# Baseline quantitative CT predicts rate of decline in forced vital capacity and clinically relevant outcomes in patients with progressive pulmonary fibrosis: results from the INBUILD trial.

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Objective

To evaluate the prognostic potential of quantitative CT scores, derived using the University of California Los Angeles (UCLA) and e-Lung (Brainomix) algorithms, for FVC decline or death in a sub-study of the INBUILD trial in patients with PPF.
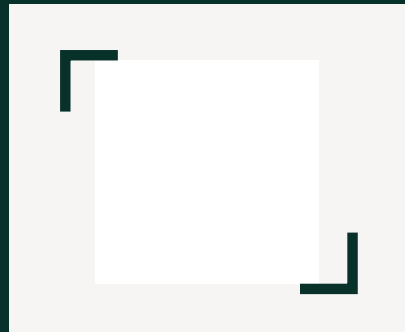
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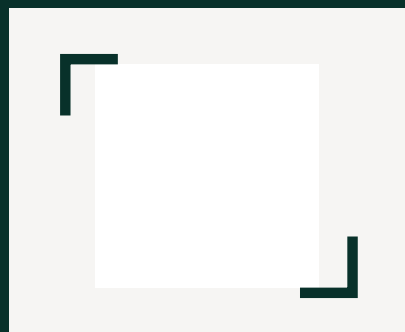
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Introduction

- Quantitative measurements of the extent of ILD or lung fibrosis on CT have been shown to be predictive of decline in FVC[1-4] and short-term mortality[2-8] in patients with various ILDs.
- More information is needed on the prognostic potential of quantitative CT measurements for clinical outcomes in patients with PPF.

Methods

The INBUILD trial[9] and its HRCT sub-study

- Patients in the INBUILD trial had an ILD other than idiopathic pulmonary fibrosis, an extent of fibrosis on HRCT >10%, and met criteria for ILD progression within the prior 24 months.
- Patients were randomized to receive nintedanib or placebo.
- In a sub-study of the INBUILD trial, HRCT scans were taken at baseline, week 24 and week 52. Non-contrast volumetric HRCT was performed with contiguous slices with ≤1 mm thickness in supine position at full inspiration, with no iterative reconstruction.

Quantitative CT parameters

- The UCLA algorithm classifies abnormal lung tissue based on pixel density or texture.[10]
  – Quantitative lung fibrosis (QLF) score: extent of reticular patterns with architectural distortion due to fibrosis
  – Quantitative honeycomb (QHC) score: extent of honeycomb cysts
  – Quantitative ground glass opacity (QGGO) score: extent of ground glass opacities
  – The total of these scores is the quantitative ILD (QILD) score.
- e-Lung is an artificial intelligence-developed image processing module.[6] Features analyzed include:
  – Weighted Reticulovascular Score (WRVS): Measure of fibrosis combining reticular abnormalities and vascular structures
  – Total Disease Extent (TDE): Combines ground glass opacification and reticulovascular structures to provide a total ILD extent.

Analyses

- In the placebo group, we evaluated:
  – Associations between baseline QILD score, QLF score, e-Lung TDE and e-Lung WRVS (analyzed as continuous variables) and rate of decline in FVC over 52 weeks, using random coefficient regression.
  – Rate of decline in FVC over 52 weeks by baseline QILD score, QLF score, e-Lung TDE and e-Lung WRVS ≤ vs > median, using random coefficient regression.
  – Associations between baseline QILD score, e-Lung TDE, QLF score and e-Lung WRVS ≤ vs > median and time to the following, using Cox regression:
    » absolute decline in FVC % predicted ≥10% or death over 52 weeks
    » death over the whole trial.

