Bronchiectasis patients move in and out of a state of exacerbation. There are two kinds: event-based exacerbations (EBEs) and symptom-based exacerbations (SBEs).

Ascertainment of EBEs requires contact with a clinician. SBE status is determined by adjudication of patient-recorded symptom scores (ordinal, 0–4) for sputum volume, sputum purulence and dyspnoea. Daily symptom diaries kept by 140 bronchiectasis patients over a 6 month period studied by Wong et al. (2012) were manually adjudicated. EBEs and wellbeing (St. George’s Resp. Q’aire) were also recorded.

Manual adjudication of SBEs is labour intensive and based on a complicated scoring rule.

A new definition of SBE is proposed based on a prediction rule validated against clinically adjudicated EBEs. The prediction rule is derived by regressing current EBE status on current and previous symptom scores and previous EBE status.

### Discussion

#### Conclusions

- A new definition of SBE was proposed which can be calculated with useful precision.
- SBE was no more associated with patient-reported wellbeing than clinically adjudicated EBE.
- Future work will investigate joint validation against patient-reported wellbeing and EBE.

#### Limitations

- Assigned equal loss for both types of misclassification; differential loss could improve predictive performance.
- Error in the predicted EBE state, $\text{Var}(\text{EBE}_{t,t})$, was not propagated.

### References


### Method

#### Overview

1. Build a retrospective prediction model for $\text{EBE}(t_0)$ using observed symptom scores and observed EBEs at times $t \in (t_0 - \tau, t_0)$.
2. Convert to a prospective model for $\text{EBE}(t_0)$ using observed symptom scores and $\text{EBE}_{t}$ at times $t \in (t_0 - \tau, t_0)$.

#### Retrospective Prediction Model

- EBE status at current time, $t$, dependent on current and past symptom scores and $\text{EBE}$ status at $t - \delta$, $0 < \delta \leq \tau$.
- Used generalized linear mixed model with logit link, rand. intercepts for patient (a ‘regressive logistic’ with random effect, Bonney, 1987) to predict the time-ordered, clustered, binary outcome, EBE, estimated with ML:
  \[
  \logit \ Pr(\text{EBE}_{t,t} = 1) = f(X_{t,t}, \text{EBE}_{t,t-5}) \beta + Z_i b_l + \epsilon_{i,t}
  \]
- Entries $\{x_{i,t}\}$ in $X_{t,t}$ are diarized symptom scores at times $t \in (t_0 - \tau, t_0)$, $f(\cdot)$ indicates an averaging scheme, $b_i \sim \text{Normal}(0, \tau^2)$, $\epsilon_{i,t} \sim \text{Normal}(0, \sigma^2)$.
- Used area under the ROC curve to search among models defined by $\{f, \delta, X_{t,t}\}$.
- Binary prediction by dichotomizing at the threshold where $\text{sens.} = \text{spec}$.

#### Prospective Prediction Model

- Fitted prospective model by sequentially fitting the retrospective model with predicted EBE in place of observed:
  \[
  \logit \ Pr(\text{EBE}_{t,t} = 1) = f(X_{t,t}, \text{EBE}_{t,t-5}) \beta + Z_i b_l + \epsilon_{i,t}
  \]
- Re-estimated the dichotomization threshold.
- Two-fold cross-validation used to estimate predictive performance.

### Wellbeing

- Assessed daily from St. George’s Resp. Q’aire total score, dichotomized (1, 2 = “bad”; 3, 4, 5 = “good”).
- Dichotomization threshold determined by regressing dichotomized wellbeing under each threshold on symptom scores, and selecting that which led to a model with best prediction performance.