Continuous digital cough monitoring during 6-month pulmonary tuberculosis treatment

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Cough counts rapidly drop in the intensive phase and remain at a low level by the end of successful TB treatment. Continuous cough monitoring is feasible in low-resource settings. Improvement is needed to optimise its use as treatment response biomarker. https://bit.ly/4eKoo2k

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Abstract

Background Recent advances in digital and wearable technologies with artificial intelligence (AI) enable the use of continuous cough monitoring (CCM) to objectively monitor symptoms as surrogate markers of treatment efficacy in pulmonary tuberculosis (PTB). The objectives of this study were to describe the evolution of cough during PTB treatment in adults and to assess the feasibility of community-based CCM.

Methods We prospectively enrolled PTB adult participants upon treatment initiation. Participants' coughs were continuously monitored during 6 months with a smartphone loaded with an app able to detect cough by using an AI algorithm.

Results 22 participants were included. The median (interquartile range (IQR)) age was 28.5 (22–42) years and 62% were male. The median (IQR) coughs per hour (medCPH) was 11.0 (7.0–27.0) at week 1. By the end of the intensive phase of PTB treatment at week 8, the medCPH was 3.5 (1.5–7.0), which was significantly lower than the medCPH at week 1 (p=0.002). At week 26 (end of treatment), the medCPH was 1.0 (1.0–2.5). The adherence to CCM was high during the first 13 weeks of PTB treatment and then waned over time. The adherence was similar during daytime and night-time.

Conclusion Cough counts rapidly drop during the intensive phase of PTB treatment and then slowly decrease to a low baseline level by the end of the treatment. Community-based CCM using digital technology is feasible in low-resource settings but requires evaluation of alternative approaches to overcome adherence issues and technical limitations (mobile internet and electricity availability).

Introduction

Tuberculosis (TB) remains a major public health challenge in low- and middle-income countries, particularly in African and South-East Asia regions [1]. In 2022, the World Health Organization estimated that 10.6 million individuals developed TB, but only 7.5 million cases were diagnosed and notified [1]. This gap is partly attributable to limited access to screening and diagnosis testing, especially at the community level [2]. In Madagascar, the estimated incidence of TB is 233 cases per 100 000 inhabitants, with 46 420 cases of all forms of TB notified in 2023 [3]. TB most frequently presents as a pulmonary disease although extrapulmonary manifestations occur in 10–42% of cases [4]. Cough is a common clinical

symptom of active pulmonary TB (PTB) and cough duration ⩾2 weeks often serves as a clinical screening marker [5, 6]. However, cough is a complex symptom that can be evaluated using several of its characteristics, including cough duration, cough counts and cough sound features [7–9]. With the development of objective tools that can be used to assess cough counts, there is a growing interest in ambulatory cough monitoring for various respiratory diseases, including TB [10]. Early cough monitoring systems have demonstrated high accuracy for cough detection but have several limitations, including poor ergonomics for patients, recording time generally limited to 24 h due to battery and internal storage memory capacity, and the need for manual sound processing, which considerably limit their potential usefulness in long-term continuous cough monitoring (CCM) in ambulatory settings [7, 10]. Recent advances in mobile device technology, such as smartphones, combined with artificial intelligence (AI) sound processing models have facilitated cough detection and recording, and have enhanced the ways in which cough sounds can be processed and analysed [7].

Studies have suggested that cough is correlated with microbiological outcome in TB, making it an interesting biomarker for assessing treatment response and outcome [11, 12]. Current existing and recommended methods to assess anti-TB treatment response have limitations. Both sputum smear microscopy and mycobacterial culture have low sensitivity and moderate specificity for predicting treatment response, and need sputum samples which are not always available across all TB populations and amongst patients responding well to TB treatment [13, 14]. In addition, mycobacterial culture is not widely available and requires a long turnaround time [15]. Chest radiography is also used for treatment monitoring but is limited by interobserver variability and may not be accurate to predict treatment failure or relapse [16]. Clinical symptoms assessment during anti-TB treatment is recommended and is simple, but is subject to interobserver variability and lack of measurement objectivity [13].

