Early View

Original research article

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Acoustic surveillance of cough for detecting respiratory disease using artificial intelligence

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Take home message

Artificial intelligence software installed in smartphones can detect changes in cough frequency

associated to medical consultations. With adequate uptake and usage, these tools could help detect the

onset of respiratory disease in a population.

Clinical study registration number: NCT04762693

Abstract

Research question: Can smartphones be used to detect individual and population-level changes in cough frequency that correlate with the incidence of COVID-19 and other respiratory infections?

Methods: This was a prospective cohort study carried out in Pamplona (Spain) between 2020 and 2021 using artificial intelligence cough detection software. Changes in cough frequency around the time of medical consultation were evaluated using a randomization routine, significance was tested by comparing the distribution of cough frequencies to that obtained from a model of no difference. The correlation between changes of cough frequency and COVID-19 incidence was studied using an autoregressive moving average (ARIMA) analysis, and its strength determined by calculating its auto-correlation function (ACF). Predictors for the regular use of the system were studied using a linear regression. Overall user experience was evaluated with a satisfaction questionnaire and through focused group discussions.

Results: We followed up 616 participants and collected over 62,000 coughs. Coughs per hour surged around the time cohort subjects sought medical care (difference = +0.77 coughs/hour, p= 0.00001) There was a weak temporal correlation between aggregated coughs and the incidence of COVID-19 in the local population (ACF= 0.43). Technical issues affected uptake and regular use of the system.

Interpretation: Artificial intelligence systems can detect changes in cough frequency that temporarily correlate with the onset of clinical disease at the individual level. A clearer correlation with population-level COVID-19 incidence, or other respiratory conditions, could be achieved with better penetration and compliance with cough monitoring.

Introduction

Syndromic surveillance relies on the recognition of symptomatic patients by healthcare systems and proves challenging for identification of emerging, rapidly transmissible pathogens. (1)

Cough is a key symptom of most respiratory diseases, including infections of public health interest, like COVID-19, or influenza. Approximately 57% of all COVID-19 patients will develop cough during the early stages of infection and its presence is probably correlated with contagiousness. (2, 3) The ubiquitous presence of cough in respiratory infections, and its low frequency in healthy individuals make it an attractive marker for syndromic surveillance. (4)

The limited portability and automation of existing cough monitoring limits their usefulness for protracted use. Furthermore, none has so far been used to monitor community-level cough.(5) Incorporation of cough monitoring into epidemiological surveillance programs is also hampered by a limited understanding of the epidemiology of cough.

Artificial intelligence systems can be trained to recognize the well-described acoustic characteristics of cough. (6, 7) (8) These patterns can be identified by a wide range of machine learning techniques such as convolutional neural networks. (6, 9) The widespread use of smartphones provides an opportunity to deploy these systems at the scale needed to construct a community-based surveillance network. (10, 11) We hypothesized that these systems could detect changes in an individual's clinical condition, and that aggregated data could help estimate the incidence of respiratory infections, such as COVID-19. Although cough detection systems have been used in clinical research for years, this is the first attempt to apply such a tool on a community scale. (12-15)

Methods

Study subjects

Participants were recruited between November 2020 and June 2021 at the University of Navarra in Pamplona (Spain), and the neighboring communities of Zizur Mayor and the Cendea de Cizur. Recruitment strategies included direct solicitation, advertisements through municipal authorities, and the university's communication platform and social networks. Through these activities, we expected to reach up to 30,000 people.

Eligible participants needed to be 1) 13 years or older, 2) own an Android or iOS smartphone able to run Hyfe, 3) be willing to install and use Hyfe as instructed, 4) accept and comply with Hyfe's privacy policy and terms of use, 5) grant access to their medical records during their participation in the study, 6) visit the University of Navarra regularly, or be a current resident of Navarra. All participants provided informed consent. This project was approved by the Ethics Committee for Medical Research of Navarra (Pamplona, Spain, reference number: PI2020/107) and the Comité d'éthique à la recherche du Centre Hospitalier de l'Université de Montréal (Montréal, Canada, reference number: 2021-9247)

Study design

This was a prospective observational study. The primary objective was to assess the value of digital cough surveillance as a proxy for community incidence of COVID-19. Secondary objectives were to (i) determine if changes in cough frequency were associated with the moment of medical consultation, and (ii) quantitatively and qualitatively assess the barriers and facilitators to participation in smartphone-based acoustic surveillance programs. A full protocol describing sample size estimations and enrollment strategies was previously published. (11)