Results

Baseline characteristics of placebo groups

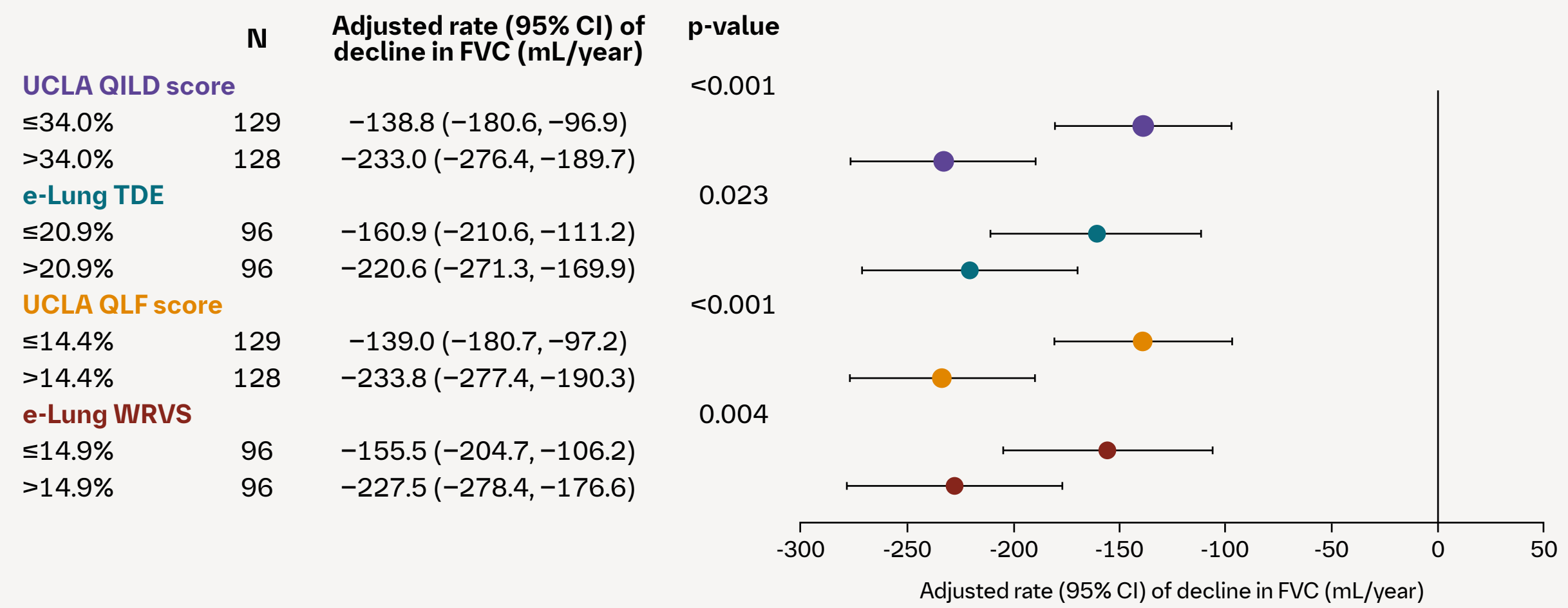|	INBUILD trial (n=331)	HRCT sub-study of INBUILD trial (n=238)
Male	177 (53.5)	132 (55.5)
Age, years	66.3 (9.8)	66.2 (10.0)
Current/former smoker	169 (51.1)	121 (50.8)
UIP-like fibrotic pattern on HRCT	206 (62.2)	151 (63.4)
Time since diagnosis of ILD, years	3.9 (3.7)	3.9 (3.6)
FVC % predicted	69.3 (15.2)	69.7 (14.8)
DLco % predicted	47.9 (15.0)	48.4 (15.7)

Data are n (%) or mean (SD).

Prognostic potential of quantitative CT parameters at baseline for rate of decline in FVC (mL/year) over 52 weeks

	Estimate (95% CI) of rate of decline in FVC (mL) per unit higher $\log_2$ value of parameter	p-value
UCLA QILD, %	−19.8 (−36.7, −2.8)	0.022
e-Lung TDE, %	−24.1 (−45.3, −2.8)	0.027
UCLA QLF, %	−23.6 (−41.5, −5.7)	0.010
e-Lung WRVS, %	−28.6 (−51.9, −5.2)	0.017

N=257 for UCLA assessments and n=192 for e-Lung assessments. Random coefficient regression with fixed effects for HRCT pattern, baseline quantitative CT value ($\log_2$), baseline FVC (mL), and including baseline quantitative CT ($\log_2$)–by–time and baseline FVC–by–time interactions.

Rate of decline in FVC (mL/year) over 52 weeks by baseline quantitative CT values ≤ vs >median

	N	Adjusted rate (95% CI) of decline in FVC (mL/year)	p-value
UCLA QILD score			<0.001
≤34.0%	129	−138.8 (−180.6, −96.9)	
>34.0%	128	−233.0 (−276.4, −189.7)	
e-Lung TDE			0.023
≤20.9%	96	−160.9 (−210.6, −111.2)	
>20.9%	96	−220.6 (−271.3, −169.9)	
UCLA QLF score			<0.001
≤14.4%	129	−139.0 (−180.7, −97.2)	
>14.4%	128	−233.8 (−277.4, −190.3)	
e-Lung WRVS			0.004
≤14.9%	96	−155.5 (−204.7, −106.2)	
>14.9%	96	−227.5 (−278.4, −176.6)	