A previous study assessed the evolution of cough counts in 64 adult PTB patients for 62 days following treatment initiation with continuous recording for the first 2 weeks and then at three specific time-points until the end of the study follow-up period [17]. The study found a significant decrease in cough counts during the first 14 days of TB treatment, which continued until the end of the study follow-up period [17]. However, the study used an obtrusive audio recording device with a lapel mini-microphone, a separate recorder and an external battery attached to the participant's waist [18]. A more recent study explored CCM using the Hyfe Research smartphone app amongst 565 suspected PTB patients in high TB burden countries and explored its feasibility and its potential as a biomarker for monitoring treatment response [19]. In that study, participants were monitored 24 h a day for 14 days [19]. The use of a smartphone in that recent study offers the advantage of operating with a device commonly used in everyday life that has a trivial impact on the participant's routine [10, 19]. Monitoring coughs continuously for a longer period would be valuable especially when assessing treatment response as the treatment for PTB would last at least 6 months for drug-susceptible TB and longer for drug-resistant TB.

In this proof-of-concept study, we assessed smartphone-based CCM over the full 6 months of standard PTB treatment. The aims of this study were: 1) to describe the evolution of cough amongst adult PTB patients over the course of 6 months of standard TB treatment and 2) to assess the feasibility of community-based CCM in adult PTB patients in Madagascar.

Methods

Study design, setting and population

We conducted a prospective cohort study in two clinical sites in Madagascar (Antananarivo and Fianarantsoa) from September 2021 to March 2022. We enrolled participants aged ⩾18 years, presenting to five TB outpatient clinics in Antananarivo and eight TB outpatient clinics in Fianarantsoa. Eligible participants had a cough for >2 weeks and a clinical suspicion of PTB.

All study procedures took place in regional hospitals. Participants attending outpatient clinics in Antananarivo were directed to the Department of Infectious Diseases of the University Hospital Joseph Raseta Befelatanana and participants attending outpatient clinics in Fianarantsoa were directed to the Department of Infectious Diseases of the University Hospital Tambohobe.

Inclusion criteria

All participants were enrolled as part of a larger study that aimed to develop a TB screening classification algorithm [20]. All participants provided three sputum samples for PTB confirmation tests including smear microscopy using auramine O staining, Xpert MTB/RIF Ultra and culture in Löwenstein–Jensen media. TB treatment was initiated for confirmed PTB participants in the referring TB outpatient clinic according to the national TB guideline in Madagascar [21]. All confirmed PTB participants were given a 6-month

standard TB regimen including a 2-month intensive phase with rifampicin, isoniazid, ethambutol and pyrazinamide and a 4-month continuation phase with rifampicin and isoniazid [22].

A subset of participants with PTB confirmed by Xpert MTB/RIF Ultra were offered to participate in this longitudinal CCM study over the 6-month duration of standard TB treatment where their spontaneous cough sounds were passively monitored. Confirmed PTB participants who had been on TB treatment for <48 h, who were willing to participate in the 6-month CCM and in whom CCM was deemed feasible by the study teams were included in the 6-month CCM. The feasibility of the CCM was assessed at the participant's home by a social worker. Participants were considered eligible to join the CCM subanalysis if they were able to interact with a smartphone, were independent, accepted to only use the smartphone for calls and texts but not for mobile internet or taking photos, and agreed not to use or install apps. Factors that influence recording quality were also considered, including the participant's home environment (noise, space available, number of rooms, number of roommates, distance between roommates during bedtime and availability of a bedside table for the bedtime recording), the participant's hobbies and job, availability of a power source for charging the smartphone's battery, and willingness to wear the smartphone in the dedicated bag attached around their neck. Participants also had to be available for regular follow-up during the CCM, including clinical visits and home visits. Finally, the level of security in the participant's living environment was considered, to allow them to safely wear the smartphone every day. All these factors were taken into account but did not constitute strict criteria to include or exclude potential participants from the CCM and the research team tried to be as supportive as possible to allow participation in the CCM. The participants from this subgroup were followed up at month 2 and month 5 of TB treatment. The follow-up visits included clinical data collection, sputum collection for TB testing (smear microscopy with auramine O staining and culture) and chest radiography. TB treatment outcome at the end of the 6 months of treatment was abstracted from routine data collected at the TB outpatient clinics.

