

Patient-reported outcomes as pragmatic predictive biomarkers for survival among lung cancer patients receiving radiation therapy

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BACKGROUND

- Patient-reported outcomes (PROs) associated with improved cancer outcomes in clinical trials.
- Their benefit in routine clinical care is far less clear. Surveys exist to identify treatable toxicity, completion voluntary, and compliance uneven.

HYPOTHESIS

PROs collected for routine symptom management can serve as predictive biomarkers for overall survival in lung cancer patients receiving thoracic radiation.

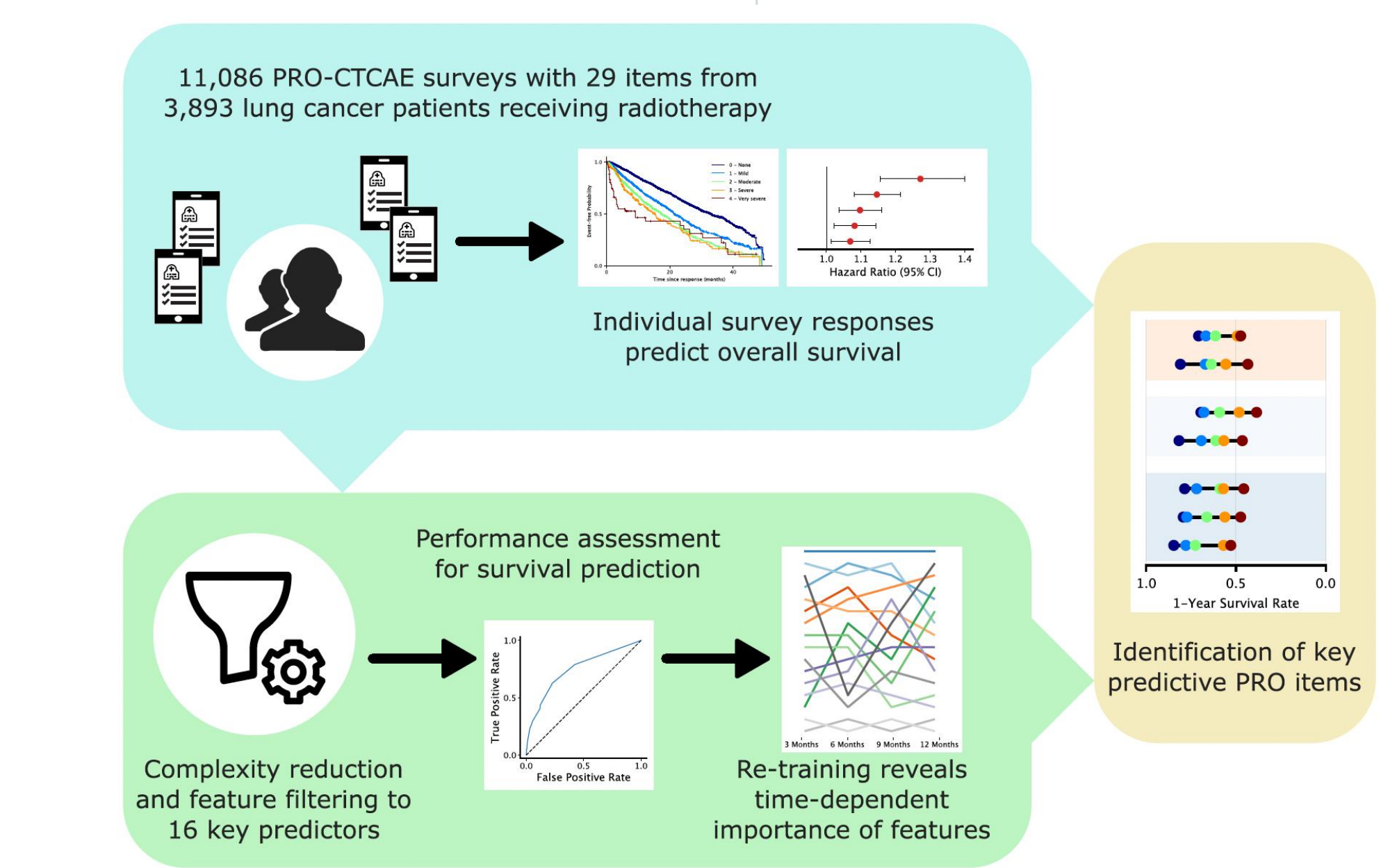
METHODS

- Retrospective analysis of routinely collected PRO-CTCAE surveys.
- Individual survey response, not the patient, served as the unit of analysis.
- Cox proportional hazards models to identify independent symptom predictors of overall survival.
- Random forest classifier trained to predict 6-month survival from the PRO survey date.
- 5-fold patient-based cross-validation kept every patient's responses within a single fold, preventing leakage between train and test.
- Permutation importance reduced the question bank to a minimal predictive set, testing whether a shorter survey retains performance.