Methods

Participants were asked to monitor their cough using Hyfe Cough Tracker (henceforth referred to as Hyfe, https://www.hyfe.ai), a free, automated cough detection application, downloaded on their personal phones. Hyfe monitors ambient sounds without continuously recording. It uses a convolutional neural network (CNN) to analyze explosive sounds. A cough prediction score is assigned to each sound by the machine learning model, if this score lies above a predetermined threshold (in this study 0.7 out of a maximum score of 1), the sound is classified as a cough, stored in the participant's smartphone, and relayed to a cloud-based central dataset. Individual coughs detected at least 0.5 seconds from each other are counted independently. Preliminary data indicate that Hyfe has a sensitivity of 96.34% and a specificity of 96.54% differentiating coughs from other detected sounds. (11) Further validation to determine its performance when undetected explosive sounds are accounted for is underway [NCT05042063].

Participants were instructed to keep Hyfe active for at least 6 hours per day during the night-time, in order to minimize interference with normal day-time routines, but encouraged to use it continuously, if possible. They were instructed to monitor their cough for a 30-day period, with the possibility of prolonging their participation. Daily push notifications and periodic emails were sent to participants to maintain retention.

Study personnel reviewed medical records of participants every eight weeks at the Clínica Universidad de Navarra and the regional public health system (Osasunbidea), looking for consultations associated with a diagnosis of respiratory disease. During each round of reviews the national ID numbers of participants were searched in a centralized dataset, and registered consultations associated with respiratory symptoms (including COVID-19 screening tests), or a confirmed diagnosis of respiratory disease (COVID-19, influenza, respiratory syncytial virus, pneumonia, asthma, bronchitis, pharyngitis, chronic cough, chronic obstructive pulmonary disease, gastro-esophageal reflux disease, or other nonspecific respiratory

tract infections) was recorded. Daily incidence of COVID-19 in the study area was obtained from public sources (16).

Upon withdrawal, participants were instructed to rate the digital cough monitoring application on a 0-5 scale (0= very unsatisfactory, and 5=very satisfactory). Participants were divided into two groups, high (≥100 hours of monitoring) and low participation users (<100 hours of monitoring).

Participants were invited to join virtual focus group discussions (FGDs) to evaluate the importance given to cough and their experience using the digital cough monitoring application.

Analysis

The main outcome measure of this study was cough frequency (measured in coughs/person-hour). Secondary outcome measures included daily COVID-19 incidence in the study area, average daily usage of the application (measured in minutes/day), and the mean application's appreciation score (in a 0-5 scale).

Cough frequency and changes in clinical status

A medical consultation period was defined as the 10 days centered on the date of consultation (days -5 to +4, with day 0 being the date of consultation). All data outside of the consultation period were defined as the user's cough frequency history and further divided into a pre- (before day -5) and post-consultation history (after day +4). Participants who attended at least one medical consultation during the enrollment period and for which at least 24 hours of cough monitoring was achieved within and outside the consultation period were included in the analysis.

Comparison tests were carried out using a randomization routine, which protects results against bias from individual-level effects (large differences in user activity and/or cough rates) while preserving uncertainties inherent to low sample sizes. Cough rates during the consultation period and the

participant's whole history were calculated for each user, their differences (consultation - history) were determined. The mean of these differences is treated as the average effect size in the sampled population.

To determine the significance of this observed effect size, it was compared to a distribution of effect sizes that would be expected under a null model of no difference between the two levels. This was determined using 1,000 iterations of a randomization routine in which the user records were shuffled (specifically, the field indicating days since consultation), and the average of the users' cough rate difference was recalculated. This routine produced a null distribution of simulated effect sizes. The proportion of null values greater than the observed value is treated as a *p*-value.

Acoustic surveillance and COVID-19 incidence

Participants with at least one hour of cough monitoring were included in this analysis. Cough was aggregated in time to create a cough frequency curve. An epidemic curve including all cases of COVID-19 diagnosed in the study area was superposed to cough data. An autoregressive moving average (ARIMA) analysis was carried out to compare confirmed cases of COVID-19 with cough frequency in the cohort, excluding participants with less than an hour of data on any specific day. The strength of the association between both variables was expressed with the auto-correlation function (ACF). This parameter ranges from -1 to +1, with values closer to 1 representing a stronger association. This analysis was only carried out for COVID-19, due to the low circulation of other respiratory pathogens during the study period.

