1 **Title: Feasibility and Utility of a Smartphone Application-Based Longitudinal Cough Monitoring in**

2 **Chronic Cough Patients in a Real-World Setting**

3 Seung-Eun Lee[1], Matthew Rudd[2], Tae-Hwa Kim[1], Ji-Yoon Oh[3], Ji-Hyang Lee[3], Lola Jover[4], Peter M.

4 Small[4,5], Kian Fan Chung[6], Woo-Jung Song[3]

5 [1]Department of Internal Medicine, Pusan National University School of Medicine, Pusan National

6 University Yangsan Hospital, Yangsan, Korea.

7 [2]Department of Mathematics and Computer Science, The University of the South, Sewanee, TN, USA.

8 [3]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of

9 Medicine, Seoul, Korea.

10 [4]Hyfe Inc, Wilmington, DE, USA.

11 [5]Department of Global Health, University of Washington, Seattle, WA, USA.

12 [6]National Heart and Lung Institute, Imperial College London, London, UK.

13

14 **Corresponding author**

15 Woo-Jung Song, MD, PhD

16 Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of

17 Medicine, Seoul, Korea.

18 E-mail: swj0126@amc.seoul.kr; Tel: +82-2-3010-3288

19

20 **Short title: Feasibility of Longitudinal Monitoring of Chronic Cough**

21 **Abstract word count: 246**

22 **Manuscript word count: 2,824**

23 **Number of Tables: 5**

24 **Number of Figures: 3**

25

33

34   **Author contributions:**

35   WJS is the full guarantor of this manuscript. SEL, PMS, KFC, and WJS contributed to the study

36   conception and design, and data interpretation. THK, JYO, JHL, and LJ have made contributions to the

37   data acquisition. SEL and MR performed formal analysis. SEL and WJS drafted the first version of the

38   manuscript. PMS, KFC, and WJS supervised and revised the manuscript. All authors approved this

39   version of the manuscript for submission.

40

ABSTRACT

Purpose: This study evaluated the feasibility and utility of longitudinal cough frequency monitoring with the Hyfe Cough Tracker, a mobile application equipped with cough-counting artificial intelligence algorithms, in real-world patients with chronic cough.

Methods: Patients with chronic cough (>8 weeks duration) were monitored continuously for cough frequency with the Hyfe app for at least one week. Cough was also evaluated using the Leicester Cough Questionnaire (LCQ) and daily cough severity scoring (0-10). The study analyzed adherence rate, the correlation between objective cough frequency and subjective scores, day-to-day variability, and patient experience.

Results: Of 65 subjects consecutively recruited, 43 completed the study. The median cough monitoring duration was 13.9 days, with a median adherence of 91%. Study completion was associated with baseline cough severity, and the adherence rate was higher in younger subjects. Cross-sectional correlation analyses showed modest or weak correlations between objective and subjective cough measures at the group level. However, in time-series correlation analyses, correlations between objective and subjective measures widely varied across individuals. Cough frequency had greater day-to-day variability than daily cough severity scores in most subjects. A patient experience survey found that 70% of participants found the cough monitoring helpful, 86% considered it acceptable, and 84% felt it was easy-to-use.

Conclusion: Monitoring cough frequency longitudinally for at least one week may be feasible. The substantial day-to-day variability in objective cough frequency highlights the need for continuous monitoring. Grasping the implications of daily cough variability is crucial in both clinical practice and clinical trials.

Keywords: chronic cough, cough frequency, cough monitor, patient-reported outcome

65 **INTRODUCTION**

66 Cough is a forced expulsive maneuver against a closed glottis and has a characteristic sound, which

67 can be used to measure cough frequency [1]. Cough frequency counting has potential applications in

68 epidemic surveillance, monitoring treatment response, and predicting acute exacerbations of

69 respiratory diseases [2-10]. Cough itself can also define a disease, particularly in patients with chronic

70 cough [11]. Objective cough frequency serves as the primary endpoint in clinical trials of antitussive

71 drugs and in guideline decision-making for chronic cough [12-15]. VitaloJAK and the Leicester Cough

72 Monitor (LCM) are currently the leading tools for the objective measurement of cough frequency

73 [16,17]. However, the utility for real-time analysis is limited since counting is not automated, and

74 recordings are mostly restricted to a 24-hour period at specific time points in research setting.

75 Individuals with chronic cough may have substantial day-to-day variability in cough frequency [18,19].

76 With advances in digital technology, real-time continuous cough frequency monitoring may

77 be realized using mobile applications with cough-counting artificial intelligence (AI) algorithms. There

78 are several smartphone apps and wearable device technologies for cough detection [20-26]. Given

79 that smartphones and wearable devices are widely utilized, the combination of such technologies with

80 AI has the potential for integration into routine clinical practice for patients with chronic cough.

81 Continuous cough monitoring may provide comprehensive information on cough patterns and

82 changes over time.

83 In the present study, we hypothesized that continuous cough frequency monitoring (≥1 week)

84 based on a smartphone app is feasible and useful for the clinical management of patients with chronic

85 cough who are attending cough clinics. We utilized the Hyfe Cough Tracker smartphone application,

86 which uses AI algorithms to measure cough frequency [6-8,27], and evaluated data for the following

87 outcomes: i) adherence to continuous cough frequency monitoring, ii) correlations of objective cough

88 frequency with subjective cough scores and iii) patient experience.

89

90   **METHODS**

91   *Participants*

92   Patients with chronic cough (>8 weeks in duration) were recruited consecutively from two referral

93   clinics in South Korea. Eligible patients were 19- to 80-years-old, used a smartphone, had active coughs,

94   and did not have any red flag signs, such as hemoptysis, severe dyspnea, fever, weight loss, peripheral

95   edema, dysphagia, vomiting, a history of recurrent pneumonia, or a medically significant abnormal

96   finding on physical examination or chest radiography. During the initial study visit (V1), patients'

97   baseline clinical characteristics were evaluated, including cough duration and comorbid conditions.

98   Participants received the usual care recommended by international and national cough guidelines

99   [12,28]. The follow-up visit day (V2) aligned with clinical appointment schedules. The institutional

100   review boards (IRB) of the two institutions approved the study, and all patients provided written

101   informed consent [IRB No. 2021-1632 and IRB No. 05-2021-281].