Study procedures

Coughs were recorded using an android smartphone (Motorola G9 Play) equipped with the Hyfe Research app ("Hyfe"; www.hyfe.ai). The smartphone model was chosen to allow good sound recording quality. Furthermore, the smartphone model should have enough RAM and internal storage, and most importantly, must allow the Hyfe app to run continuously in the background. The Hyfe app can differentiate coughs from other explosive sounds using an AI-based algorithm and showed an excellent performance in detecting (sensitivity 91% and specificity 98%), recording and counting coughs [23]. The Hyfe app was also previously used in coronavirus disease 2019 studies and showed similar performance (sensitivity and specificity 96%) for detecting cough sounds using human listeners as gold standard [24, 25]. In addition, a technical validation was done as part of the main study (CODA TB DREAM Challenge), of which this substudy was part of, and found similar performance for classification of cough sounds [20].

The research team had a total of 40 study smartphones at their disposal (20 smartphones for each site). Participation in the CCM was proposed to eligible confirmed PTB individuals whenever a study smartphone was available to the research team. For the CCM, participants were asked to wear the smartphone in a small bag attached around their neck with the microphone pointing toward the mouth during daytime (supplementary figure S1). They were asked to place the smartphone on a bedside table within 1.5 m of their head while sleeping. All cough data recorded were stored locally on the smartphone. The research team periodically collected the smartphone to upload the cough data to the Hyfe app's cloud-based server. When this happened, participants were provided with a new phone to ensure continuity in cough monitoring. Depending on the amount of cough data recorded, the upload took between a few days to a few weeks. The frequency of the exchange of the smartphone depends on the amount of data recorded, which is linked to the frequency of coughing. During the first 2 months of anti-TB treatment, smartphones were exchanged biweekly according to a defined scheduled. Afterwards, the exchange was done approximately once a month.

Longitudinal cough analysis

Cough counts were summarised using median cough count per hour (medCPH) per week over the 6-month duration of the follow-up, as used in previous studies [17, 19]. LOESS (locally estimated scatterplot smoothing) was applied to weekly medCPH values to visualise the cough trajectory over time. Paired Wilcoxon tests were used to assess the change in weekly cough counts over time.

Adherence to CCM

Adherence to CCM was assessed using the Hyfe app's activity data, which indicates the number of hours per day the smartphone was actively recording. Whenever the phone is on, the app is launched in the background and is actively recording. Another app was installed on each smartphone to lock changes of

the smartphone's settings and to prevent de-activation or removal of the Hyfe app. Therefore, if the smartphone is on 24 h over a day, the app is also actively detecting and recording cough sounds for 24 h and the adherence will be 100% for that 24-h period. We reported mean daytime (from 07:00 to 22:00), night-time (from 22:00 to 07:00) and total weekly adherence.

When a CCM interruption was detected by the study teams, the participant was asked for the reasons of discontinuation if such interruptions were intentional.

Results

A total of 327 participants were included in the primary study cohort. Of these individuals, 134 were confirmed PTB. 22 of the confirmed PTB individuals were invited to participate in the 6-month CCM. All 22 participants accepted and were included in the 6-month CCM, of whom 10 were recruited from Fianarantsoa and 12 from Antananarivo. The rest of the participants (n=112) were not invited to participate in the 6-month CCM and were not further assessed for eligibility due to the unavailability of the smartphone for the CCM at the study site at the time they were present (supplementary figure S2).

Baseline characteristics data and follow-up

Baseline characteristics of the participants included in the 6-month CCM and the entire cohort of confirmed PTB participants are described in table 1. The baseline characteristics of participants included in the 6-month CCM were not significantly different from the remaining confirmed PTB patients. The median (interquartile range (IQR)) follow-up time was 171.5 (166.5–184.0) days. The median (IQR) cumulative time during which the patient's smartphone was actively recording amounted to 143.6 (116.4–173.2) days.