Usage and perception of the acoustic syndromic surveillance system

Predictors of regular use were evaluated using a linear regression model to compare differences in the average daily monitoring period by age, gender, operating system (Android or iOS), number of medical consultations during the study period, and number of email reminders sent to each participant.

Mean appreciation scores for the application from participants who completed the end-of-study questionnaire were disaggregated by operating systems and compared with a two-tailed unpaired t-test.

Barriers and facilitators for uptake and use were qualitatively assessed in FGDs.

Data was organized and analyzed using R Studio version 1·3 (RStudio Team, 2020. RStudio: Integrated Development for R. RStudio, PBC, Boston, MA), and SPSS Statistics version 28 (IBM Corp, Armonk, NY)

Results

Characteristics of the cohort

A total of 930 participants were enrolled. However, only 616 used the application for at least one hour (Figure 1). Although this is the largest cough cohort continually monitored to date, it represents just 1.7% of the 35,000 people estimated to have been reached in the recruitment campaign. Participants were aged 14-76 years, (Median: 21, IQR: 20-25), mostly female (64.9%) and iOS users (56%). In total, 178 (28.9%) participants registered more than 100 hours of monitoring, and 21 (3.4%) registered at least 240 hours, equivalent to ten days of continuous monitoring. The latter groups were older (median age for those with 100 hours or more: 50, IQR: 39-56), as presented in table 1.

Cough frequency is higher around the time of medical consultation

Two-hundred and seventy-two participants attended at least one medical consultation during the study period (425 consultations in total, supplementary material), 33 of whom had at least 24 hours of monitoring both during and outside the consultation period (Figure 1). For these 33 patients, hourly cough rates were higher during the consultation period, than during the rest of the monitoring history, with a difference of 0.77 coughs/hour (*p* value < 0.00001), equivalent to approximately 19 extra coughs per day. This effect was driven by lower cough rates during the post-consultation history (after day +4, difference:

1.08 coughs/hour, p < 0.00001). When exclusively compared to the pre-consultation history (before day - 5), cough rates were not significantly different (p= 0.855). (Figure 2, table 2) Similar results were observed when comparing subdivisions of the consultation period to the rest of the monitoring history (supplementary material).

Syndromic surveillance and COVID-19 incidence

Over 79,000 aggregated hours of monitoring, equivalent to 3,316 person-days (or 9.08 person-years) and 62,401 coughs were registered between November 2020, and August,2021 (n= 616 participants). Of these, 79% were recorded between 20:00 and 8:00. Peaks of coughs were registered in February, April-May, and August 2021 (Figure 3, panel B).

In total 14,051 cases of COVID-19 were diagnosed in the study area, in three clear waves: in January and February, late March, and April, and between July and August 2021 (Figure 3, panel A). Only 72 new cases were diagnosed among study participants (51 of which occurred among participants who recorded one hour or more).

Cough frequency in the cohort and COVID-19 incidence in the population correlated, notably during the first and last waves (Figure 3, panel A and B). The ARIMA model analysis confirmed this association which reached maximum strength (ACF= 0.43) when lagging the cough time series by 17 days compared to the COVID-19 incidence. This indicates that cough increased, in average, 17 days after peaks in COVID-19 cases.

The number of users registering coughs changed throughout the study period such that changes in cough frequency were based on a diminishing number of participants (Figure 3, panel D). Specifically, during the February COVID-19 wave, approximately 40 participants were contributing a combined total of over 555 hours of monitoring time per day. At the time of the third peak there were only about 12 participants

contributing 111 hours of monitoring time per day. Upon closer inspection, it was noted that almost half of all coughs registered during this wave came from a single chronic cougher who did not have COVID-19. Further investigation revealed that during this period, her cough increased to approximately 400 per day, following the discontinuation of antitussive medication. The smaller peak observed in February also coincides with this participant's recruitment into the study.

While the peak in coughs during the summer remains evident after excluding this participant from the ARIMA model (Figure 3, panel C), the strength of the correlation markedly reduced (ACF= 0.28), indicating that given the low number of participants, trends were influenced by one person with severe chronic cough.

Usage and perception of the application

Participants with at least 1 hour of monitoring (n=616) registered an average of 130 hours of total data (range: 1 to 5000 hours) and used the application for an average of 336 minutes/day (SD: +/- 188 minutes), equivalent to 5.6 hours. Average daily usage was discretely increased in participants who received more email reminders ($\mathbb{Z}=5$ minutes per reminder, p < 0.001), and those older ($\mathbb{Z}=4.5$ minutes per year, p < 0.001). On the contrary, using iOS rather than Android was associated with significantly reduced daily usage time ($\mathbb{Z}=-103$ minutes, p < 0.001). Results for other predictors can be found in the supplementary material.