102

103   *Cough frequency monitoring*

104   The hourly cough rate was calculated for each day throughout the monitoring period, using the Hyfe

105   Cough Research App (Wilmington, DE, USA, https://www.hyfeapp.com). It is a smartphone application

106   that measures the frequency of coughs using AI algorithms to distinguish cough sounds from ambient

107   noise. It operates as a smartphone background application, monitors ambient sound levels, and

108   records short snippets of "explosive" sounds (<0.5 s) [7]. The half-seconds containing at least one

109   explosive sound are transferred to a server and analyzed on a server-based convolutional neural

110   network (CNN) AI model, which differentiates cough sounds from non-cough sounds. The CNN model

111   was demonstrated to have greater than 96.0% sensitivity and specificity [8,27,29].

112

113   *Cough frequency monitoring set-up*

114   At V1, participants were provided with research smartphones or were allowed to use their personal

115 smartphones with the application installed. Research coordinators instructed the participants on how

116 to install and use the application. The training covered the following content: (1) the smartphone must

117 be carried within a 1.5-m distance of the subject for cough monitoring, including during the nighttime,

118 (2) the battery should be frequently charged to avoid complete discharge, (3) the application should

119 be reactivated when the microphone was commandeered by another application using an audio

120 system, and (4) the smartphone should be connected to Wi-Fi at least once every three days so that

121 the measured cough data are automatically transmitted to the server. Participants were provided with

122 a small pouch to carry their phone during the study period. Monitoring continued for a full 24-hour

123 cycle, including nighttime. Instructions were also provided as a single-page leaflet. The time spent on

124 the set-up and training was measured. Patients were not aware of cough frequency data during the

125 monitoring period.

126

127 ***Subjective cough measures***

128 At V1, the participants recorded their cough severity using the numerical rating scale (NRS) (0-10),

129 Leicester Cough Questionnaire (LCQ), and Cough Hypersensitivity Questionnaire (CHQ). The NRS score

130 for daily cough severity was also recorded in a paper diary every evening of the monitoring period. At

131 the follow-up visit day (V2), the participants indicated their cough status by responding to the severity

132 NRS and LCQ.

133

134 ***Adherence to continuous cough monitoring***

135 We determined the actual recording time of the application from the monitoring record. Adherence,

136 which indicates application usage, was defined as the percentage of actual operation to the

137 monitoring period. For analysis, we categorized adherence as "good" (≥75%) and "excellent" (≥85%).

138

139 ***Correlations between objective cough frequency and subjective cough scores***

140   In subjects with excellent adherence to continuous cough monitoring, the relevance of objective

141   cough frequency was explored using correlation analyses of objective cough frequency and subjective

142   cough scores, as indicated by cough severity NRS and LCQ scores.

143

144   ***Day-to-day variability of cough***

145   The changing patterns of objective cough frequency and cough severity score were initially assessed

146   through visual inspection of daily changes and subsequently analyzed using time-series correlation

147   analyses. To measure day-to-day variability of objective cough frequency and cough severity score,

148   the variance index was calculated by dividing the standard deviation by the mean daily cough

149   frequency (or severity score) for each subject.

150

151   ***Patient experience survey***

152   At V2, study participants were provided with a paper report on daily cough frequency between V1 and

153   V2. Physicians and patients discussed the cough report and their clinical course. Then, patients were

154   presented with 14 questions about their user experience, including the convenience, usefulness, and

155   acceptability of the tool. Responses were recorded as answers to open-ended questions and on a 5-

156   point Likert scale.

157

158   ***Statistical analysis***

159   Descriptive data were expressed as means ± standard deviations, medians (interquartile range [IQR]),

160   or percentages. Subject characteristics were compared according to study completion or adherence

161   rate. Categorical variables were analyzed using the chi-square test, and continuous variables were

162   analyzed using the t-test, Mann-Whitney U-test, or Wilcoxon signed-rank test. The correlation

163   between the variables was evaluated using the Spearman or Pearson correlation coefficient,

164   depending on the variable distribution. Data were analyzed using the R software version 4.2.2 (R Core

165   Team, 2022) and the Stata/SE 17.0 software package (Stata Corporation, College Station, TX, USA). All

166   tests were two-sided, and p values were significant at <0.05.

167

168 **RESULTS**

169 *Baseline characteristics*

170 A total of 65 subjects with chronic cough were recruited consecutively for the study. Their median age

171 was 47.0 years (IQR: 36.0 to 59.0), and 70.8% of them were female. The median duration of cough

172 was 30 months (IQR: 4.0 to 120.0). Of the patients recruited, 13 missed the follow-up visit (V2). For

173 another nine subjects, the operating time of the cough monitoring device did not align with the study

174 period (e.g., due to delayed initiation or early termination of cough monitoring by the subjects).

175 Therefore, 43 participants (66.2%) were deemed to have completed the study and provided reliable

176 cough monitoring data for comprehensive quantitative analysis.

177   The baseline characteristics of subjects according to study completion are summarized in

178 Table 1. Subjects who completed the study (n=43) had significantly higher baseline cough severity NRS

179 scores. There were no significant differences in other baseline parameters, such as age, sex, body mass

180 index, cough duration, smoking history, comorbid conditions, pulmonary function, LCQ scores, and

181 CHQ scores. The average setup time was 191 s, and setup took longer in the group that completed the

182 study—a median of 206.0 s (IQR: 170 to 230) vs. a median of 185 s (IQR: 170 to 191; Table 1).