Random coefficient regression with fixed effects for HRCT pattern, dichotomized baseline quantitative CT value, baseline FVC (mL), and including dichotomized baseline quantitative CT–by–time, and baseline FVC–by–time interactions.
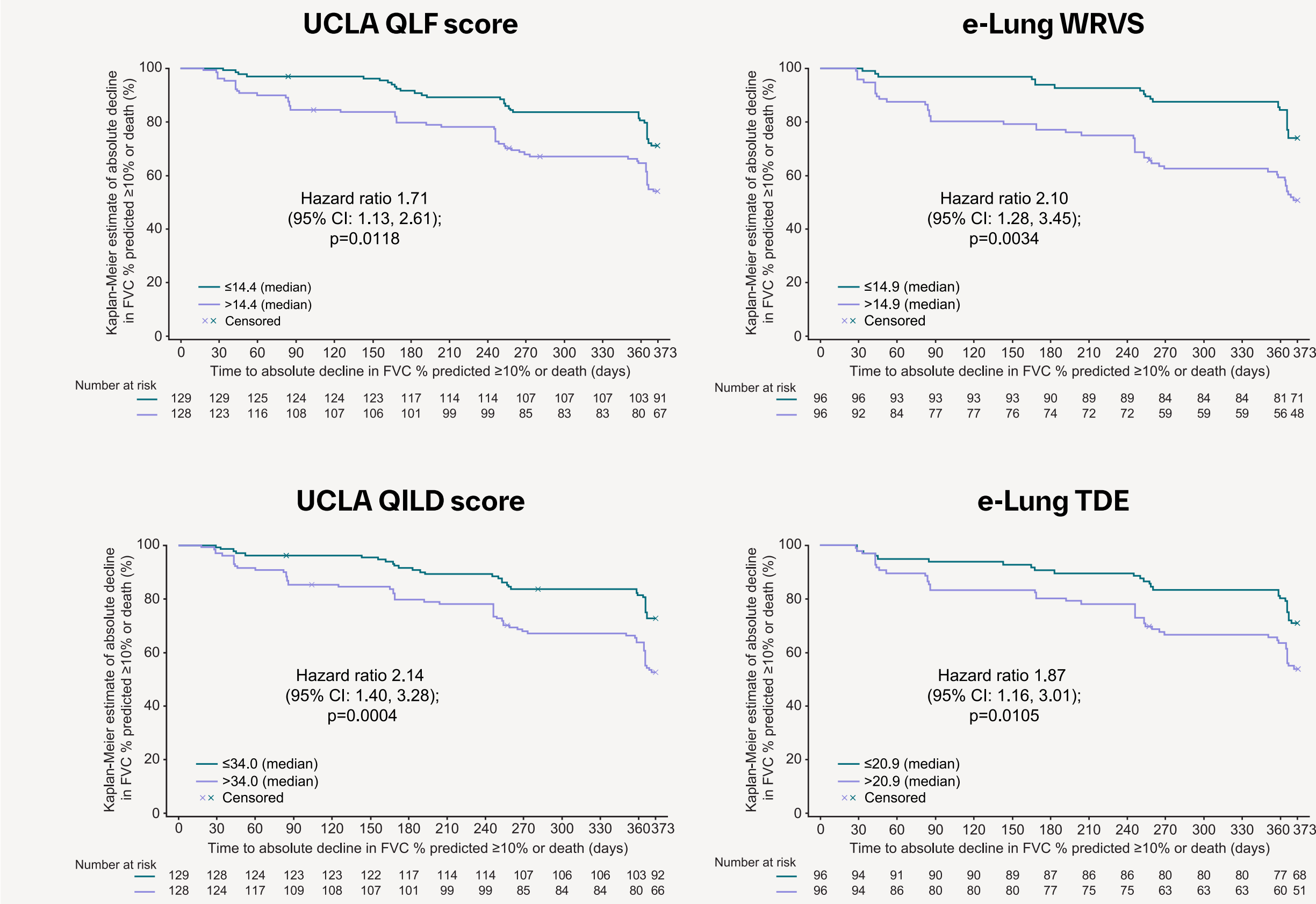
Time to absolute decline in FVC % predicted ≥10% or death over 52 weeks by baseline QCT parameters

Hazard ratios are based on Cox regression model with continuous covariate age, binary covariate dichotomized baseline quantitative CT value, and categorical covariate inclusion criterion for progressive ILD, and stratified by HRCT pattern (UIP-like pattern versus other fibrotic patterns).

Time to death over whole trial by baseline QCT parameters

Hazard ratios are based on Cox regression model with continuous covariate age, binary covariate dichotomized baseline quantitative CT value, and categorical covariate inclusion criterion for progressive ILD, and stratified by HRCT pattern (UIP-like pattern versus other fibrotic patterns).

