

Evaluation of COPD Exacerbations Using the EXACT-U

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BACKGROUND

The EXACT (Exacerbations of COPD Tool) is a patient-reported daily diary to evaluate the frequency, severity, and resolution of exacerbations of COPD and chronic bronchitis.(1-2) The instrument is comprised of items that evaluate symptoms as well as systemic manifestations of the condition. Reporting utilities from the EXACT enables a more accurate account of change during an exacerbation for economic evaluations than current methods. The EXACT-U was developed to quantify the utility of exacerbating patients from the EXACT daily diary.

Methods to develop the EXACT-U included:

1. EXACT-U Item Identification – Classical Test Theory (CTT) using Principal Components Analysis, and Item Response Theory (IRT) using Rasch analysis
2. Content Validation and Health State Development – group of patients debriefed on selected items. Items and response options grouped to form selected health states
3. Preference Data Collection – TTO interviews with 400 members of UK general public
4. Model Development – Using statistical inference (SI) and multi-attribute utility theory (MAUT) methods
 - ◆ Statistical analyses for SI model development
 - ◆ Statistical analyses for MAUT model development
5. Predictive Validity – SI and MAUT models tested for predictive ability using independent dataset

Further assessment of model performance is necessary to evaluate performance of the EXACT-U models in a clinical setting.

OBJECTIVE

To evaluate and compare discriminant validity and responsiveness of two EXACT-U scoring algorithms for use in cost-effectiveness studies.

METHOD

EXACT-U algorithms using the SI and MAUT methods were previously developed.(3) For this study, algorithms were applied to an independent dataset to evaluate discriminant validity and responsiveness.

Dataset Study Details:

Previously collected data were available on COPD patients with and without exacerbations, completing the EXACT and other clinical measures.

- ◆ Stable group: 188 stable COPD with EXACT daily diary responses from Day 1-7.
 - ◆ Acute group: 222 acute exacerbations with EXACT daily diary responses from Day 1-29 and 60-66.
- All patients had: clinician-assessed COPD severity and FEV¹ (within 1 year).
 Acute group had: clinician-assessed exacerbation diagnosis, severity, and resolution.

Statistical Analyses:

Discriminant validity:

The extent to which an instrument can differentiate among known groups.(4) Analyses conducted to evaluate differentiation among stable and acute states, and all 4 severity levels of an exacerbation, as assessed by a clinician.

- ◆ Assessed by order of mean utilities, magnitude of differences, and statistical significance ($P < 0.05$) for stable and acute groups; for mild, moderate, severe, and very severe exacerbations.
- ◆ Box and whisker plots reported and include the five-number summaries: the smallest observation (sample minimum), lower quartile (Q1), median (Q2), upper quartile (Q3), and largest observation (sample maximum) for each severity level.

METHOD (CONT'D)

Responsiveness:

A component of construct validity and refers to the ability of an instrument to reflect underlying change, in this case, response to treatment.(4) Analyses conducted to evaluate the change from exacerbation treatment, contrasted by change at stable state. Clinicians identified many patients as either "much better" or "completely resolved" after 10 days; therefore change will be assessed for the initial 2-week period. Day 60-66 will be assessed, as this was pre-determined as the "stable" period for the acute group.

- ◆ Acute Group only: Assessed by effect size ((mean baseline – mean follow-up)/SD baseline scores) from from Day 1-14 and 60-66.
- ◆ Linear graphs include mean utility values for the stable group and acute group for Day 1-14 and 60-66.