183

184 **Adherence to continuous cough monitoring**

185 Adherence, defined as the percentage of actual app operation duration in relation to the monitoring

186 period (V2-V1), was calculated in 43 subjects who completed the study (Table 2). Median cough

187 monitoring duration, calculated based on the time elapsed between the initiation and termination of

188 the app usage, was 13.9 days (IQR: 7.3 to 14.3). The overall adherence rate for monitoring was 91%

189 (IQR: 74 to 100). Adherence was categorized as good (≥75%) for 74.5% of participants (n=32) and as

190 excellent (≥85%) for 60.5% of participants (n=26). Table 3 compares subjects' baseline characteristics

191 according to their adherence rate. Subjects with adherence ≥85% (n=26) were significantly younger

192 (median 36.5 [IQR: 29.0 to 53.0] vs. 62.0 [IQR: 47.0 to 65.0]; p=0.001], compared with those whose

193   adherence was <85% (n=17). However, there were no significant differences in hourly cough rates or

194   in baseline cough severity NRS, CHQ, or LCQ scores. At V2, subjects with adherence ≥85% had lower

195   LCQ scores than did those with poor adherence, but the difference was not statistically significant

196   (median 12.4 [IQR: 9.1 to 14.9] vs. 15.3 [IQR: 12.2 to 18.5]; p=0.071; Table 3).

197

198   **Correlations between hourly cough rates and subjective cough scores**

199   Correlations of continuous cough frequency with PRO scores were examined in 25 subjects with

200   adherence ≥85% (V1 and V2 data combined). The hourly cough rate showed a moderate correlation

201   with the LCQ score (r=-0.566, p<0.001) and with the cough severity NRS score (r=0.609, p<0.001;

202   Figures 1A and 1B).

203

204   **Day-to-day variability of cough**

205   Longitudinal changes in hourly cough rate and daily cough severity NRS score were plotted in Figure

206   2. Time–series correlations between hourly cough rate and subjective cough severity were

207   summarized in Table 4; and the degree of correlations between objective and subjective measures

208   varied widely between individuals, and the degree did not correlate with adherence (r=-0.100,

209   p=0.646). The variance index of hourly cough rates was higher than that of cough severity scores in

210   most subjects (19 of 25) (Figure 3).

211

212   **Patient experience**

213   Patient experience is summarized in Table 5. More than 80% of the participants responded that the

214   measurement of cough frequency was important to and helpful for cough treatment. In addition, 70%

215   responded that the monitoring was helpful, 86% reported that the tool's use was acceptable, and 84%

216   found the app easy to use. The most common reason for characterizing the tool as unacceptable was

217   the inconvenience of continuously carrying the device (n=14). Additional technical issues included

218   difficulty with using other audio-enabled apps simultaneously (n=3), increased battery usage (n=2),

219   and application freezing (n=2). Two subjects also expressed concern about confounding by ambient

220   noise or another person's coughs.

221

DISCUSSION

In this feasibility study, we used the Hyfe Cough Tracker, a smartphone application for longitudinal monitoring of cough frequency in patients with chronic cough as they go about their daily lives. Of the 65 subjects recruited, 43 (66.2%) completed the study visits and were considered to have reliable cough frequency data suitable for full quantitative analysis. The median duration of continuous cough monitoring was 13.9 days (IQR: 7.3 to 14.3), and the adherence rate during the study period was a median of 0.93 (IQR: 0.74 to 1.0).

Very few studies have reported the feasibility and utility of monitoring cough frequency longitudinally over several days in real-world practice. In a retrospective analysis examining the feasibility of using the LCM, Vertigan and colleagues found that 75% of participants used the monitors correctly, most cough recordings (93%) were interpretable, and the set-up time was between 10 and 20 minutes, suggesting that such monitoring is potentially feasible [30]. However, this analysis was limited to only 24 hours of monitoring experience. Kuhn et. al evaluated the 7-day performance and wearability of a novel, small, wearable cough detector (SIVA-P3) in 27 patients with chronic cough [26]. Using cough epochs collected in the first 24 hours (compared against a human operator), they reported the algorithm's sensitivity and specificity to be approximately 85% and 99%, respectively. The monitor was comfortable for most participants to wear. However, the researchers did not report the feasibility and utility of continuous cough monitoring over multiple days.

In this study, of the 65 subjects recruited, only 66.2% (43 subjects) completed the study visits. Among those, 60.5% achieved an adherence rate of ≥85%. The reasons behind the relatively high rate of study incompletion are presently ambiguous and might be diverse. In our baseline comparison, no specific characteristic linked to study incompletion was identified. Nonetheless, given the relatively long duration of monitoring (a median of 13.9 days [IQR: 7.3 to 14.3]), the adherence rate may not be considered poor. The finding that the adherence rate was significantly associated with younger age underscores the practical challenges of implementing these technologies in current practice. We

247 anticipate that adherence will improve with enhanced device wearability, such as the adoption of

248 smart watches.

249 We examined the correlations of objective cough frequency with subjective cough PRO

250 scores in a group of subjects with adherence ≥85%. The cross-sectional correlations were found to be

251 modest, which aligns with observations made for the VitaloJAK, LCM, and Hull Automatic Cough

252 Counter [31-33]. However, upon visual inspection of longitudinal changes, it was observed that

253 subjective daily cough scores often did not respond to changes in cough frequency in some subjects.

254 This reaffirms the idea that cough severity might be an overarching concept that encompasses various

255 dimensions of cough, including its frequency [34,35]. The pattern of daily changes also varied between

256 individuals (Figure 2). In time–series correlation analyses, the degree of correlations varied widely

257 between individuals (Table 4). Furthermore, cough frequency exhibited greater day-to-day variability

258 compared to daily cough severity scores in most subjects (Figure 3). These findings suggest that daily

259 cough severity scoring may not be well responsive to actual changes of daily cough frequency.

260 Continuous measurements spanning several days or longer may be preferable to single-day

261 measurements to address the variability of cough.

262 In our user experience survey, more than half of the participants responded that the

263 measurement of cough frequency was relevant, acceptable, and easy to use. However, approximately

264 10 to 20% of participants responded negatively. Some respondents mentioned that they perceived

265 low importance in measuring the frequency of coughs, primarily because the cough symptoms

266 improved rapidly. Additionally, individuals with low adherence often expressed concerns about its

267 usefulness and convenience. Notably, the most frequent complaint was the inconvenience of carrying

268 the device. Additional issues included difficulty with using other audio-enabled apps, battery usage,

269 and the application freezing. These issues indicate the need for improving the wearability of the tool

270 or developing a dedicated unobtrusive device for long-term continuous monitoring.