Amongst the 22 participants, 18 were able to provide follow-up sputum at month 2; five out of 18 were smear positive and three out of 18 were culture positive. At month 5, five out of 22 individuals were able to provide follow-up sputum and all were smear and culture negative.

All participants in the 6-month CCM but one were classified as cured at the end of their TB treatment at the TB outpatient clinics where they were followed up. One participant was classified as a treatment failure at the TB outpatient clinic but this was not based on a microbiological test.

Data on the participant's household environment were available for 20 out of 22 participants (11 from Antananarivo and nine from Fianarantsoa). The participants reported a median (IQR) of 4 (3–5) people per household. The median (IQR) number of rooms per household was 2 (1–3.5). Only six participants (30%) had their own room. The remaining lived with a median (IQR) of 2 (1–3) people in the same room. All but one of the participants had access to electricity at home.

Evolution of cough counts during the course of TB treatment

Cough counts decreased throughout treatment amongst all participants (figure 1). Cough counts were highest during the first week of treatment, with a medCPH (IQR) of 11.0 (7.0–27.0). This reduced to a medCPH (IQR) of 7.0 (5.0–18.5) at week 2 ($p=0.023$). By the end of the intensive phase of TB treatment at week 8, the medCPH (IQR) was 3.5 (1.5–7.0), which was significantly lower than the medCPH at week 1 ($p=0.002$) and at week 2 ($p=0.021$). By the end of treatment at week 26, the medCPH (IQR) was 1.0 (1.0–2.5), which was not significantly different from the medCPH at week 8 ($p=0.358$). Individual cough trends are detailed in supplementary figure S1.

Adherence to CCM

The adherence to CCM was high during the first 12–13 weeks of the TB treatment and then waned over time (figure 2a). This occurred both during the daytime and at night (figure 2b and c). There was a noticeable improvement in adherence to CCM at ∼18–19 weeks of TB treatment before dropping off around week 22. Adherence to CCM was the lowest by the end of the TB treatment.

Amongst the 22 participants, 16 (72%) admitted that they momentarily discontinued recording: six (50%) amongst the 12 participants included in Antananarivo and nine (90%) amongst the 10 participants included in Fianarantsoa. Amongst participants who reported a discontinuation of the CCM, the duration was clearly reported by 14 participants. The median (IQR) duration of the CCM discontinuation was 35 (17–45.5) days. One participant abandoned the CCM after 40 days of monitoring and two participants reported repeated intermittent discontinuation over the 6-month CCM. The reasons for CCM discontinuation are described in supplementary table S1.

TABLE 1 Baseline demographic and clinical characteristics of pulmonary tuberculosis (PTB) individuals included in the 6-month continuous cough monitoring (CCM) compared to the remaining PTB cohort

