## Ultrasensitive Circulating Tumour DNA Detection for Risk Stratification in Early-Stage NSCLC

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Circulating tumour DNA (ctDNA) analysis is a promising tool for assessing clinical risk in early-stage non-small cell lung cancer (NSCLC). However, its clinical utility has been constrained by the sensitivity of current approaches. We utilized a tumour-informed liquid biopsy platform capable of detecting ctDNA at concentrations as low as 1-3 parts per million (PPM). A total of 2990 plasma samples from 432 lung cancer patients enrolled in the TRACERx study were analyzed to evaluate the prognostic impact of ultrasensitive ctDNA detection. ctDNA detection below 80 PPM at a postoperative landmark timepoint identified an intermediate-risk group, distinct from those with undetectable ctDNA and those with ctDNA levels above 80 PPM. Additionally, integrating preoperative ctDNA status enabled further stratification of relapse risk and survival outcomes in lung adenocarcinoma. Our findings highlight the value of ultrasensitive ctDNA detection for improved risk stratification in early-stage lung cancer. This approach has the potential to refine prognostic assessment and inform clinical decision-making, advancing personalized management strategies in NSCLC.