271   The present study has several limitations. First, its aim was not validation, but to evaluate the

272   feasibility in a routine practice setting. The accuracy has not been fully assessed, and its real-world

273   validity requires further investigation. Second, we limited our quantitative analysis to subjects with an

274   adherence rate ≥85%, as the cough frequency data obtained from those with poor adherence group

275   might be unreliable. Nevertheless, there is a potential risk of selection bias that needs to be

276   acknowledged. Third, while we confirmed that the app was active and patients received verbal and

277   written instructions to constantly keep their phones nearby, we did not ensure the actual patient's

278   proximity to the phone, potentially leading to some undercounting of coughs or overcounting from

279   external sources. Although we recommended using a small pouch, the carrying method was not

280   strictly controlled. We calculated adherence (as the percentage of actual operation per the monitoring

281   period) to assess potential operational interruptions of the app during the study. Nevertheless, we

282   recognize this as an indirect measure of adherence. Fourth, there might be sex differences in the

283   manner of carrying the phone. Investigation of the impact on adherence and cough frequency is

284   warranted. Fifth, the current version of the application relies solely on acoustic signals. Incorporating

285   the accelerometer present in smartphones could help address the limitations of the acoustic signal-

286   based cough counting algorithm. Finally, if other individuals coughed within the 1.5-meter operational

287   range of the phone, their coughs could have been mistakenly attributed to the study participant. While

288   we acknowledge these factors might contribute to the day-to-day variability of cough frequency, we

289   also believe that there is an inherent variability that requires consideration. This suggests the need for

290   measuring cough frequency over an extended period of several days.

291   Despite these limitations, this study represents the first effort to evaluate the feasibility and

292   potential value of a smartphone application-based, longitudinal, continuous cough monitoring (for a

293   duration of ≥1 week) in patients with chronic cough receiving care in the real world. The analysis of

294   the adherence rate points to the practical challenges of implementing such technologies in current

295   practices. However, we anticipate that adherence will improve as device wearability advances. The

296   day-to-day variability in objective cough frequency, combined with the limited responsiveness of daily

297   subjective scoring, underscores the importance of introducing continuous cough frequency

298   monitoring. Furthermore, understanding the significance of day-to-day cough variability is essential

299   for both clinical practice and in clinical trials.

300

REFERENCES

1. Morice AH, Fontana GA, Belvisi MG, Birring SS, Chung KF, Dicpinigaitis PV, Kastelik JA, McGarvey LP, Smith JA, Tatar M, Widdicombe J, European Respiratory S (2007) ERS guidelines on the assessment of cough. Eur Respir J 29 (6):1256-1276

2. Crooks MG, den Brinker AC, Thackray-Nocera S, van Dinther R, Wright CE, Morice AH (2021) Domiciliary Cough Monitoring for the Prediction of COPD Exacerbations. Lung 199 (2):131-137

3. Faruqi S, Sykes DL, Crooks MG, Brindle K, Thompson J, Morice AH (2020) Objective Assessment of Cough: An Early Marker of Response to Biological Therapies in Asthma? Lung 198 (5):767-770

4. Do W, Russell R, Wheeler C, Javed H, Dogan C, Cunningham G, Khanna V, De Vos M, Satia I, Bafadhel M (2022) Performance of cough monitoring by Albus Home, a contactless and automated system for nocturnal respiratory monitoring at home. ERJ Open Research 8 (4)

5. Porter P, Brisbane J, Abeyratne U, Bear N, Claxton S (2022) A smartphone-based algorithm comprising cough analysis and patient-reported symptoms identifies acute exacerbations of asthma: a prospective, double blind, diagnostic accuracy study. J Asthma:1-9

6. Huddart S, Asege L, Jaganath D, Golla M, Dang H, Lovelina L, Derendinger B, Andama A, Christopher D, Nhung N (2023) Continuous cough monitoring: a novel digital biomarker for TB diagnosis and treatment response monitoring. Int J Tuberc Lung Dis 27 (3):221-222

7. Altshuler E, Tannir B, Jolicoeur G, Rudd M, Saleem C, Cherabuddi K, Dore DH, Nagarsheth P, Brew J, Small PM, Glenn Morris J, Grandjean Lapierre S (2023) Digital cough monitoring - A potential predictive acoustic biomarker of clinical outcomes in hospitalized COVID-19 patients. J Biomed Inform 138:104283

8. Gabaldón-Figueira JC, Keen E, Giménez G, Orrillo V, Blavia I, Doré DH, Armendáriz N, Chaccour J, Fernandez-Montero A, Bartolomé J (2022) Acoustic surveillance of cough for detecting respiratory disease using artificial intelligence. ERJ Open Research 8 (2)

9. Tinschert P, Rassouli F, Barata F, Steurer-Stey C, Fleisch E, Puhan MA, Kowatsch T, Brutsche MH (2020) Nocturnal cough and sleep quality to assess asthma control and predict attacks. J Asthma Allergy:669-678

10. Zhang M, Brindle K, Robinson M, Ingram D, Cavany T, Morice A (2022) Chronic cough in cystic fibrosis: the effect of modulator therapy on objective 24-h cough monitoring. ERJ Open Research 8 (2)

333   11.   McGarvey L, Gibson PG (2019) What is chronic cough? Terminology. J Allergy Clin Immunol
334   Pract 7 (6):1711-1714

335   12.   Morice AH, Millqvist E, Bieksiene K et al. (2020) ERS guidelines on the diagnosis and
336   treatment of chronic cough in adults and children. Eur Respir J 55 (1)

337   13.   McGarvey LP, Birring SS, Morice AH et al. (2022) Efficacy and safety of gefapixant, a P2X(3)
338   receptor antagonist, in refractory chronic cough and unexplained chronic cough (COUGH-1
339   and COUGH-2): results from two double-blind, randomised, parallel-group, placebo-
340   controlled, phase 3 trials. Lancet 399 (10328):909-923

341   14.   Dicpinigaitis PV, Morice AH, Smith JA et al. (2023) Efficacy and Safety of Eliapixant in
342   Refractory Chronic Cough: The Randomized, Placebo-Controlled Phase 2b PAGANINI Study.
343   Lung 201 (3):255-266