Conclusions

- In the INBUILD trial in patients with PPF, a greater extent of ILD (QILD score or e-Lung TDE) or lung fibrosis (QLF score or WRVS) at baseline was associated with a greater rate of decline in FVC over 52 weeks and a greater risk of death over the whole trial.
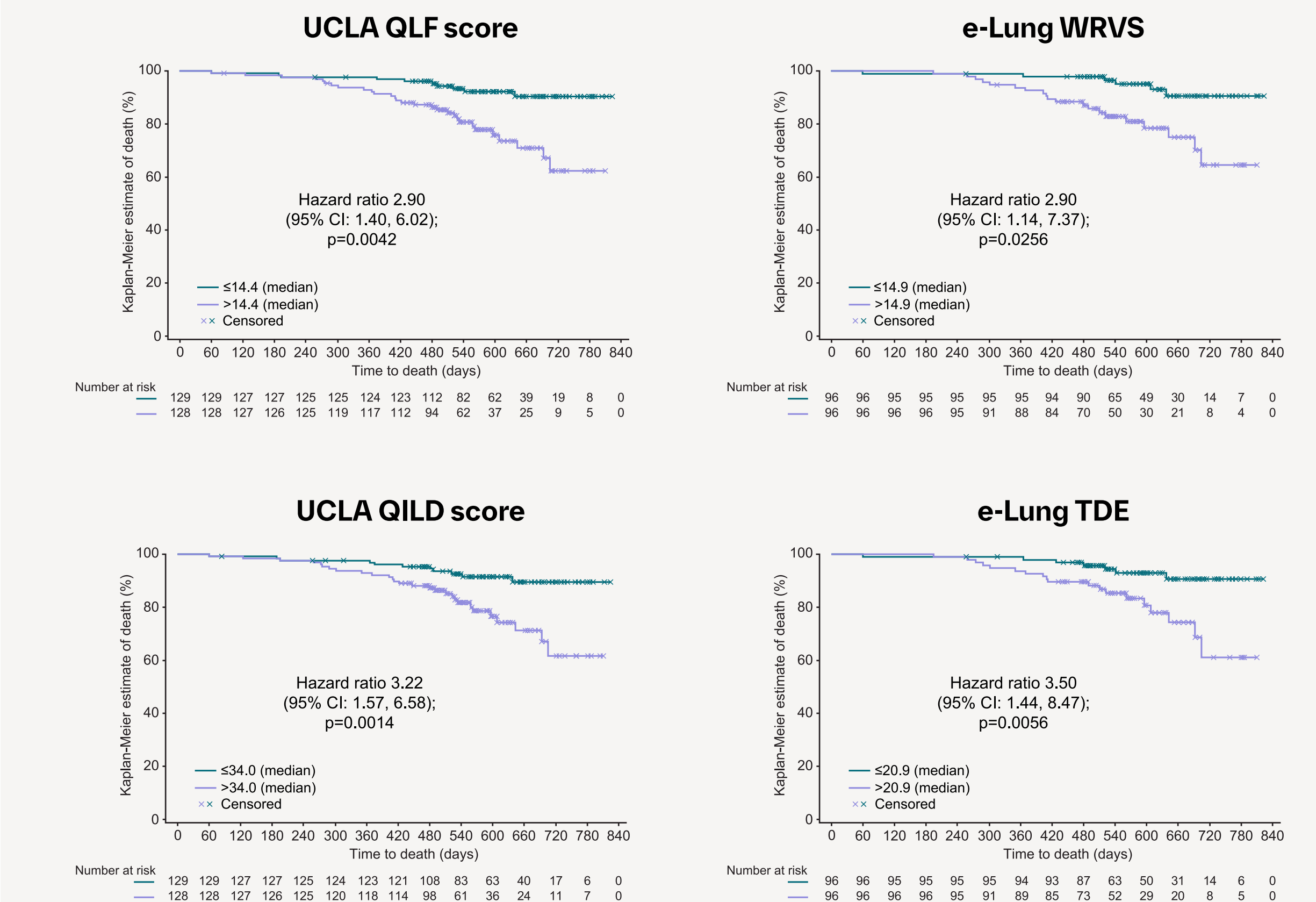
- These findings suggest that quantitative CT methods can facilitate the prediction of clinically relevant outcomes in patients with PPF.

References
1. Walsh SLF et al. Eur Respir Rev 2024;33:230055; 2. Khanna D et al. Arthritis Res Ther 2015;17:372; 3. Kim GHJ et al. Eur Radiol 2020;30:726–34; 4. Lee JS et al. J Clin Med 2021;10:3812; 5. Devaraj A et al. Am J Respir Crit Care Med 2024;209:1168-9; 6. Jacob L et al. Eur Respir J 2017;49:1; 7. George PM et al. ERJ Open Res 2024;00570-2024; 8. Yeo J et al. Rheumatology (Oxford) 2023;62:3690-9; 9. Humphries SM et al. Chest 2024:S0012-3692(24)05472-2; 10. Flaherty KR et al. N Engl J Med 2019;381:1718-27; 11. Kim HG et al. Clin Exp Rheumatol 2010;28:S26–35.