The average appreciation score was 3.6, n=217, SD: +/-1.02). Scores were also higher among Android users (3.82, 95%CI: 3.64 - 4.00), compared to iOS users (3.38, 95%CI 3.18-3.58, p= 0.001). The most common reason to withdraw were technical problems while running the application (95, 43.8%), mostly among iOS users (60 out of 95, supplementary material).

Nine participants took part in FGDs. Participants were aged 21 to 65 years (median= 48 years). Two were male (22.2%) and seven female (77.8%). Seven belonged to the high usage group (registered 100 hours or more), while two belonged to the low usage group. In the former, cough was perceived as important only if it affected daily routines, either because it was associated with a known respiratory disease, or with certain lifestyle characteristics, such as smoking. The main motivator behind constant usage was interest in helping the study team, with little importance given to its perceived health benefits. However, two participants with a history of chronic respiratory disease indicated that seeing changes in longitudinal cough trends, and their link to certain behaviors, were important motivators. Notifications were not well received in the low participation group. Repeated bugs in the iOS version were noted in both groups, confirming results from the quantitative analysis. Summary tables with common answers provided by participants can be found in the supplementary material.

Discussion

This is the first population-based syndromic surveillance study using passive digital cough monitoring. Over the course of the study, we monitored over 9 years of person-time and detected 62,000 cough sounds. We showed that cough monitoring can detect changes in cough frequencies at individual and community levels.

Our observation that cough frequency is higher around the time that individuals seek medical care suggests that passively detected changes in cough patterns could be noticed by participants, and partially influence health-seeking behaviors. While it is true that other symptoms apart from cough are likely to contribute to this process, these findings suggest that upon further refinement, smartphone-based tools could be used to detect changes of clinical relevance in cough patterns, in the context of patient monitoring, or evaluation of response to treatment. These changes were driven by reductions after the 5 days following consultations. The lack of a significant difference with the pre-consultation history is likely

a result of the fact that many of these participants were recruited during COVID-19 testing sessions, when many were already symptomatic, making their pre-consultation history short or non-existing

We also demonstrated that longitudinal changes in aggregate cough data from this cohort were temporally associated with the incidence of COVID-19 in the community. However, the causal nature of this association is challenged by the fact that the cough frequency peaked, on average, 17 days after COVID-19 incidence, long after the period within which most symptoms of mild infection resolve. (17)

Further confounding in this association came from a large proportion of coughs originated by a single individual with chronic cough. As discussed below, the lack of a stronger temporal association is likely caused by a low population coverage, and the low incidence of COVID-19 in the cohort. It may also be due to a low percentage of patients experiencing cough, confounding by other infectious and non-infectious causes of cough within the cohort, or exposure to other environmental tussive stimuli.

Nonetheless, the fact that the association remains visible in more than one COVID-19 wave, and after removing the chronic cougher, might indicate that some subjects in the cohort were infected in the last part of a community wave and remained undiagnosed.

Limitations

This study failed to reach an adequate uptake to produce representative data of the population (only 1.7% of the estimated reached individuals ended up using the application). Similarly, only 2/3 of these participants provided useful data, and only 21 used it regularly throughout the study period. Addressing these issues seems complicated, considering low uptakes reported for similar contact tracing software in the past. (18). Larger multicentric projects, ideally supported by public health authorities, might help increase the number of participants in future studies.

Another important limitation is the fact that participants were instructed to preferentially monitor night-time cough. While this likely facilitated compliance by reducing interference with routine cell phone use, sleep is an inhibitor of cough, (19) and we in fact, observed a higher cough frequency from 10 am to 8 pm, with coughs sharply reducing after midnight (REF to ERJOR-00001-2022). This means that the value of longer monitoring periods will rely on longer daytime monitoring. The fact that technical problems were the leading cause for discontinuation is encouraging, as these are solvable engineering challenges, many of which have already been implemented, indicating that future studies with protracted daytime monitoring time are feasible. Human factors of maintaining interest and ensuring privacy may be harder to address.

The fact that only a few participants were monitoring their cough regularly also made the results susceptible to the effect of outliers, as was indeed observed, with large changes in the cohort's aggregated cough rate being driven by a single participant with chronic cough. Despite this, the fact that a modest correlation remained visible after excluding this participant, and the system's capacity to detect changes in cough frequency associated to medical consultations are encouraging.