344   15.   McGarvey L, Smith JA, Morice A et al. (2023) A Randomized, Double-Blind, Placebo-
345   Controlled, Parallel-Group Phase 2b Trial of P2X3 Receptor Antagonist Sivopixant for
346   Refractory or Unexplained Chronic Cough. Lung 201 (1):25-35

347   16.   Birring SS, Fleming T, Matos S, Raj AA, Evans DH, Pavord ID (2008) The Leicester Cough
348   Monitor: preliminary validation of an automated cough detection system in chronic cough.
349   Eur Respir J 31 (5):1013-1018

350   17.   Smith JA, Holt K, Dockry R, Sen S, Sheppard K, Turner P, Czyzyk P, McGuinness K (2021)
351   Performance of a digital signal processing algorithm for the accurate quantification of cough
352   frequency. Eur Respir J 58 (2)

353   18.   Kang YR, Oh JY, Lee JH, Small PM, Chung KF, Song WJ (2022) Long-COVID severe refractory
354   cough: discussion of a case with 6-week longitudinal cough characterization. Asia Pac Allergy
355   12 (2):e19

356   19.   Rudd M, Song W-J, Small PM (2022) The Statistics of Counting Coughs: Easy as 1, 2, 3? Lung
357   200 (5):531-537

358   20.   Rassouli F, Tinschert P, Barata F, Steurer-Stey C, Fleisch E, Puhan MA, Baty F, Kowatsch T,
359   Brutsche MH (2020) Characteristics of asthma-related nocturnal cough: a potential new
360   digital biomarker. Journal of Asthma and Allergy:649-657

361   21.   Liaqat D, Liaqat S, Chen JL, Sedaghat T, Gabel M, Rudzicz F, de Lara E Coughwatch: Real-
362   world cough detection using smartwatches. In: ICASSP 2021-2021 IEEE International
363   Conference on Acoustics, Speech and Signal Processing (ICASSP), 2021. IEEE, pp 8333-8337

364   22.   Jokić S, Cleres D, Rassouli F, Steurer-Stey C, Puhan MA, Brutsche M, Fleisch E, Barata F (2022)
365   TripletCough: cougher identification and verification from contact-free smartphone-based

366   audio recordings using metric learning. IEEE Journal of Biomedical and Health Informatics 26
367   (6):2746-2757

368 23. Kruizinga MD, Zhuparris A, Dessing E, Krol FJ, Sprij AJ, Doll RJ, Stuurman FE, Exadaktylos V,
369   Driessen GJ, Cohen AF (2022) Development and technical validation of a smartphone-based
370   pediatric cough detection algorithm. Pediatric Pulmonology 57 (3):761-767

371 24. Barata F, Cleres D, Tinschert P, Iris Shih CH, Rassouli F, Boesch M, Brutsche M, Fleisch E
372   (2023) Nighttime Continuous Contactless Smartphone-Based Cough Monitoring for the
373   Ward: Validation Study. JMIR Form Res 7:e38439

374 25. Shim J-S, Kim M-H, Lee SM, Kim S-H, Kwon J-W, Song C, Ahn K-M, Kang S-Y, Park H-K, Park H-
375   W (2023) An Artificial Intelligence Algorithm-based Smartphone Application for Daily Cough
376   Monitoring. Allergy

377 26. Kuhn M, Nalbant E, Kohlbrenner D, Alge M, Kuett L, Arvaji A, Sievi NA, Russi EW, Clarenbach
378   CF (2023) Validation of a small cough detector. ERJ Open Res 9 (1)

379 27. Gabaldón-Figueira JC, Keen E, Rudd M, Orrilo V, Blavia I, Chaccour J, Galvosas M, Small P,
380   Lapierre SG, Chaccour C (2022) Longitudinal passive cough monitoring and its implications
381   for detecting changes in clinical status. ERJ Open Research 8 (2)

382 28. Song DJ, Song WJ, Kwon JW et al. (2018) KAAACI Evidence-Based Clinical Practice Guidelines
383   for Chronic Cough in Adults and Children in Korea. Allergy Asthma Immunol Res 10 (6):591-
384   613

385 29. Gabaldon-Figueira JC, Brew J, Dore DH, Umashankar N, Chaccour J, Orrillo V, Tsang LY, Blavia
386   I, Fernandez-Montero A, Bartolome J, Grandjean Lapierre S, Chaccour C (2021) Digital
387   acoustic surveillance for early detection of respiratory disease outbreaks in Spain: a protocol
388   for an observational study. BMJ Open 11 (7):e051278

389 30. Vertigan AE, Kapela SL, Birring SS, Gibson PG (2021) Feasibility and clinical utility of
390   ambulatory cough monitoring in an outpatient clinical setting: a real-world retrospective
391   evaluation. ERJ Open Res 7 (4)

392 31. Kelsall A, Decalmer S, Webster D, Brown N, McGuinness K, Woodcock A, Smith J (2008) How
393   to quantify coughing: correlations with quality of life in chronic cough. European Respiratory
394   Journal 32 (1):175-179

395 32. Faruqi S, Thompson R, Wright C, Sheedy W, Morice AH (2011) Quantifying chronic cough:
396   objective versus subjective measurements. Respirology 16 (2):314-320

397 33. Birring SS, Matos S, Patel RB, Prudon B, Evans DH, Pavord ID (2006) Cough frequency, cough
398   sensitivity and health status in patients with chronic cough. Respir Med 100 (6):1105-1109

399   34.   Kum E, Guyatt GH, Devji T, Wang Y, Bakaa L, Lan L, Liu E, Mastrolonardo A, Couban R,

400   O'Byrne PM, Satia I (2021) Cough symptom severity in patients with refractory or

401   unexplained chronic cough: a systematic survey and conceptual framework. Eur Respir Rev

402   30 (161)

403   35.   Kum E, Guyatt GH, Munoz C et al. (2022) Assessing cough symptom severity in refractory or

404   unexplained chronic cough: findings from patient focus groups and an international expert

405   panel. ERJ Open Res 8 (1)

