-21, with higher scores representing better quality of life.

Statistical Analysis

All analyses were performed using SPSS version 13.0 (SPSS Inc, Chicago, Ill). Day, night, and overall cough rates, for all three methods, were positively skewed; logarithmic transformation (base 10) normalised the distributions. As night time VAS and night time cough rates contained zero values, one unit was added to each data point to allow logarithmic transformation.

Results

Subjects

We studied 70 subjects with chronic unexplained cough (mean age 55years (SD \pm 11.7yrs), 73% female, median duration was 4.8 years (IQR 2.5-10.0)); 2 subjects did not complete the cough VAS.

Cough quantification

The median cough rates for the three different cough units are given in Table 1. All three methods for quantifying cough were highly correlated (Table 2). The strongest correlation was between explosive phases and cough seconds (shared variance $r^2=0.98$) but the correlation for both these measures and cough epochs was less strong (cough seconds and cough epochs, $r^2=0.84$ and explosive phases and cough epochs, $r^2=0.80$) (Table 2 and Figure 3).

Table 1 Diurnal variation in cough rate per hour; medians and interquartile ranges for three units of cough.

Quantification Method	24 hrs	Day	Night
Explosive Phases	15.9 (8.6-23.0)	19.3 (11.4-33.6)	4.5 (1.3-10.6)
Cough Seconds	12.2 (6.8– 18.1)	16.3 (9.2-26.2)	3.4 (1.0-9.1)
Cough Epochs	5.1 (2.9-7.1)	6.4 (3.6-9.5)	1.4 (0.4-3.2)

Table 2: Pearson correlations between different units of cough.

	Log cough seconds	Log cough epochs
Log explosive phases	r=0.99, p=<0.001	r=0.90, p=<0.001
Log cough seconds	N/A	r=0.92, p=<0.001

N/A = not applicable.

The median epoch length was 2.9 (IQR 2.1-3.6) explosive phases per epoch. There was no difference between the median epochs length for day (2.7, IQR 2.0-3.7) or night (3.1, IQR 2.1-4.2), p=0.12.

Subjective measures and quality of life

Mean total LCQ score was 12.3 (SD ±3.8), median daytime VAS score was 40.0mm (IQR 21.5-62.8 mm) and median night time VAS score was 18.0mm (IQR 5.3 - 45.8mm). Over 24 hours, rates of explosive phases and cough seconds had identical correlation coefficients with the LCQ, explaining 28% of the variance (Table 3). Cough epochs correlated slightly less strongly and explained 21% of the variance. Correlations between the VAS and cough units showed a similar pattern.

Table 3: Correlations between different units of cough and subjective measures. Note that negative correlations are present for the LCQ as lower scores and worse quality of life were associated with higher cough rates.

		LCQ	LCQ	Day VAS	Night VAS
Log Explosive phases	Day	r=-0.53 p=<0.001	r=-0.49 p=<0.001	r=0.45 p=<0.001	
	Night		r=-0.36 p=0.002		r=0.67 p=<0.001
Log Cough seconds	Day	r=-0.53 p=<0.001	r=-0.50 p=<0.001	r=0.44 p=<0.001	
	Night		r=-0.35 p=0.003		r=0.64 p=<0.001
Log Cough epochs	Day	r=-0.46 p=<0.001	r=-0.36 p=0.002	r=0.40 p=0.001	
	Night		r=-0.31 p=0.008		r=0.60 p=<0.001

Discussion

This the first study to compare the three commonest methods for quantifying coughs during ambulatory monitoring. We found that the measurements of explosive phases and cough seconds are extremely strongly correlated with one another, sharing 98% of their variance and hence are virtually interchangeable. Moreover, both measures are similarly related to cough-related quality of life and the patients' subjective estimate of cough severity. Cough epochs were less closely related to either explosive phases or cough seconds, sharing 80% and 84% of variance respectively, and were less well correlated with patients' reports.

Quantification in terms of epochs effectively ignores epoch length; the poorer correlation with cough quality of life/VAS implies that epoch length is important to patients.