It is also possible that the monitoring system detected background coughs, not produced by study participants, particularly if they used it while visiting crowded areas. The fact that participants were mostly instructed to use the application at night and in their homes, as well as the fact that louder sounds are more likely to trigger the classification algorithm, are expected to limit this confounding effect, but this should be explored in future studies.

Acoustic surveillance systems are technically capable of detecting changes in cough frequency associated with the onset and evolution of respiratory disease in individuals and populations. However, the discussed limitations prevented us from reliably responding to whether they can be used to infer the incidence of respiratory disease.

Authors contributions

Conceptualization: SGL, JCGF, CCh. Methodology: SGL, JCGF, CCh, EK, GG, NU. Software: EK, GG. Formal analysis: JCGF, EK, GG, NU. Investigation: JCGF, CCh, VO, IB, NA, JCh, AFM, JB. Data Curation: JCGF, CCh. Writing - Original Draft: JCGF, CCh. Writing - Review & Editing: all authors. Visualization: EK, GG. Funding acquisition: SGL

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Competing interests

EK, GG, and PS are employees of Hyfe, Inc. CCh has received consultancy fees and owns equity in Hyfe Inc.

All other authors declare no conflict of interest.

Data availability statement

Datasets including deidentified records with the date of medical consultation of individual participants, responses to the satisfaction questionnaire, and individual cough and monitoring data are available upon request from this <u>direction</u>. A complete study protocol, including the statistical analysis plan, and samples of informed consent forms has been published (11), and can also be found on <u>www.clinicaltrials.gov</u> under the registration number NCT04762693.

Table 1: Cohort characteristics and cough monitoring periods

	Recruited	One hour	100 hours	240 hours	
Median age (IQR)	21 (20-24)	21 (20-25)	25 (21-50)	50 (39-56)	
Operating System					
Android Users (%)	366 (39-4)	269 (43·7)	127 (71·3)	18 (85·7)	
iOS users (%)	559 (60·1)	345 (56)	51 (28·7)	3(14·3)	
Not specified (%)	5 (0.5)	2 (0.3)	0		0
Total	930	616	178	:	21

Table 2: Changes in cough rates during the consultation period and participant monitoring history

Compared groups (Day 0= Date of consultation)		n	Observed difference in cough rate (coughs/hour) Mean cough rate (SD)	<i>p</i> -value
Consultation period (days -5 to +4)	Full user history	33	+0·77 (2·62)	< 0.00001
	Pre-consultation history (before day -5)	23	-0·25 (1·89)	0.855
	Post-consultation history (after day +4)	29	+1.08 (2.92)	< 0.00001

Figure legends

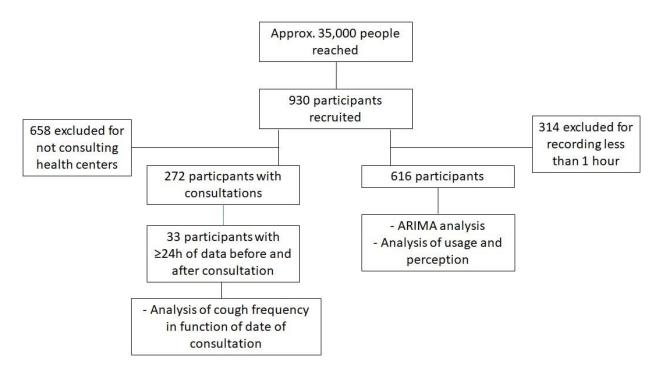


Figure 1: Flow chart of participants analysed in the study

Approximately 35,000 people were estimated to have been reached via social network information campaigns. Of these, 930 were enrolled in the study. Only 616 participants recorded data for one hour or more, and were therefore included in the ARIMA and usage analyses. Similarly, only 272 participants consulted medical services during the study period. Of these, only 33 recorded at least 24 hours of data both in, and outside the consultation period, and were included in the analysis of cough frequency changes in function of consultation dates.

