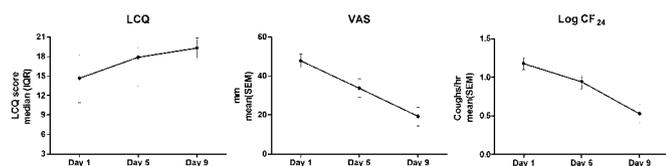


spent on over-the-counter cough medicines annually, despite limited evidence to support their efficacy. The optimal cough assessment outcome parameter for clinical evaluation of anti-tussive drugs is not known. We investigated the natural course of acute cough with objective and subjective cough assessment tools.

**Methods** 32 healthy subjects with acute cough due to upper respiratory tract infection (median (IQR) age 30 (32–35) years, 63% female, mean (SEM) duration of cough 4.2 (0.4) days) were recruited for evaluation. Subjects taking anti-tussives were excluded. Assessments of cough severity included objective 24-h ambulatory cough frequency monitoring with the Leicester Cough Monitor, health related quality of life (HRQOL) with the Leicester Cough Questionnaire-Acute (LCQ) and cough severity visual analogue scale (VAS). Assessments were performed at baseline (day 1) and then 4 and 8 days later. Global rating of change questionnaires were completed by patients at each follow-up to assess change in cough severity and determine minimal important difference.

**Results** At baseline, the median (IQR) LCQ score was 14.7 (10.9–18.3) and mean (SEM) cough VAS was 48 (4) mm, consistent with a severe cough associated with significant impairment in HRQOL. Geometric mean (logSD) 24-h cough frequency (CF<sub>24</sub>) at baseline was 15.0 (0.4) coughs/hr, and at days 5 and 9 were 8.7 (0.5) and 3.4 (0.7) coughs/hr respectively. At day 5, 3 subjects reported no change, 9 mild, 14 moderate and 6 large change in their cough severity. At day 9, 6 subjects reported mild, 5 moderate and 20 large change in cough severity. The minimal important difference on day 5 for the LCQ was 2.0, VAS 17 mm and CF<sub>24</sub> 54% change from baseline.

**Conclusions** Acute cough is associated with a significant cough frequency and impairment in HRQOL. We suggest clinical trials of anti-tussive drugs should incorporate objective and subjective cough assessment outcome measures. Anti-tussive drugs need to demonstrate a considerable reduction in cough frequency (>54% over a 4-day interval) to establish clinically important efficacy.



Abstract S144 Figure 1 Change in health related quality of life, cough severity VAS and cough frequency in acute cough.

### S144a ENDOGENOUS INHIBITION OF EXPERIMENTALLY INDUCED COUGH IN HEALTHY SUBJECTS

doi:10.1136/thoraxjnl-2011-201054b.144a

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**Background** The pathophysiology of chronic cough may include peripheral/central sensitisation of afferent pathways and/or a failure of inhibitory pathways. Cough can be voluntarily suppressed in healthy subjects, but the role of endogenous inhibition is unknown. Endogenous inhibitory pain pathways can be activated by applying a painful conditioning stimulus to one body part, to inhibit pain elsewhere, described as “Diffuse Noxious Inhibitory Controls”.

**Aim** To investigate if a painful conditioning stimulus applied to the hand would inhibit cough in healthy subjects.

**Methods** This was a randomised, 4-way, cross-over study. The EC50 dose of capsaicin was pre-determined (inducing at least 50% maximal cough frequency) at screening, and subsequently administered at each of the 4 visits (>48 h apart) in 2 blocks (1 h apart) of 4 inhalations (15 s apart), simultaneous with a randomised intervention:

**B:** Basal-no intervention (both blocks)

**W:** Warm-hand placed in non-painful 32°C water (both blocks)

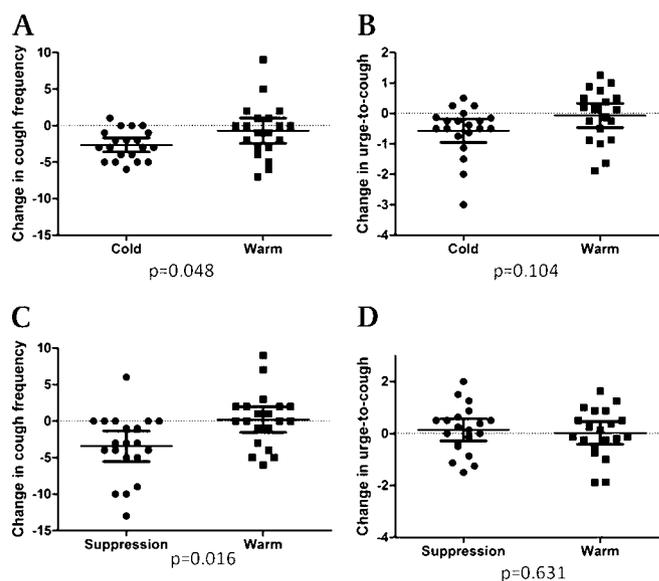
**C:** Cold-hand placed in painful 10°C or non-painful 32°C water (randomised order)

**S:** Suppression-instructed to “try not to cough” or “cough freely” (randomised order) while placing hand in 32°C warm water.

Coughs were counted and verified using sound recordings. Urge-to-cough was rated using a Modified Borg Scale (0–10).

**Analysis** The between-block change in cough frequency and urge-to-cough intensity was compared by intervention using paired t-tests after adjusting for an order-effect. Primary outcome was W versus C. Secondary outcomes were B versus W, and W versus S.

**Results** 20 non-smoking healthy subjects [10 male; mean (SD) age 55.05 (14.2) yrs] with normal lung function and median (IQR) EC50 of 15.6 (23.50) μM capsaicin completed the study. Compared to B, W had no significant effect on cough (p=0.623) or urge-to-cough (p=0.285). Compared to W, C significantly reduced cough (p=0.048) (Abstract S144a figure 1A) and showed a trend towards a reduction in urge-to-cough (p=0.104) (Abstract S144a figure 1B). Compared to W, S significantly reduced cough (p=0.016) (see Abstract S144a figure 1C) but urge-to-cough did not change (p=0.631) (Abstract S144a figure 1D).



Abstract S144a Figure 1 Change in total cough frequency (A,C) and urge-to-cough intensity (B,D) between blocks. Horizontal lines show mean, error bars ±95% CI.

**Conclusion** Applying a painful stimulus to the hand inhibits cough in healthy subjects, and may be a useful model for measuring endogenous inhibition of coughing. Further studies to investigate whether chronic cough patients demonstrate impaired inhibition using this experimental paradigm are underway.