Cough related quality of life and VAS are becoming widely used to assess patients with cough. Whilst all units of cough were significantly correlated with both subjective measures, the correlation coefficients are at best moderate, so the majority of the variance in these scores is not explained by objective cough frequency. It is inevitable that subjective scores and quality of life are influenced by much more than just the number of coughs, regardless of the units used. The intensity or effort involved in coughing is ignored, but it is likely that the most intense coughs that have the greatest impact for patients. Anxiety and depression are common in chronic cough(19, 20) and may also be important. We have recently shown that anxiety scores significantly predict cough related quality of life(21). Vigilance and recall may also differ between patients. Cough is an episodic symptom, some subjects may be better than others at recalling the frequency of cough and associated disruption; this is likely to be related to how much attention they pay to the symptom.

These issues highlight the limitations of using subjective scores or objective quantification of coughing alone. A comprehensive assessment of cough requires both measures. In future,

methods that would allow an objective measure of cough intensity would be a valuable addition to cough monitoring.

One limitation of this study is that we could only examine cough epochs defined as continuous coughing without a two second pause. When monitored coughing from sound alone, it is not possible to count cough epochs defined as a single expiratory effort with multiple explosive phases. A simultaneous measure of respiratory rate would be needed and may give different results.

We conclude that different units of cough quantification are remarkably highly correlated. Explosive phases and cough seconds are correlated sufficiently closely, to be interchangeable and correlate moderately with cough related quality of life and subjective assessment of cough severity. Cough epochs are a less satisfactory alternative.

Figure Legends

Figure 1 Typical cough sound waveform showing the acoustic phases. Inset A shows the explosive phase on an expanded time base, demonstrating the irregular, noise-like appearance. Inset B shows the contrasting regular, periodic appearance of the voiced phase.

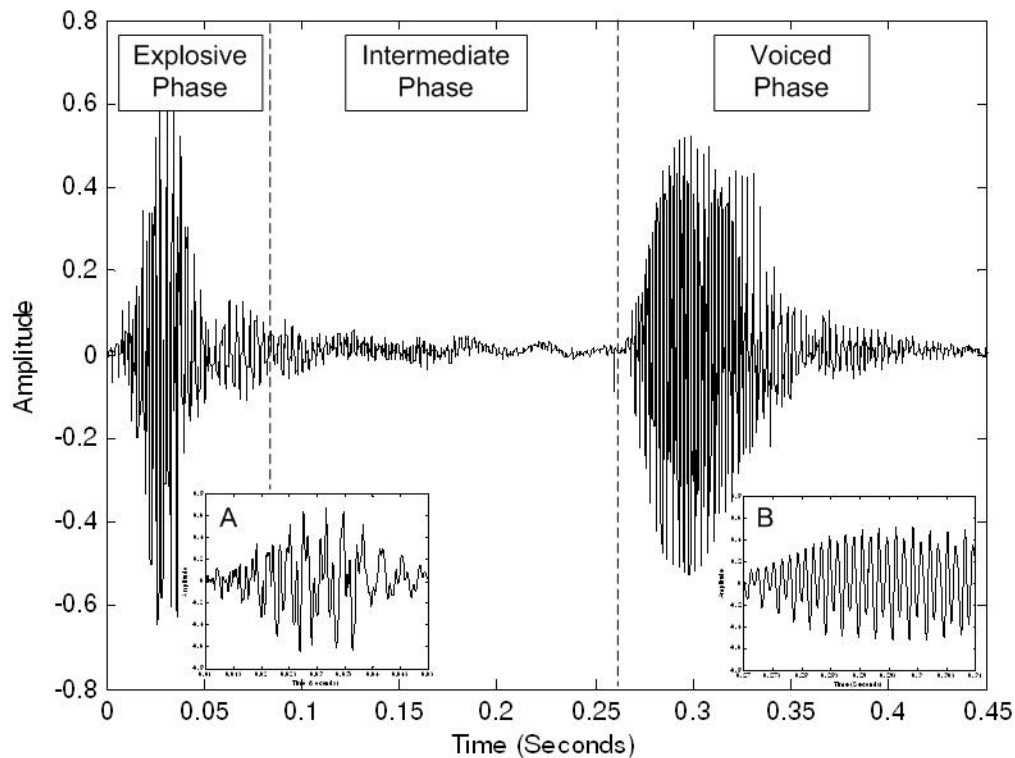


Figure 2 Comparison of different methods for quantifying cough sound recordings. A) Explosive and voiced phases in cough waveforms, B) counting explosive phases, C) counting cough seconds and D) counting cough epochs (see also online sound file).