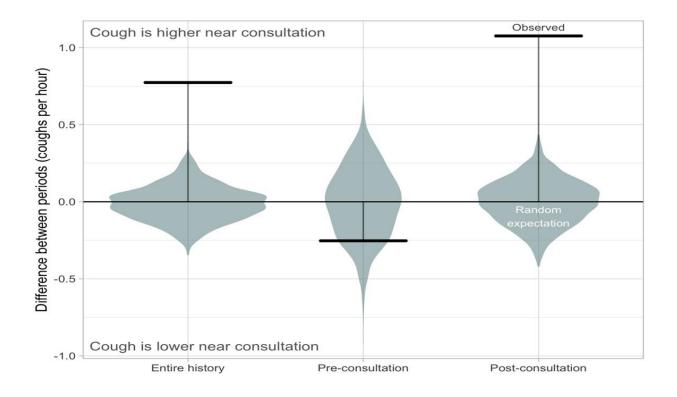


Figure 2: Difference between cough rates in the consultation period compared to the participants' monitoring history

Cough frequency during the consultation period is compared to the entire monitoring history (n=33), and the parsed pre-(n=23) and post-consultation history (n=29). Shaded areas represent the distribution of effect sizes predicted under a null model of no difference. The black line represents the actual observed difference between the consultation period and compared periods. Cough frequency during the consultation period significantly increased when compared to the entire history and the post-consultation history (p < 0.00001 in both cases), but not when compared to the pre-consultation history (p = 0.855)

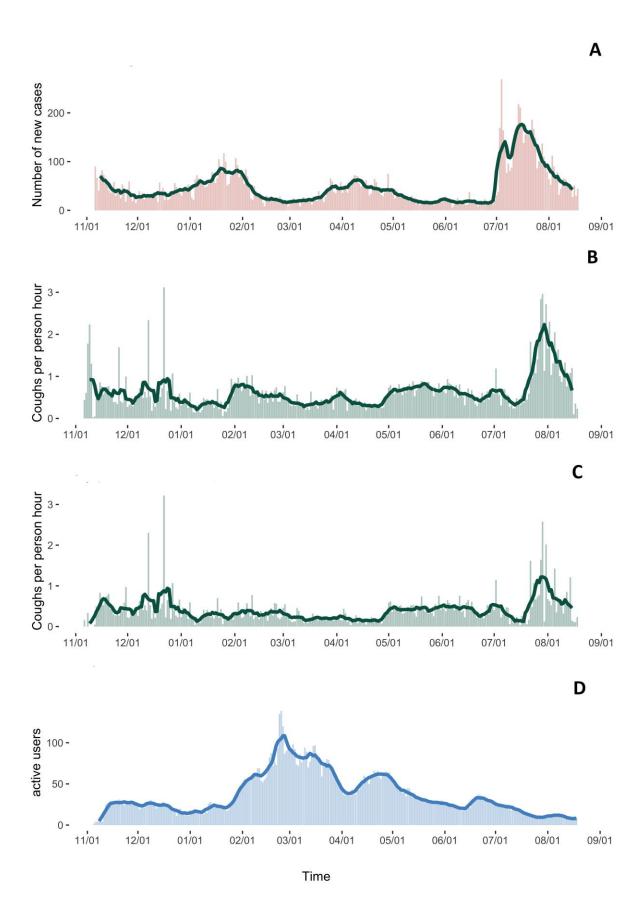


Figure 3: Cough and usage trends compared to COVID-19 incidence.

Incidence of COVID-19 in the entire study area (A) compared to the evolution of cough trends in the monitored cohort (B), after the exclusion of the participant with chronic cough C) and compared to the number of active users (D). The continuous line represents the 7-day rolling average.

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Supplementary Material

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Changes in cough rate around the time of medical consultation

Figure 1: Diagram of time windows compared among participants who registered medical consultations

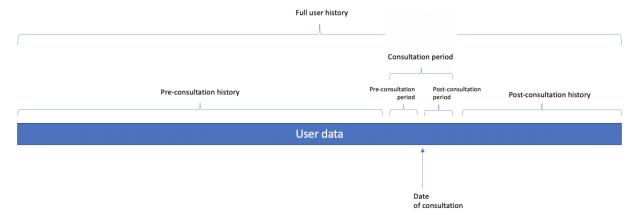
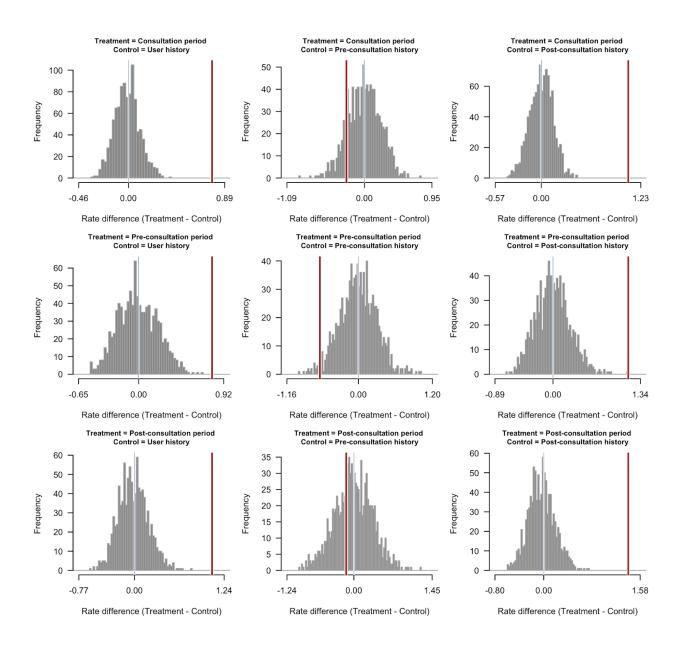