	PTB cohort that participated in the 6-month CCM (n=22)	PTB cohort that did not participate in the 6-month CCM (n=112)	p-value[#]
Age (years)	28.5 (22–42)	31 (24.5–42.5)	0.251
Sex			0.462
Female	7 (32)	45 (40)	
Male	15 (68)	67 (60)	
Smoked in the last 7 days	2 (9)	24 (21)	0.245
Prior chronic respiratory disease	1 (5)	1 (1)	0.302
Prior PTB	1 (5)	12 (10)	0.693
Previous household exposure to TB	6 (27)	20 (18)	0.307
Cough duration (days)	30 (21–60)	35 (28–65)	0.502
Haemoptysis	6 (27)	27 (24)	0.753
Fever	20 (91)	90 (80)	0.364
Night sweats	17 (77)	98 (88)	0.312
Loss of appetite	17 (77)	82 (73)	0.796
Weight loss	21 (95)	106 (94)	1
BMI ($kg \cdot m^{-2}$)	18.4 (16.7–19.9)	18.2 (16.1–20.5)	0.650
HIV negative	22 (100)	97 (86)	0.270
Sputum smear			0.358
Negative	2 (9)	18 (16)	
Scanty (1–9 AFB/100 fields)	2 (9)	1 (1)	
1+ (1–9 AFB/10 fields)	3 (14)	17 (15)	
2+ (1–9 AFB/field)	4 (18)	22 (20)	
3+ (>9 AFB/field)	11 (50)	52 (46)	
Not done	0 (0)	2 (2)	
Xpert MTB/RIF Ultra			
Trace	2 (9)	2 (2)	0.178
Very low	2 (9)	3 (3)	
Low	3 (14)	20 (18)	
Medium	4 (18)	16 (14)	
High	11 (50)	63 (56)	
Not done	0 (0)	8 (7)	
Positive culture on Löwenstein–Jensen media	21 (95)	106 (95)	1
Chest radiography (n=127)			0.036
Normal	3 (13.6)	2 (2)	
Abnormal	19 (86)	103 (98)	
Abnormal chest radiography with cavitation (n=122)	13 (68)	55 (53)	0.226

Data are presented as median (interquartile range) or n (%), unless otherwise stated. BMI: body mass index; AFB: acid-fast bacilli. [#]: Mann–Whitney test for continuous variables and Chi-squared test or Fisher's exact test for categorial variables.

The most common reasons for CCM discontinuation amongst the 16 participants who reported repeated intermittent or temporary discontinuation of the CCM were due to insecurity or feeling unsafe having a smartphone visible and electricity issues (outage or unavailability). However, the reason for CCM discontinuation was not clearly identified for five individuals. Those patients had not reported any discontinuation; however, it was noted from the app dashboard that recording had paused for a prolonged period of time (ranging from 12 to 48 days).

Discussion

Our proof-of-concept study assessed cough during the course of 6 months of TB treatment. We showed that cough counts decreased rapidly during the initial 2 weeks of treatment, following the initiation of the anti-TB treatment, which corroborates prior findings [17, 19, 26, 27]. Cough counts continued to decrease through the intensive phase of treatment and the continuation phase, but at a slower rate. By the end of treatment, medCPH had decreased significantly compared to levels at treatment initiation; however, it remained detectable. This low level of cough could correspond to the baseline cough counts that could be found even in healthy adults [28]. Residual coughs could also be attributed to post-TB lung disease, where cough is reported by over a fifth of patients [29]. Nevertheless, the lack of a control group did not allow for a definitive interpretation of the residual cough observed at the end of TB treatment in this cohort.