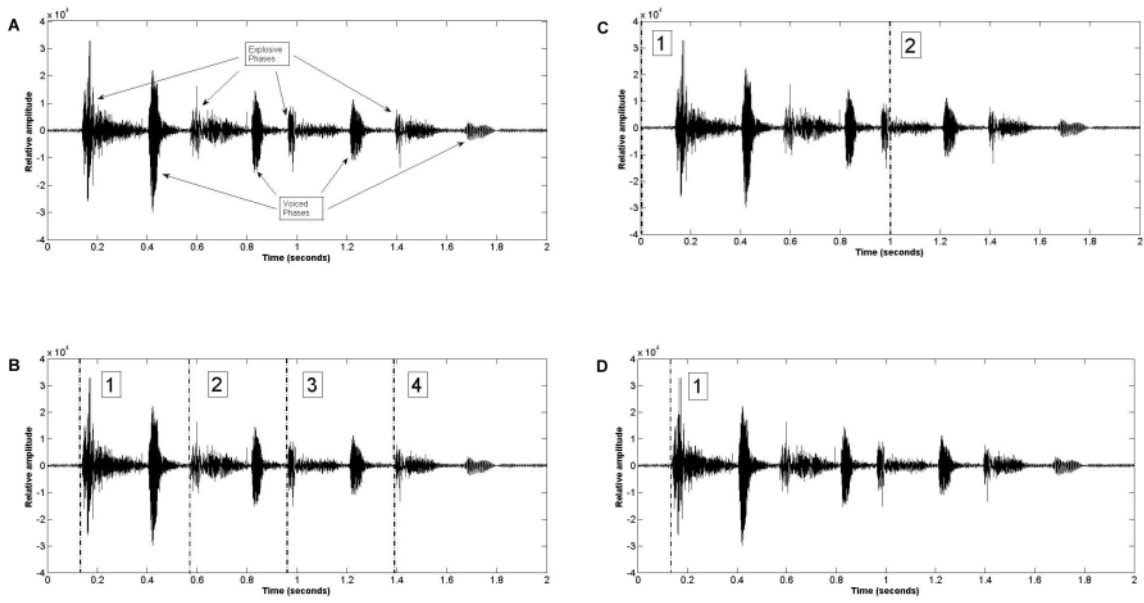
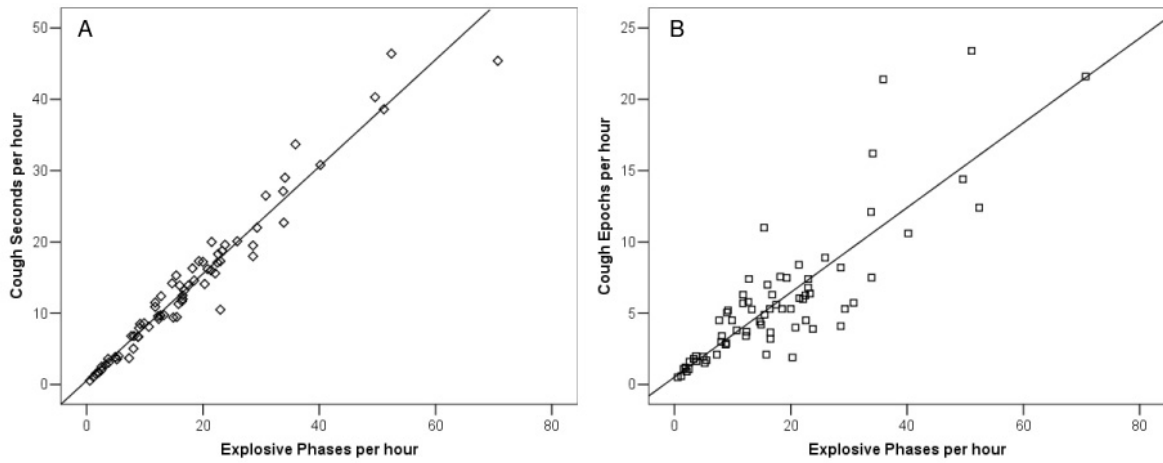


Figure 3 A) Correlation between cough seconds and explosive phases and B) correlation between cough epochs and explosive phases.