Table 1: Changes in cough rates during the two components of the consultation period

Compared groups (Day 0= Date of consultation)		n	Observed difference in cough rate (coughs/hour) Mean cough rate (SD)	p-value
Pre-consultation period (days -5 to -1)	Full user history	22	0.79 (3.24)	< 0.00001
	Pre-consultation history (before day -5)	18	-0.62 (1.80)	0.980
	Post-consultation history (after day+4)	19	1.15 (3.63)	< 0.00001
Post-consultation period (days 0 to +4	Full user history	27	1-07 (2.91)	< 0.00001
	Pre-consultation history (before day -5)	18	-0.14 (2.41)	0.662
	Post-consultation history (after day+4)	25	1.38 (3.15)	< 0.00001

Figure 2: Observed cough differences compared with expected effect size distributions under the null hypothesis between different monitoring periods.



Results of the randomization analysis. Each pane represents the results of a single comparison test between the cough rates in a treatment period (e.g., consultation period) and a control period (e.g., remainder of user history). The grey histogram represents the distribution of differences expected under a null model of no pattern/random chance. These

distributions are centered about zero (white/blue line). The red line represents the actual difference observed. If the none (or very little) of the null distribution is bisected by the red line, that observation cannot be explained as a byproduct of random chance.

Table 2: Diagnoses associated with respiratory symptomatology in the studied cohort

Final diagnosis	n	%
Unspecified upper respiratory symptomatology	247	58.1
COVID-19	72	16.9
Contact with COVID-19 case	38	8.9
COVID-19 (follow up visits)	29	6.8
Tonsillitis	15	3.5
Sinusitis/rhinitis	10	2.4
Acute gastroenteritis	3	0.7
Chronic cough of unknown cause	3	0.7
Asthma crisis	2	0.5
Bronchial hyperresponsiveness	1	0.2
Allergic bronchopulmonary aspergillosis	1	0.2
Dyspnoea of unknown cause	1	0.2
GERD	1	0.2
Otitis	1	0.2
Pulmonary nodule under evaluation	1	0.2
Total	425	100.0

GERD: Gastroesophageal reflux disease.

Analysis of predictors of usage

Table 3: Descriptive statistics of the cohort

	N	Minimum	Maximum	Mean	Std. Deviation
Total visits	616	0	6	0.49	0.925
Total reminders	616	0	16	7.09	3.991
Female	616	0	1	0.65	0.478
Age	609	14	76	26.57	11.688
Self. Rep History of Resp. Disease	616	0	1	0.7	0.459
Total conditions reported	616	0	9	1.53	1.549

iOS/Android	616	0	1	0.56	0.497
Coughs	616	0	149.9289	2.066626	8.325265
Seconds of usage	616	791.1667	83298.09	20162.28	11257-28
Valid N (listwise)	608				

Table 4: Linear regression, dependent variable is seconds of application usage

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	В	Std. Error	Beta		
(Constant)	11125.55	56419.49		0.197	0.844
Day of recruitment	0.065	1.273	0.002	0.051	0.959
Total visits	-23.211	419.821	-0.002	-0.055	0.956
Total reminders	307.431	103.268	0.11	2.977	0.003
Female	1370.449	810.428	0.059	1.691	0.091
Age	218.511	35.406	0.232	6.172	0.001
Self. Rep. Hist	780.591	1065.618	0.032	0.733	0.464
Total conditions	-441.354	319.359	-0.062	-1.382	0.167
iOS/Android	-6187.88	785.623	-0.278	-7.876	0.001
Coughs	368.685	47.471	0.28	7.767	0.001