406

407 **Table 1.** Baseline patient characteristics according to study completion

Characteristic	Subjects who completed study protocols (n=43)	Subjects who did not complete study protocols (n=22)	P-value
Age, years[†]	47.0 [34.0 to 61.5]	46.5 [38.0 to 56.0]	0.967
Female sex (%)	33 (76.7)	13 (59.1)	0.233
BMI, kg/m^2[†]	23.6 [22.3 to 25.9]	23.9 [22.5 to 25.6]	0.857
Cough duration, months[†]	30.0 [4.0 to 120.0]	30.0 [4.0 to 120.0]	0.819
Previous diagnosis			
Asthma, n (%)	12 (27.9)	3 (13.6)	0.327
AR or CRS, n (%)	15 (34.9)	10 (45.5)	0.576
GERD, n (%)	8 (18.6)	6 (27.3)	0.627
Hypertension, n (%)	9 (20.9)	4 (18.2)	1.000
Never smoker, n (%)	33 (76.7)	17 (77.3)	0.999
FEV1/FVC, %[†]	82.0 [78.0 to 87.0]	82.0 [75.5 to 87.5]	0.764
FEV1% of predicted[†]	90.0 [83.0 to 95.0]	92.0 [85.5 to 100.0]	0.712
FVC% of predicted[†]	89.0 [82.0 to 98.0]	98.0 [82.5 to 104.5]	0.243
Abnormal chest X-ray, n (%)	7 (20.0)	6 (28.6)	0.683
FeNO, ppb[†]	17.0 [13.0 to 30.0]	11.0 [8.0 to 19.0]	0.011
CHQ[†]	10.0 [7.5 to 12.5]	10.0 [6.0 to 11.0]	0.573
Cough severity NRS[†]	7.0 [5.0 to 7.5]	5.0 [3.0 to 6.0]	0.015
LCQ[†]	9.7 [8.0;12.7]	11.4 [9.8 to 12.6]	0.238
Set-up time, seconds[†]	206 [170 to 230]	185 [170 to 191]	0.020

408   [†]Median [IQR]; AR, allergic rhinitis; BMI, body mass index; CHQ, Cough Hypersensitivity Questionnaire;

409   CRS, chronic rhinosinusitis; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in

410   the first second; FVC, forced vital capacity; GERD, gastroesophageal reflux disease; LCQ, Leicester

411   Cough Questionnaire; NRS, numeric rating scale.

412

413   **Table 2.** Adherence to continuous cough monitoring using the Hyfe Cough Tracker[*]

Subjects, n	43
Monitoring period in days, median [IQR]	13.9 [7.3 to 14.3]
Participants who continued recording for at least 5 days, n (%)	37 (86.0)
Adherence (%), median [IQR]	91 [74 to 100]
Adherence<50, n (%)	5 (11.6)
Adherence≥50, <75, n (%)	6 (14.0)
Adherence≥75, <85, n (%)	6 (14.0)
Adherence≥85, ≤100, n (%)	26 (60.5)

414   [*]Adherence was defined as the operation time of the application per the total expected monitoring

415   time.

416   **Table 3.** Comparison of patient characteristics according to adherence to continuous cough

417   monitoring

Characteristic	Adherence ≥85% (n=26)	Adherence <85% (n=17)	P-value
Age, years[†]	36.5 [29.0 to 53.0]	62.0 [47.0 to 65.0]	0.001
Female sex, n (%)	18 (69.2)	15 (88.2)	0.283
BMI, kg/m^2[†]	24.0 [21.5 to 26.5]	23.6 [23.0 to 24.5]	0.737
Cough duration, months[†]	12.0 [2.0 to 120.0]	48.0 [10.0 to 72.0]	0.344
Previous diagnosis			
Asthma, n (%)	4 (15.4)	8 (47.1)	0.055
AR or CRS, n (%)	9 (34.6)	6 (35.3)	1.000
GERD, n (%)	6 (23.1)	2 (11.8)	0.595
Hypertension, n (%)	5 (19.2)	4 (23.5)	1.000
Never smoker, n (%)	19 (73.1)	14 (82.4)	0.060
FEV1/FVC, %[†]	84.5 [81.0 to 87.5]	79.0 [74.0 to 83.0]	0.009
FEV1% of predicted[†]	91.5 [82.0 to 98.5]	89.0 [84.0 to 94.0]	0.653
FVC% of predicted[†]	87.5 [78.0 to 100.5]	89.0 [82.0 to 95.0]	0.731
FeNO, ppb[†]	19.0 [16.0 to 31.0]	14.0 [9.0 to 25.0]	0.128
Abnormal chest X-ray, n (%)	3 (14.3)	4 (28.6)	0.546
Cough monitoring duration (days)[†, ††]	14.0 [10.5 to 17.0]	13.0 [7.0 to 14.0]	0.214
CHQ at V1[†]	11.0 [8.0 to 13.0]	10.0 [6.0 to 12.0]	0.501
Cough severity NRS at V1[†]	6.5 [4.0 to 7.0]	7.0 [5.0 to 8.0]	0.389
Cough severity NRS at V2[†]	3.0 [2.0 to 4.0]	3.0 [1.2 to 4.0]	0.627
LCQ at V1[†]	9.5 [7.5 to 13.0]	10.2 [9.1 to 12.5]	0.517
LCQ at V2[†]	12.4 [9.1 to 14.9]	15.3 [12.2 to 18.5]	0.071

Hourly cough rate at V1, coughs/hour†	11.4 [3.4 to 27.2]	9.8 [4.4 to 12.0]	0.514
Hourly cough rate at V2, coughs/hour†	2.9 [0.6 to 9.4]	2.8 [0.7 to 6.0]	0.645

418   †Median (IQR)

419   ††Cough monitoring duration (in days) was calculated based on the time between the initiation and

420   termination of app usage.