PRO-CTCAE SURVEY ITEMS

- Each symptom rated on up to three attributes, 7-day recall period:
- **Item Sets (13):** difficulty swallowing, decreased appetite, nausea, shortness of breath, cough, heart palpitations, radiation skin reaction, mental concentration, general pain, insomnia, fatigue, anxiety, sadness
- **Severity at its worst**
None, Mild, Moderate, Severe, Very severe
- **Frequency**
Never, Rarely, Occasionally, Frequently, Almost constantly
- **Interference with usual activities**
Not at all, A little bit, Somewhat, Quite a bit, Very much

PATIENTS AND SURVEYS



RESULTS

- 3893 (54.9%) of patients responded to at least one survey
- Cox models showed that routine symptom monitoring stratifies short-term survival risk. Independent **predictors of overall survival** were **sex** (HR 1.27, male vs. female, $p < 0.01$), **decreased appetite severity** (HR 1.15, $p < 0.01$), **fatigue severity** (HR 1.09, $p = 0.02$) and **difficulty swallowing severity** (HR 1.09, $p = 0.02$).
- Feature reduction retained **16 features** associated with 6-month survival, led by decreased appetite severity, pain frequency and fatigue severity.
- Random forest classifier on these factors resulted in a **c-index of 0.737**.
- The strongest signals were **constitutional** — appetite, fatigue, pain — rather than local pulmonary symptoms most associated with thoracic radiotherapy. Cough and shortness of breath were not independently predictive.
- Because roughly half of patients completed a questionnaire, estimates describe **responders**. Non-response is not random and may itself carry prognostic information.
- Hazard ratios are per one-level increase on the five-point PRO-CTCAE scale, so effects compound across the scale rather than describing a single step.

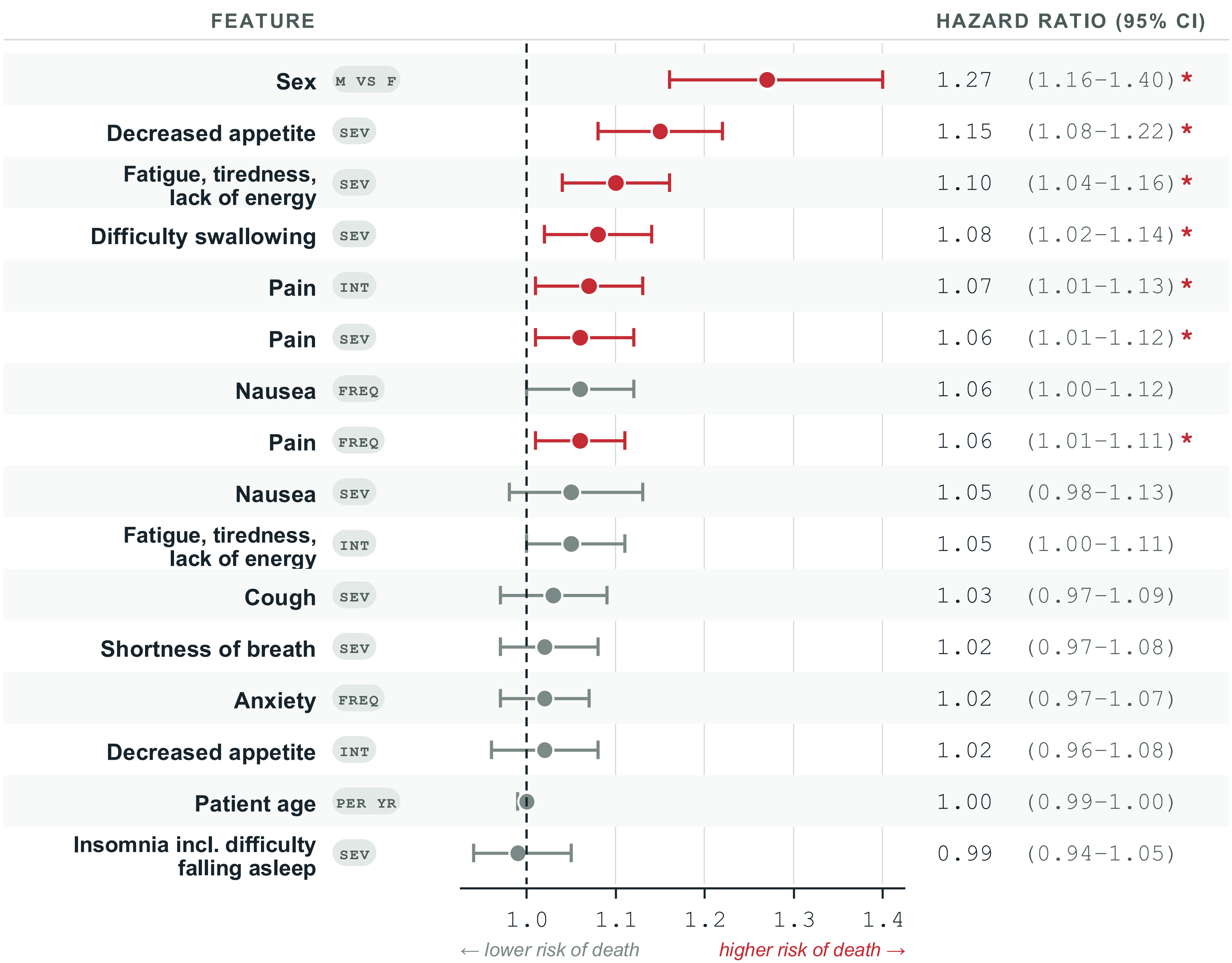
CONCLUSIONS

- Routinely collected PROs showed **potential prognostic value** in lung cancer patients.
- **Feature reduction** preserved ability to predict survival, indicating **lower resource avenues** to stratify patients by survival risk.
- **Additional validation studies** required for generalization.

How often did you have pain? PRO-CTCAE ITEM



SYMPTOMS AND ASSOCIATION WITH 6-MONTH SURVIVAL



* $p < 0.05$ · SEV severity · FREQ frequency · INT interference

FIGURE 1 Top features associated with 6-month survival after feature reduction. Hazard ratios with 95% confidence intervals from Cox proportional hazards models