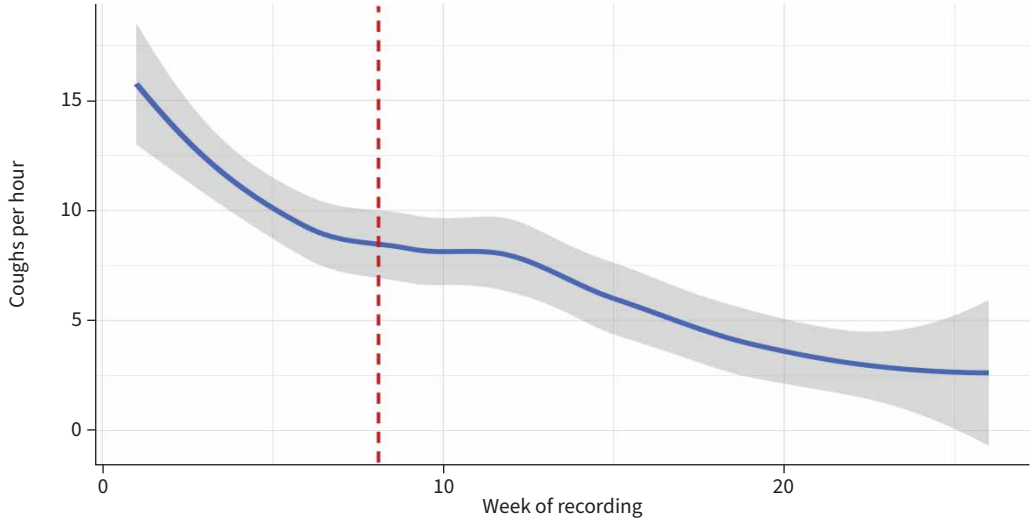

FIGURE 1 LOESS (locally estimated scatterplot smoothing) applied to median coughs per hour per week during the 6 months of tuberculosis (TB) treatment amongst participants. The shaded area indicates the LOESS confidence interval. The dashed red vertical line indicates the transition from the intensive phase to the continuation phase of the TB treatment.

The adherence to CCM was high during the first 12–13 weeks of the TB treatment, which includes the intensive phase of TB treatment. The absence of difference in adherence during daytime and night-time recording informs us on the acceptability of carrying a smartphone in a pouch around the neck during the day. This high adherence during the first 2 months of the study can be attributed to the frequent interaction between the participants and the study team (for smartphone exchanges for data uploading) and the TB clinics (for TB treatment supply in accordance with TB recommended standard of care) [30]. After the intensive phase of treatment, treatment delivery and interactions with the research team were less frequent. Additionally, the participants coughed less often, which may explain the lower adherence of the participants to CCM. A combination of clinical improvement, less frequent follow-up and recording fatigue could all contribute to the progressive waning of CCM adherence over time. We hypothesised that the increase in CCM adherence observed at week 18–19 was related to the month 5 visit that participants have to undergo as part of routine TB care. Hence, CCM may be enhanced by frequent contact with research staff or healthcare providers, which is resource intensive and would make remote cough monitoring for TB treatment response difficult to implement. Intermittent cough monitoring, defined as continuous recording for a few hours or days at predefined time-points during the course TB treatment, may be a more cost-effective and a more feasible alternative. However, shorter recording periods may compromise the ability to detect meaningful changes in cough rates [31, 32]. Reasons for CCM discontinuation were centred on the participant's sense of safety as robbery and mugging are frequent in the urban area where the participants lived. However, the overall duration of the discontinuation reported by the participants seems acceptable when compared to the intended total duration of CCM, given the technical constraints that may arise during long-term continuous recording. Indeed, the median duration of discontinuation reported by the participants was 35 days, which actually corresponds to ∼19% of the 6-month intended monitoring duration. Seven participants had probably experienced technical issues that resulted in unintentional CCM discontinuation. The cause of these technical issues was undetermined. However, the amount of data lost due to technical issues was low compared to a previous study where up to 42% of the recordings could not be processed due to technical issues, despite a shorter monitoring duration [17]. Smartphone technology with an AI-powered app for cough detection offers a simpler, less burdensome solution that is less prone to technical issues that cause loss of data, especially in the context of continuous monitoring over a long period of time.

A major limitation was the high cost of mobile phone data plans in Madagascar, which prevented real-time upload of cough data to the cloud. Instead, the data upload was done in each clinical facility using a less costly Wi-Fi internet connection. This process resulted in delays in the upload of data, spanning several days to weeks as the amount of cough data stored in the smartphone was extensive. To avoid any disruption in CCM, participants were given a new smartphone for recording. Consequently, at least two