Table 5: Causes of withdrawal among participants who completed the end-of-study questionnaire

Reason for withdrawal	Operating system					
	Android		iOS	Unknown	To	otal
Completion of requested period		20	3			23
Loss of interest		33	38		2	73
Privacy concerns		10	5			15
Technical issues		35	60			95
Other		3	2			5
Unknown		3	3			6
Total		104	111		2	217

Table 6: Response patterns observed in the heavy use group (over 100 hours monitored)

Key aspect	P1 (Female, Apple, 65 years)	P2 (Female, Android, 39 years)	P3 (Female, Android, 61 years)	P4 (Female, Android, 56 years)	P5 (Female, Apple, 36 years)	P6 (Male, Android, 35 years)	P9 (Male, Apple, 48 years)
Is cough important?	 Depends if sick or not. Number less important than changes in trend. 	Not important Checks number out of curiosity.	 Relationship with smoking is important. Interest in increases with smoking. 	 Important as it affects daily routines. Exact number not important but checks regularly. 	Not important.Number of coughs less important than trends.	 Only if repetitive or annoying. More important in the context of covid-19. 	Not important.
What worked?	 Only records snippets. Automatic detection of cough. 	 Simplicity Ability to access recorded cough sounds. Provides more information than other health apps. 	 Continuous monitoring. Ability to detect changes related to smoking. 	• Simplicity	 Notifications. Possibility of seeing changes in cough patterns. 	Ability to access recorded sounds.	 Simplicity and ease of use. Possibility of programming reminders and notifications. Easier to use than other health apps.
What did not work?	• Regular crashes in iPhones.	• Irregular notifications and easy to forget.	No complaints. Thinks the app works perfectly.	Lags when checking old records.	 Regular crashes in iPhone. Monitoring interrupted without warning. Boring interface. 	 The app catches other people's coughs. Inability to create different user profiles in one device. Need to activate it every day. 	It should start and stop automatically at certain times. High data consumption when not connected to Wi-Fi
What motivates?	Seeing changes in real time.	Helping the research team.Curiosity.	Providing valuable results.Seeing relationship with smoking.	• Seeing the effect of treatment on coughs.	Regular notifications.Seeing changes in time.	Collaborate with the research team.	Personal commitment with the study.
Can monitoring improve health?	• Gives an objective picture of progress.	• Only in people with resp. disease.	It helps modify a damaging behaviour (smoking)	Does not help because the cause of the cough remains unknown.	Only in people with resp. disease or risk exposure.	Additional information can help doctors.	Only if provides recommendations

Table 6 (continued): Response patterns observed in the heavy use group (over 100 hours monitored)

Key aspect	P1 (Female, Apple, 65 years)	P2 (Female, Android, 39 years)	P3 (Female, Android, 61 years)	P4 (Female, Android, 56 years)	P5 (Female, Apple, 36 years)	P6 (Male, Android, 35 years)	P9 (Male, Apple, 48 years)
How to improve the app?	 Correct regular crashes. 	• Correct some details.	• Include medical recommendations.	• No suggestions.	Make it more interactive. Increase automatization	 Program sessions to start automatically. Improve the algorithm to differentiate coughs from different people. Focus development on people with respiratory disease. 	 Allow sessions to start and stop automatically. Include an option to only upload data using Wi-Fi networks.

Table 7: Response patterns observed in participants in the light use group (less than 100 hours recorded)

Key aspect	P7 (Female, Apple, 21 years)	P8 (Female, Android, 54 years)		
Is sough important?	It's annoying, notices it when persists in time.	Not important		
Is cough important?	Objective number is important to evaluate adequately.	Does not pay attention to frequency.		
	Simplicity and accessibility.			
What worked?	No need for extensive input from user.	Simplicity and pretty design.		
		Not useful.		
What did not work?	Very easy to forget to turn it on, particularly if busy or stressed.	Daily registries of cough and reminders were stressing.		
		Need to remember to turn it on daily.		
What motivates?	Interest in the study and potential utility in the covid-19 pandemic.	Nothing. Not perceived useful.		

Table 7 (continued): Response patterns observed in participants in the light use group (less than 100 hours recorded)

Key aspect	P7 (Female, Apple, 21 years)	P8 (Female, Android, 54 years)
Can monitoring improve health?	Provides accurate picture of impact in everyday life.	Only in people with resp. disease.
How to improve the app?	Program sessions to start and stop automatically.	Does not know.