Making Cough Count in Tuberculosis
(and other respiratory diseases)

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Objectives

● Distinguish artificial intelligence-assisted *cough detection* and *cough classification*

● Identify the potential use cases of digital cough monitoring in tuberculosis control and respiratory medicine
Cough is a biological phenomenon in which specific sequential patterns of inspiration and expiration (without and then with air flow) create a classic “explosive” sound.

There is biological rationale for coughs associated with distinct lung diseases to have distinct acoustic features.

Cough is both a symptom of disease and defense mechanism.

Cough is associated with many non-TB diseases so it’s not perfectly specific.

Cough is one of the most common symptoms of pulmonary TB but it’s not perfectly sensitive either.

Current ways of assessing cough are limited by recall biases, stigma, etc.
Renewed interest in cough

Acoustic epidemiology - The analysis of human sounds (voice, coughs, sneezes, wheezing, etc) to study the determinants, patterns and distribution of disease.
Acoustics and artificial intelligence

Identification of human coughs sounds among ambient sounds
i.e. transforming cough as a “symptom” in cough as a “sign”

Enables geospatial and temporal aggregation

**Cough detection**

**Cough classification**

Identification of cough sounds associated with specific clinical conditions or stages of disease

Cough detection and classification for tuberculosis control

Making cough count in tuberculosis care

Alexandra J. Zimmer, César Ugarte-Gill, Rahul Pathri, Puneet Dewan, Devan Jaganath, Adithya Cattamanchi, Madhukar Pai & Simon Grandjean Lapierre

Fig. 2 Potential use cases for digital cough monitoring in the tuberculosis cascade of care. Each step in the TB care cascade is represented as a bar. The gaps in the cascade are in red between each step. Boxes pointing at the gaps represent possible digital cough-based solutions to address various gaps. The height of the bar graphs and the length of the gaps are not scaled to represent true values. They are intended to help illustrate the different steps of the care cascade and points at which people with TB may fall to benefit from care. (Cascade of care adapted from Fig. 1 of Subbaraman et al.).
Syndromic surveillance works

Acoustic surveillance of cough for detecting respiratory disease using artificial intelligence

Juan C. Gabaldón-Figueira 1,2, Eric Keen 3, Gerard Giménez 3, Virginia Orrillo 4, Isabel Blavia 4, Dominique Hélène Doré 5, Nuria Armendáriz 6, Juliane Chaccour 1, Alejandro Fernandez-Montero 7, Javier Bartolomé 8, Nita Umashankar 3, Peter Small 3,9, Simon Grandjean Lapierre 5,10,12 and Carlos Chaccour 1,2,11,12

Temporal association between aggregated cough rates and COVID « waves », both within the cohort and the population

Potential value in surveillance and preparedness ?
Syndromic surveillance works

Real-time temporal and geospatial aggregation of cough events among TB patients

Potential value in secondary case finding?

Tsang et al. Unpublished
Cough detection measures treatment response

Longitudinal passive cough monitoring and its implications for detecting changes in clinical status

Juan C. Gabaldón-Figueira, Eric Keen, Matthew Rudd, Virginia Orrilo, Isabel Blavia, Juliane Chaccour, Mindaugas Galvosas, Peter Small, Simon Grandjean Lapierre, and Carlos Chaccour

Digital cough monitoring data correlates with clinically significant events

Potential value in treatment response monitoring?
Cough detection measures treatment response

Both the cough rate and circadian variability rapidly regress with TB therapy

What would we see in case of failure?

Figure 2. Circadian cycle of cough frequency during treatment for study group. A. Smoothed trends in cough from day -1 to day 7 of treatment. Each day begins at 9 am, as this is the time when recordings began. B. Separate negative binomial generalized estimating equation models fitted for each day following treatment. All recordings, regardless of total length, were included (n = 12,108 hours of recording). Random-effects modeling was used to adjust for study participant. Circadian cycles of cough were reflected by sine/cosine terms.
Cough detection measures treatment response

Participants with microbiologically confirmed TB have significantly higher median cough per hour than participants with non-TB respiratory diseases.

Median cough per hour regresses following diagnosis and treatment initiation

What would we see in case of failure?
Cough detection as a pronostic biomarker

COVID-19 confirmed patients requiring hospitalization

Continuous cough monitoring in individual rooms

Continuous monitoring of oxygen support and categorical clinical outcomes (e.g. room air, noninvasive ventilation, intubation, death)
Cough detection as a pronostic biomarker

Transitional cough rate as an outcome predictor

Total enrollement

Initial 24 hours

Initial 6 hours

Decision boundary:
3.401 coughs per hour

Decision boundary:
3.417 coughs per hour

Decision boundary:
9.5 coughs per hour

AUC: 0.761

AUC: 0.792

AUC: 0.719
• Diagnostic cohort of > 2100 TB suspects self-referred to care for TB diagnostics

• High quality solicited cough sounds recording and clinical parameters

• Well characterized TB disease using composite diagnostic based on Xpert & culture

https://www.synapse.org/#!Synapse:syn31472953/wiki/
Assessing cough classification performance

F1-score = \frac{TP}{TP + \frac{1}{2}(FP+FN)}

Receiver operating characteristic (ROC) curve
Area Under the Curve (AUC)
TB cough classification

Subchallenge 1:

Predict 'positive' TB diagnosis using cough recordings only.

Subchallenge 2:

Predict 'positive' TB using cough recordings and additional demographic/clinical variables (Age, Sex, Height, Weight, BMI, Smoking, Reported Duration of Cough, Prior TB, Hemoptysis, Heart Rate, Temperature, Fever, Night Sweats, and Weight loss).

Assessment

Submissions will be scored using the two-way partial area under the receiver operator characteristic curve (pAUC) \([1]\) with Sensitivity (TPR) \(\geq 0.8\) and 1 - Specificity (FPR) \(\leq 0.4\).
Over 150 participants – Approximately 10 teams submitting classification models in the last rounds

Selected preliminary leaderboard results confirm that there is a TB acoustic signature

Final results and complementary / sub-group analyses to come
Discussion

Acoustic epidemiology is an emerging field of research
There are multiple potential niches for digital cough monitoring in TB control and respiratory medicine

Results from cough detection studies suggest that TB treatment clinical response can be objectively measured
Technological improvements are needed to facilitate unobtrusive longitudinal monitoring
Specific thresholds / patterns suggesting clinically relevant events (e.g. treatment failure) need to be identified and validated

Results from cough classification studies suggest the existence of an acoustic signature for pulmonary TB
Existing classification models can be further improved
Existing classification models could be combined with other biomarkers
The impact of cough classification for TB triage needs to be modeled and prospectively validated
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