421   AR, allergic rhinitis; BMI, body mass index; CHQ, Cough Hypersensitivity Questionnaire; CRS, chronic

422   rhinosinusitis; FEV1, forced expiratory volume in the first second; FeNO, fractional exhaled nitric oxide;

423   FVC, forced vital capacity; GERD, gastroesophageal reflux disease; LCQ, Leicester Cough Questionnaire.

424

425 **Table 4.** Time-series correlations for agreement between daily cough severity scores and hourly cough

426 rates and adherence in each subject

Subject	Spearman correlation between daily cough severity scores and hourly cough rates	Adherence for cough frequency monitoring
Case 001*	NA	1
Case 002	0.668	0.99
Case 003	0.561	1
Case 004	0.600	0.99
Case 005	-0.182	1
Case 006	0.498	1
Case 007	0.000	0.95
Case 008	-0.106	1
Case 009	0.204	1
Case 010	0.664	0.94
Case 011	-0.612	1
Case 012	0.934	0.95
Case 013	0.248	1
Case 014	0.116	1
Case 015	0.652	0.93
Case 016	-0.318	0.86
Case 017*	NA	0.89

|		
Case 018	0.863	0.88
Case 019	0.431	0.99
Case 020	0.692	1
Case 021	-0.158	0.91
Case 022	0.783	0.96
Case 023**	NA	0.95
Case 024	0.000	0.85
Case 025	0.094	0.98
Case 026	0.630	1

427 *Standard deviations were zero.

428 **Diary score was not recorded.

429   **Table 5.** User experience

Survey responses, %	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1. Monitoring cough frequency is important for cough treatment.	10	0	2	32	56
2. Monitoring cough frequency is helpful in cough treatment.	12	2	2	34	50
3. Overall, this cough monitoring tool was helpful.	16	10	4	32	38
4. This cough monitoring tool helped me identify when and how much I was coughing.	18	8	6	22	46
5. It helped me to see if my cough improved after treatment.	20	4	4	32	40
6. Overall, this cough monitoring tool was acceptable.	8	2	4	36	50
7. It was easy to learn how to use this cough monitoring tool.	6	4	0	28	62
8. This cough monitoring tool was easy to use.	6	8	2	18	66
9. It was comfortable to wear.	22	14	2	28	34
10. I wore it most of the time during the study period.	14	8	2	34	42
11. I am willing to use this cough monitoring tool in the future.	18	6	2	32	40

430

431   **Figure legends**

432   **Figure 1.** Spearman correlations between subjective cough scores and hourly cough rates in subjects with

433   adherence≥85% (n=26): Hourly cough rate compared with (A) Leicester Cough Questionnaire (LCQ) score, and
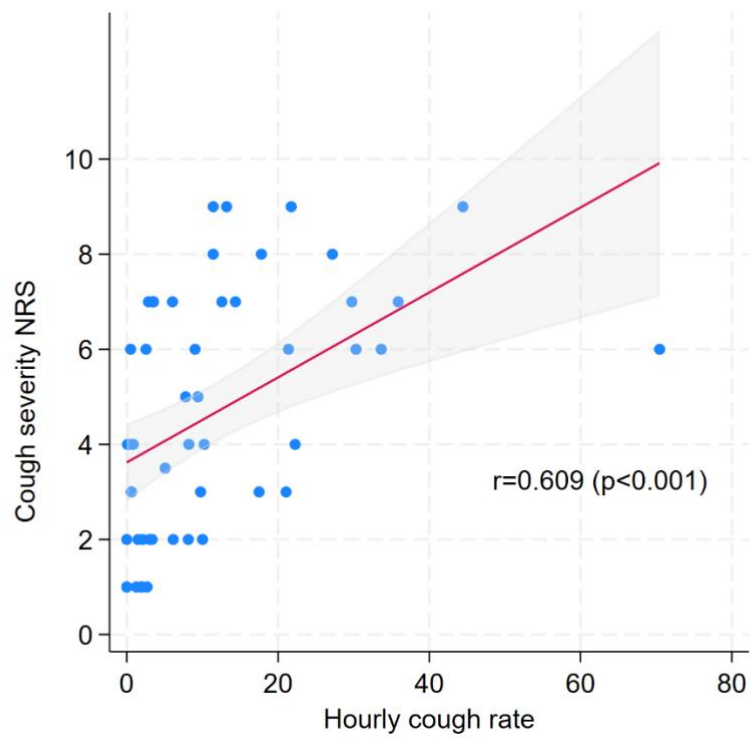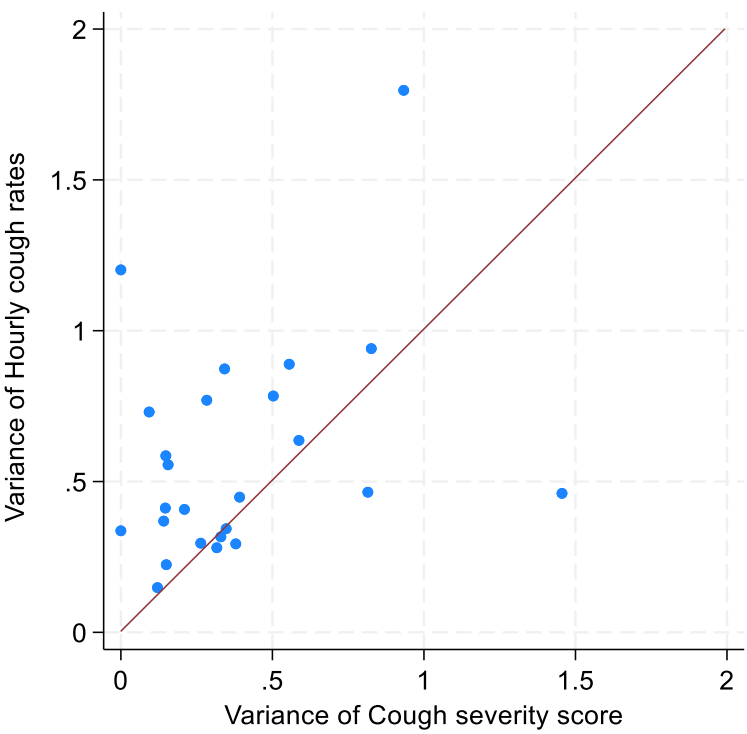
434   (B) cough severity numerical rating scale (NRS).