References

1. Coyle MA, Keenan DB, Henderson LS, Watkins ML, Haumann BK, Mayleben DW, et al. Evaluation of an ambulatory system for the quantification of cough frequency in patients with chronic obstructive pulmonary disease. *Cough*. 2005 Aug 4;1:3.
2. Matos S, Birring SS, Pavord ID, Evans DH. Detection of cough signals in continuous audio recordings using hidden Markov models. *IEEE Trans Biomed Eng*. 2006 Jun;53(6):1078-83.
3. McGuinness K, Kelsall A, Lowe J, Woodcock A, Smith JA. Automated Cough Detection: A Novel Approach [abstract]. *Am J Resp Crit Care Med*. 2007 April;175(Abstract Issue):A381.
4. Barry SJ, Dane AD, Morice AH, Walmsley AD. The automatic recognition and counting of cough. *Cough*. 2006;2:8.
5. Birring SS, Prudon B, Carr AJ, Singh SJ, Morgan MDL, Pavord ID. Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax*. 2003 April 1, 2003;58(4):339-43.
6. French CT, Irwin RS, Fletcher KE, Adams TM. Evaluation of a cough-specific quality-of-life questionnaire. *Chest*. 2002 Apr;121(4):1123-31.
7. Fontana GA, Widdicombe J. What is cough and what should be measured? *Pulmonary Pharmacology & Therapeutics*. 2007;20(4):307.
8. Morice AH FG, Belvisi MG, Birring SS, Chung KF, PV Dicipinigaitis, JA Kastelik LM, JA Smith, M Tatar, J Widdicombe. ERS Guidelines on the assessment of Cough. *Eur Respir J*. 2007 Jun;29(6):1256-76.
9. Korpas J, Sadlonova J, Vrabec M. Analysis of the cough sound: an overview. *Pulm Pharmacol*. 1996 Oct-Dec;9(5-6):261-8.

10. Decalmer S, Webster D, Kelsall A, McGuinness K, Woodcock A, J. S. Chronic Cough: How do Cough Reflex Sensitivity and Subjective Assessments Correlate with Objective Cough Counts during Ambulatory Monitoring? *Thorax*. 2007;62:329-34.
11. Smith J, Owen E, Earis J, Woodcock A. Effect of codeine on objective measurement of cough in chronic obstructive pulmonary disease. *J Allergy Clin Immunol*. 2006 Apr;117(4):831-5.
12. Smith J, Owen E, Earis J, A. W. Cough in COPD: Correlation of Objective Monitoring With Cough Challenge and Subjective Assessments. *Chest*. 2006 2006;130:379-85.
13. Smith J, Owen E, Jones A, Dood M, Webb A, Woodcock A. Objective measurement of cough during pulmonary exacerbations in adults with cystic fibrosis. *Thorax*. 2006 2006;61:425-9.
14. Smith J. Ambulatory methods for recording cough. *Pulm Pharmacol Ther*. 2007;20(4):313-8.
15. Smith J. The objective measurement of cough: University of Manchester; 2004.
16. Hsu JY, Stone RA, Logan-Sinclair RB, Worsdell M, Busst CM, Chung KF. Coughing frequency in patients with persistent cough: assessment using a 24 hour ambulatory recorder. *Eur Respir J*. 1994 July 1, 1994;7(7):1246-53.
17. Munyard P BC, Logan-Sinclair R, Bush A. A New Device for Ambulatory Cough Recording. *Pediatric Pulmonology*. 1994;18:178-86.
18. Hamutcu R, Francis J, Karakoc F, Bush A. Objective monitoring of cough in children with cystic fibrosis. *Pediatr Pulmonol*. 2002 Nov;34(5):331-5.
19. Dicpinigaitis PV, Tso R, Banauch G. Prevalence of depressive symptoms among patients with chronic cough. *Chest*. 2006 Dec;130(6):1839-43.
20. McGarvey LP, Carton C, Gamble LA, Heaney LG, Shepherd R, Ennis M, et al. Prevalence of psych morbidity among patients with chronic cough. *Cough*. 2006;2:4.

21. Decalmer S, Kelsall A, McGuinness K, Woodcock A, J.A S. Anxiety, depression and quality of life in patients with chronic persistent cough [abstract]. Thorax.

2007;62(Supplement III):A108.