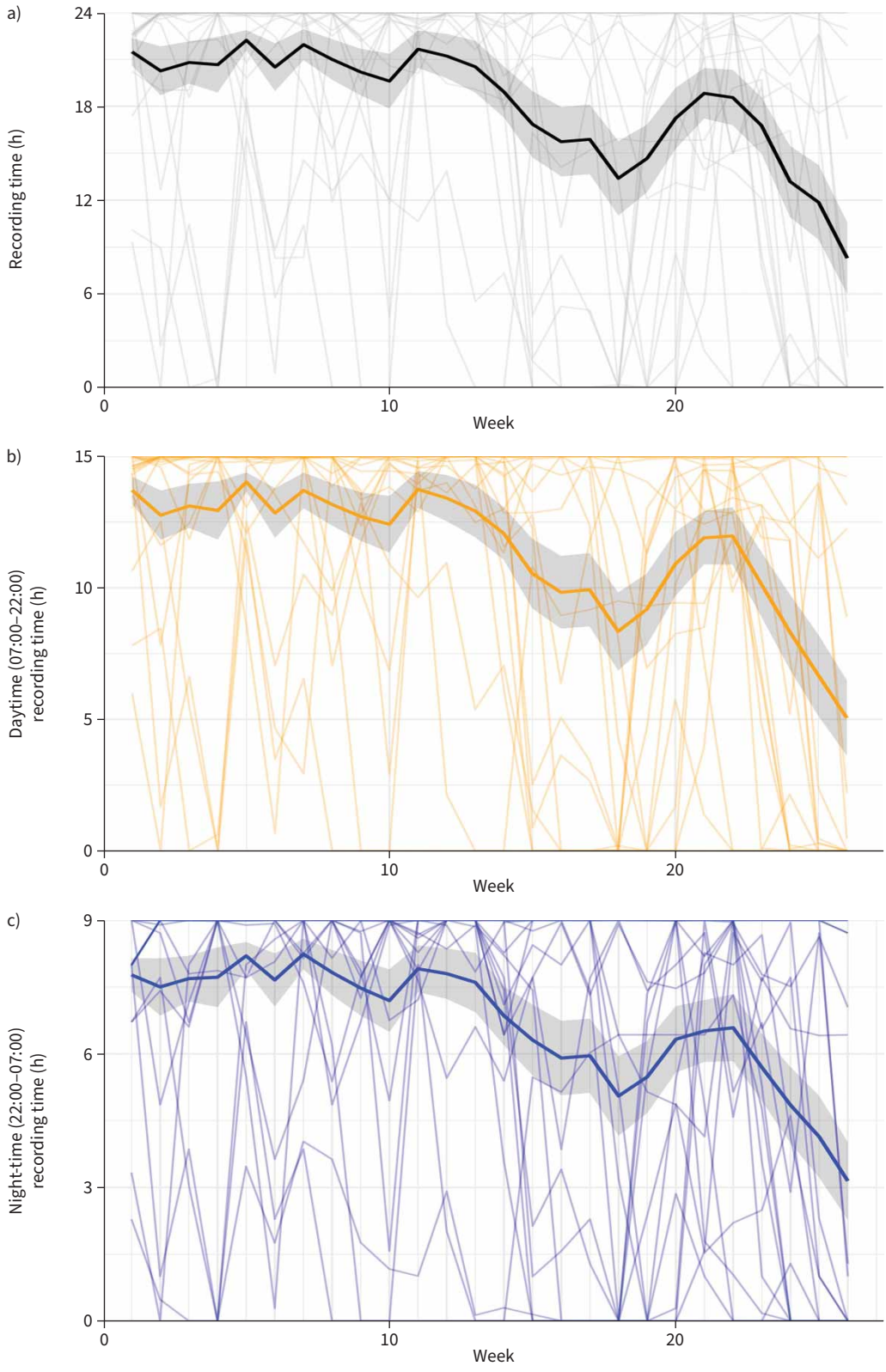

FIGURE 2 Weekly average continuous cough monitoring recordings over the 6 months of tuberculosis (TB) treatment: a) 24 h, b) daytime (07:00–22:00) and c) night-time (22:00–07:00). In each panel, the thin lines are individual average weekly recording adherence hours and the thick line represents the study sample average weekly recording adherence hours. The shaded area indicates the standard error.

smartphones were needed per participant, especially during the first 2 months of recording when participants were coughing more frequently and thus the amount of data stored locally was high. This limited the number of participants that could be enrolled and monitored for the 6-month CCM. Likewise, an alternative strategy of monitoring, such as intermittent monitoring, may overcome this issue and could allow real-time processing of the data with the use of mobile internet connection for a defined period of time while increasing the number of participants that can be tracked.