435

436

437

438
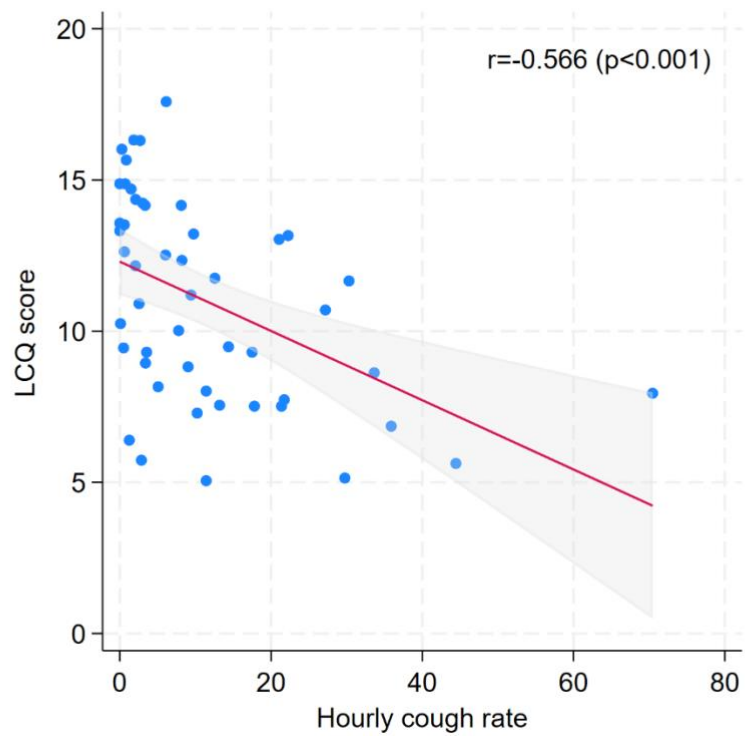
439   **Figure 2.** Longitudinal changes in hourly cough rate and daily cough severity diary score in individuals with

440   adherence≥85% (n=25). The x-axis represents the number of days since visit 1. The left y-axis denotes the

441   hourly cough rate for each day, while the right y-axis indicates the daily cough severity diary score.

442

443
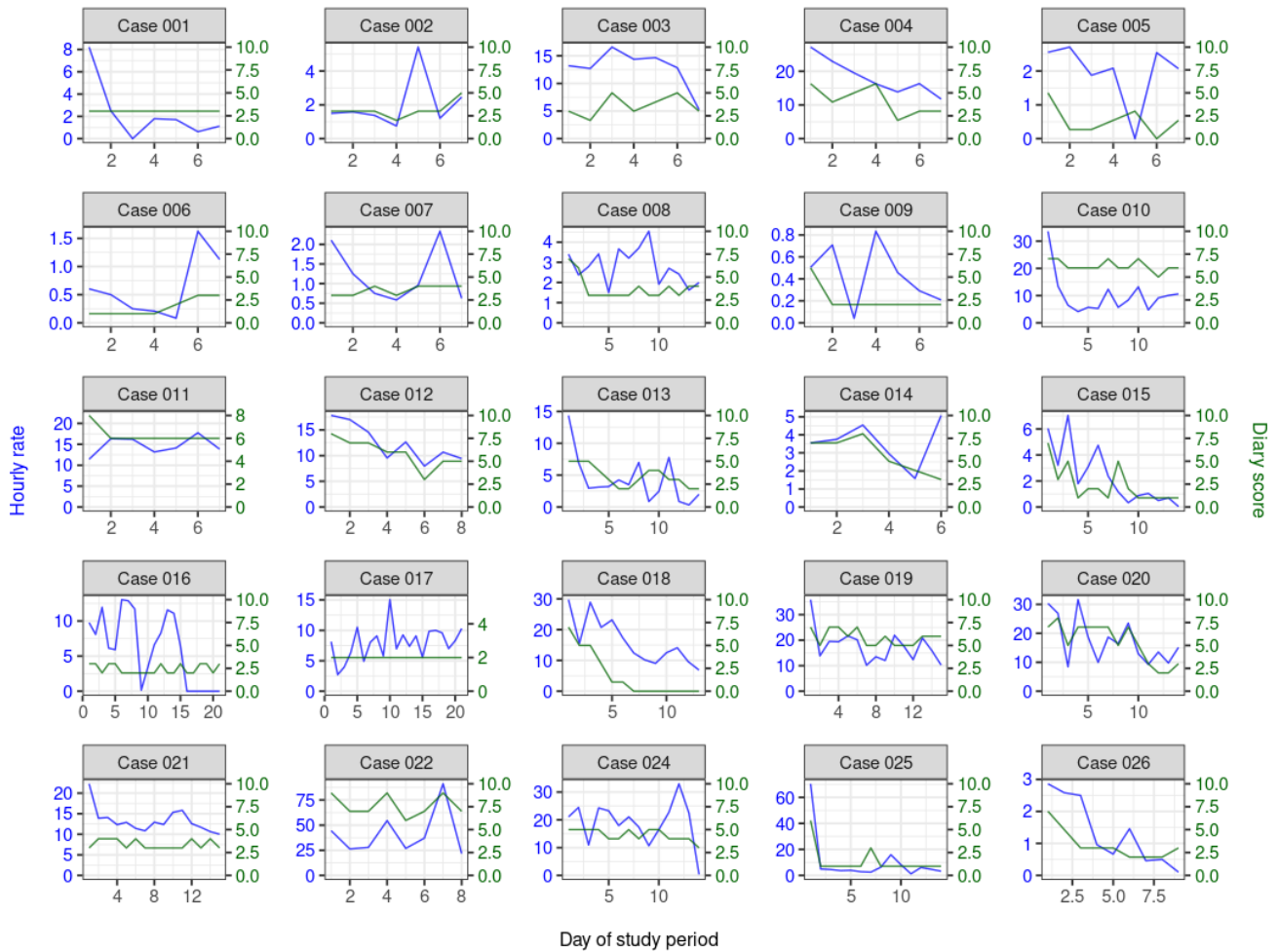
444   **Figure 3.** Scatter plot comparing variance indices of the daily cough severity diary score and hourly cough rate

445   in individuals with adherence≥85% (n=25). Each dot represents a subject, and the diagonal line is the reference

446   for an equal variance (1:1) between the cough severity score and hourly cough rate.

447

448