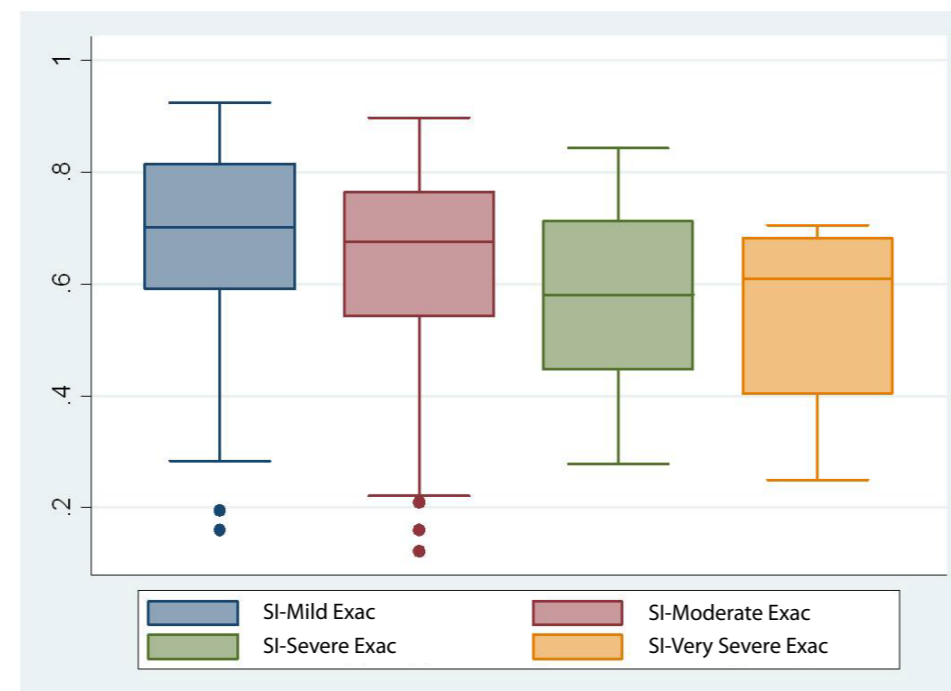
RESULTS

Discriminant Validity

SI Model:

- ◆ Figure 1 demonstrates the median, upper and lower quartiles, and min/max utilities predicted.
- ◆ Mean utilities from the SI Model at Day 1 were 0.78 for the stable and 0.63 for the acute state, reaching statistical significance ($P < 0.001$).
- ◆ SI model mean utility values for exacerbation severity were ordered and declined in order of increasing severity.
- ◆ Statistical significance reached for: mild/moderate ($P < 0.05$) and moderate/severe ($P < 0.001$) levels.
- ◆ The difference between severe and very severe exacerbations was not statistically significant ($P = 0.12$) due to the small sample size in the very severe group ($n = 4$) compared to the severe group ($n = 33$).
- ◆ Standard deviations were large across all exacerbation severity levels.

Figure 1: SI Model Utilities by Exacerbation Severity

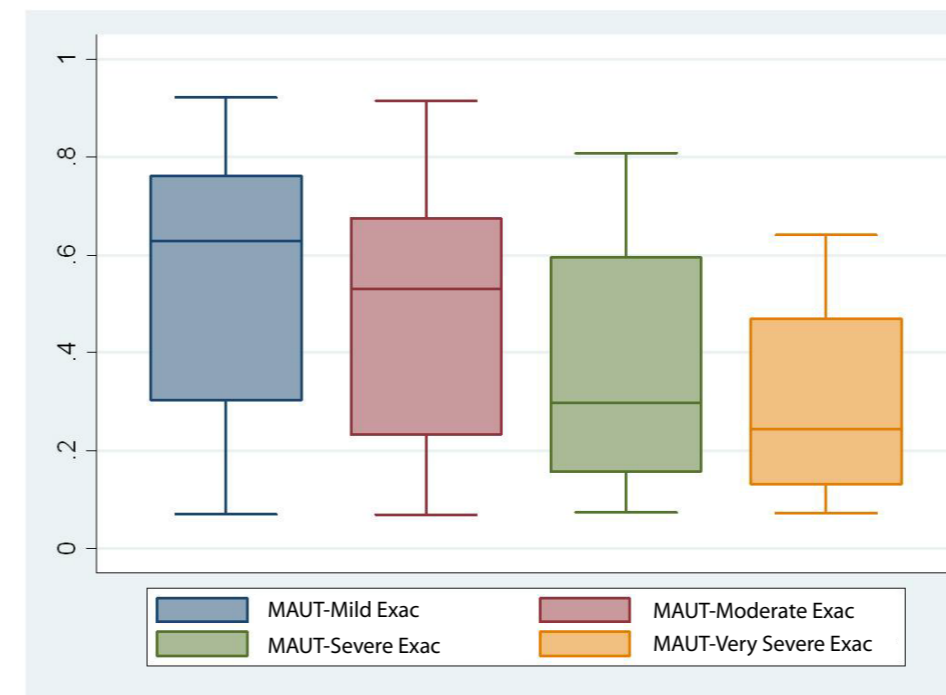


RESULTS (CONT'D)

MAUT Model:

- ◆ Figure 2 demonstrates the median, upper and lower quartiles, and minimum/maximum utilities predicted.
- ◆ Day 1 mean utilities were 0.68 for stable and 0.47 acute groups reached statistical significance ($P < 0.001$).
- ◆ MAUT model mean utility values for exacerbation severity were ordered and declined in order of increasing severity.
- ◆ Standard deviations were large and similar across all exacerbation severity levels.
- ◆ Statistical significance was reached for differences between mild/moderate ($P < 0.01$) and moderate/severe ($P < 0.001$).
- ◆ The difference between the severe and very severe groups did not reach statistical significance ($P = 0.14$) due to the small sample size in the very severe group ($n = 4$).