Another limitation of the study is inherent in the technology itself and the detection of cough using the detection of explosive sounds as a first step. The actual sensitivity and specificity of the Hyfe app in detecting coughs in various environments may be different from the performance described in validation studies. It was noted that in noisy environments, the probability of an explosive sound being a cough is low and thus the specificity of the system in that type of environment would be much lower [33]. Similarly, in environments with a high level of background noise or because of the use of the bag to wear the smartphone around the neck, the ability of the app to detect explosive sounds may be reduced and therefore the system would have higher false negatives and lower sensitivity [23]. Finally, the sensitivity of the app was only calculated by considering the explosive sound already detected by the system and assessed by a human listener, meaning that non-explosive sounds that are not captured by the system but might have contained cough sounds were not counted [33]. The waning of adherence to CCM over time may have influenced the probability of capturing cough sounds, particularly after 12 weeks of CCM when adherence started to drop. However, the progressive reduction in adherence is not sufficient to explain the reduction in cough rate over time. Since we were using medCPH, *i.e.* rate of median cough count per hour, this should have taken account of differences in recording time to a large extent. By using a rate rather than an absolute count, we were normalising the data across different recording durations. Furthermore, the use of median, which is resistant to outliers, is therefore less affected by the total duration of the recording. Additionally, the increase in CCM adherence around week 18–19 did not correlate with an increase in cough rate, suggesting that waning of adherence alone is not the only factor that explained the drop in cough rate and that this observed phenomenon was really correlated with an actual reduction in participant coughing.

The small sample size in this proof-of-concept study did not allow for a comparison of cough count trajectories according to TB treatment outcome (cured *versus* treatment failure). In addition, TB outcome assessment abstracted from routine care data may not be sufficiently reliable as TB culture is not routinely performed either for diagnosis or for follow-up during the course of the TB treatment. Finally, as we did not screen for TB or follow-up on the detection of incident TB or screen for any other respiratory conditions whose symptoms may include cough in household contacts of the participant, there is a risk of contamination of the recording by the coughing of household contacts developing TB or other respiratory diseases during the CCM.

As we performed a proof-of-concept study, a potential selection bias could have occurred because the inclusion of the participants was dependent on favourable recording conditions in the participant's environment. The absence of significant differences between the baseline characteristics and the PTB participants included in the CCM cohort and those who were not, and the descriptions of participants' home environments, which are consistent with the housing conditions of Malagasy people in urban settings, are reassuring and suggest an adequate representation of PTB participants in urban areas. However, the use of such technology for CCM would be restricted to areas where electricity and internet connection are available.

Future studies assessing cough dynamics to predict PTB treatment outcome should include more participants and measure TB treatment outcome and time to bacteriological conversion using serial culture testing [34]. In addition, longer duration of follow-up after the end of the TB treatment may be required to predict infection relapse [34]. Future studies should also explore alternative recording strategies, including intermittent continuous monitoring and use of other types of wearable devices (*e.g.* wearable watches), consider the use of mobile internet connection to allow real-time transfer and processing of cough sounds, and explore different strategies that would overcome adherence issues (*e.g.* adapting the app to be used on the participant's usual smartphone).

Conclusion

In our cohort of 22 confirmed PTB patients undergoing 6 months of TB treatment, cough counts rapidly declined during the first 2 months, corresponding to the intensive phase of treatment. Cough counts continued to decrease throughout the continuation phase until the end of treatment and remained at a low baseline level. Adherence to CCM was high during the first 12–13 weeks following the start of treatment, but declined thereafter. Reasons for CCM discontinuation were mainly related to participant's perceived

safety. Digital cough monitoring during the 6-month duration of TB treatment is feasible in low-resource settings, but patient adherence should be improved by exploring alternative approaches, especially during the continuation phase of the treatment.

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Ethics statement: The study was approved by the Comité d'Éthique de la Recherche Biomédicale du Ministère de la Santé Publique de Madagascar (number 051-MSANP/SG/AMM/CERBM) and the Comité d'Éthique de la Recherche du Centre Hospitalier de l'Université de Montréal (CHUM) in Canada. All participants provided written informed consent.

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