Daily Cough Count Variability and Correlation With PROs in Chronic Cough: Informing Antitussive Trial Endpoints

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Rationale

The accurate assessment of coughing is critical for therapeutic trials of antitussive agents. To date, this has relied upon patient-reported outcomes and human annotation of 24 hour audio recordings. Automated continuous cough monitors now enable continuous cough monitoring. We monitored cough for a month in patients with refractory or unexplained chronic cough and analyzed the value of that data for designing antitussive trials.

Methods

Thirty-five patients with refractory/unexplained chronic cough were recruited from two cough clinics. Subjects completed the Leicester Cough Questionnaire (LCQ) at the outset and conclusion of the study, the Visual Analogue Scale (VAS) daily and a usability questionnaire. Time stamps of the subject's cough were recorded for the 30-day study using the Hyfe CoughMonitor Suite (CMS).

Results

Average hourly cough rates ranged from 2.1 to 51.2 (cohort mean 13.6) with substantial variability both between individuals (**Fig 1**) and within individuals from day to day (**Fig 2**). A clear diurnal pattern was observed across the cohort, with a nadir overnight and a sharp rise between 5–10 am (**Fig 3**). Cough bouts (3 or more coughs separated by <3 seconds) were derived (**Fig 4a**).

Daily VAS scores correlated poorly with objective cough counts (r = 0.23, 95% CI 0.16–0.30), with considerable inter-individual variation. Among participants reporting VAS <40, 28% had >10 coughs per hour and 14% had >20 coughs per hour. The Pearson correlation coefficient between the first and last LCQ was 0.79; Test–retest reliability of cough monitoring improved to 0.90 with longer monitoring duration, indicating that averaging cough rate over consecutive days provides a more reliable trial endpoint than a single 24-hour measurement.

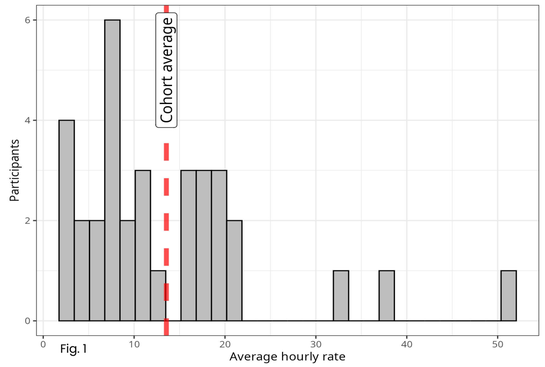

Fig. 1

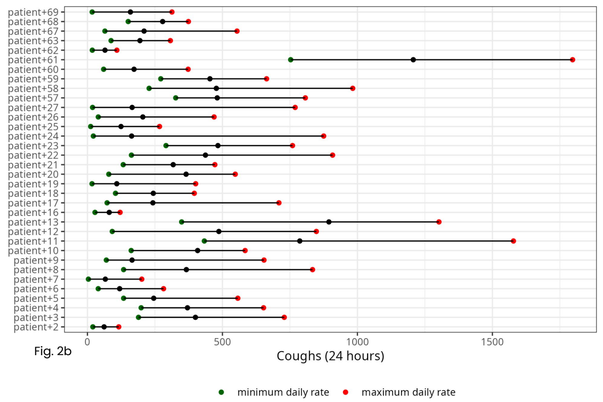

Fig. 2b

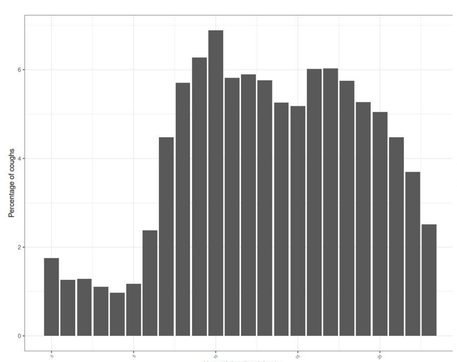

Fig. 3

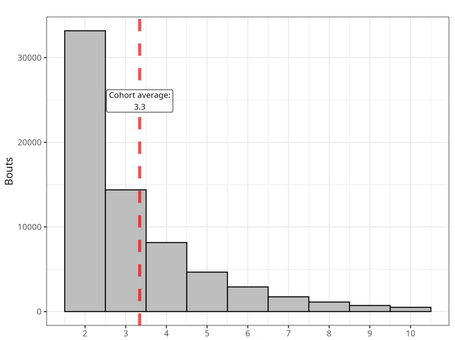

Fig. 4a

35
clinically stable RCC/UCC patients

928
person-days of monitoring

302,868
coughs recorded

0.90
test-retest reliability of continuous monitoring

Conclusions

Daily cough rates in RCC/UCC patients are highly variable, and VAS correlates poorly with objective cough frequency. Using VAS thresholds alone for trial screening risks excluding patients with objectively high cough rates.

Averaging cough rate over multiple consecutive days yields a markedly more stable endpoint than a single 24-hour measurement. Continuous cough monitoring and PROs capture different dimensions of cough and play complementary roles in antitussive trial design.

Take-Home Points

1. **Daily cough counts in chronic cough show substantial day-to-day variability.**
2. **Daily VAS correlates poorly with objective cough frequency.**
3. **Multi-day cough monitoring provides a more reliable trial endpoint than single-day counts.**
4. **Continuous cough monitoring and PROs play complementary roles in antitussive trials.**

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