Figure 2: MAUT Model Utilities by Exacerbation Severity



Responsiveness

Both algorithms demonstrated strong response to change during the first 2 weeks after diagnosis of an exacerbation. (Figure 3) Results also show the stable state immediately after an exacerbation remains lower than the stable state of a patient not recently diagnosed with an exacerbation

SI Model:

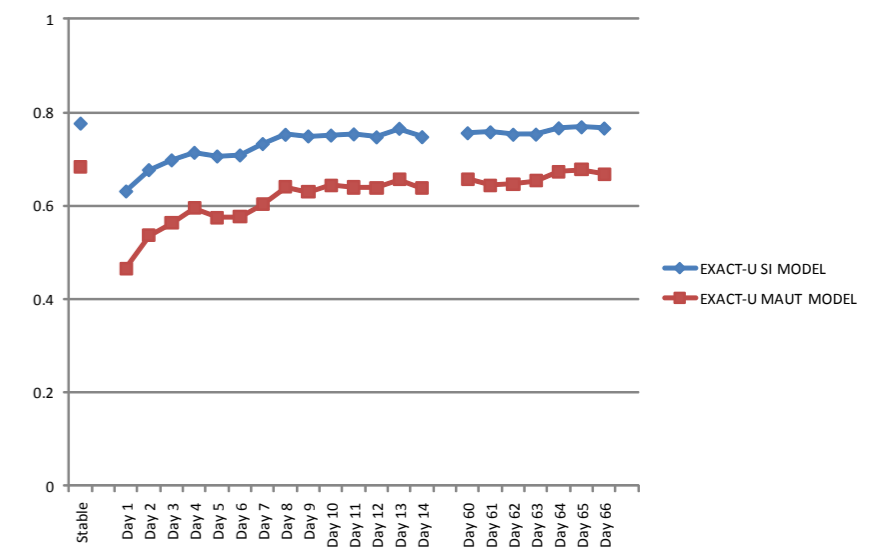
Effect size was moderate at Day 3 but increased to strong at Day 7 through the remaining assessment period: Day 3=0.38; Day 7=0.58; Day 10=0.68; Day 13=0.76.

MAUT Model:

Effect size was strong from the start through recovery: Day 3=0.52; Day 7=0.55; Day 10=0.71; Day 13=0.76.

RESULTS (CONT'D)

Figure 3: Mean Utilities for Stable at Day and Acute at Day 1-14, 60-66 by Model



CONCLUSION

- ◆ The EXACT-U can be used where EQ5D data are not available or where condition-specific utilities are preferred to report the impact of the severity, duration, and frequency of exacerbations on patients.
- ◆ Both algorithms appear to be adequately sensitive with regards to responsiveness and discriminant validity and may be used to report utilities for COPD exacerbations from the EXACT.
- ◆ Differentiation of exacerbation severity by stable COPD levels is slightly better with the MAUT model than the SI model.
- ◆ The instrument can be used in cost-effectiveness assessments to report utilities for COPD and exacerbating patients from clinical trials where EXACT data are available.

REFERENCES

1. Leidy NK, Wilcox TK, Jones PW, et al. Development of the EXacerbations of Chronic Obstructive Pulmonary Disease Tool (EXACT): A Patient-Reported Outcome (PRO) Measure. Value Health. 2010.
2. Leidy NK, Wilcox T, Roberts L, Winnette RM, Murray L. The EXACT-PRO Initiative: Development and validation of a single patient-reported outcome measure for evaluating exacerbations of chronic obstructive pulmonary disease. . International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 11th Annual European Meeting. Athens, Greece, 2008.
3. J Petrillo, J Cairns. Comparison of the Statistical Inference and Multi-Attribute Utility Theory Models to Develop a Preference-Based Instrument: The EXACT-U as a Case Study. European Health Economic Conference. Helsinki, Finland, 2010.
4. Nunnally J, Bernstein I. Psychometric Theory. 3rd ed. New York: McGraw Hill, 1994.

QUESTIONS

For questions on the poster or sponsorship/licensing of the EXACT-U, please email jennifer.petrillo@lshtm.ac.uk