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Background:

Large-scale RCT's have shown that CT lung cancer screening is effective in reducing lung cancer mortality. However, the optimal screening strategy, including risk-based intervals, remain unknown.

Objective:

To evaluate the safety, effectiveness and feasibility of risk-based personalised CT lung cancer screening and support high-quality implementation across Europe.

Design:

4-IN-THE-LUNG-RUN (4-ITLR) is a multicentre randomised controlled trial conducted across five European countries. More than 21,000 participants aged 60-79 years at high risk* of lung cancer defined as a $PLCO_{m2012}$ 6-yr risk >2.6% or smoking history of >35 PYs, with <10 yrs of quit smoking, were randomised 1:1 to annual or risk-based (biennial) screening (Figure 1).

Figure 1 – Study protocol

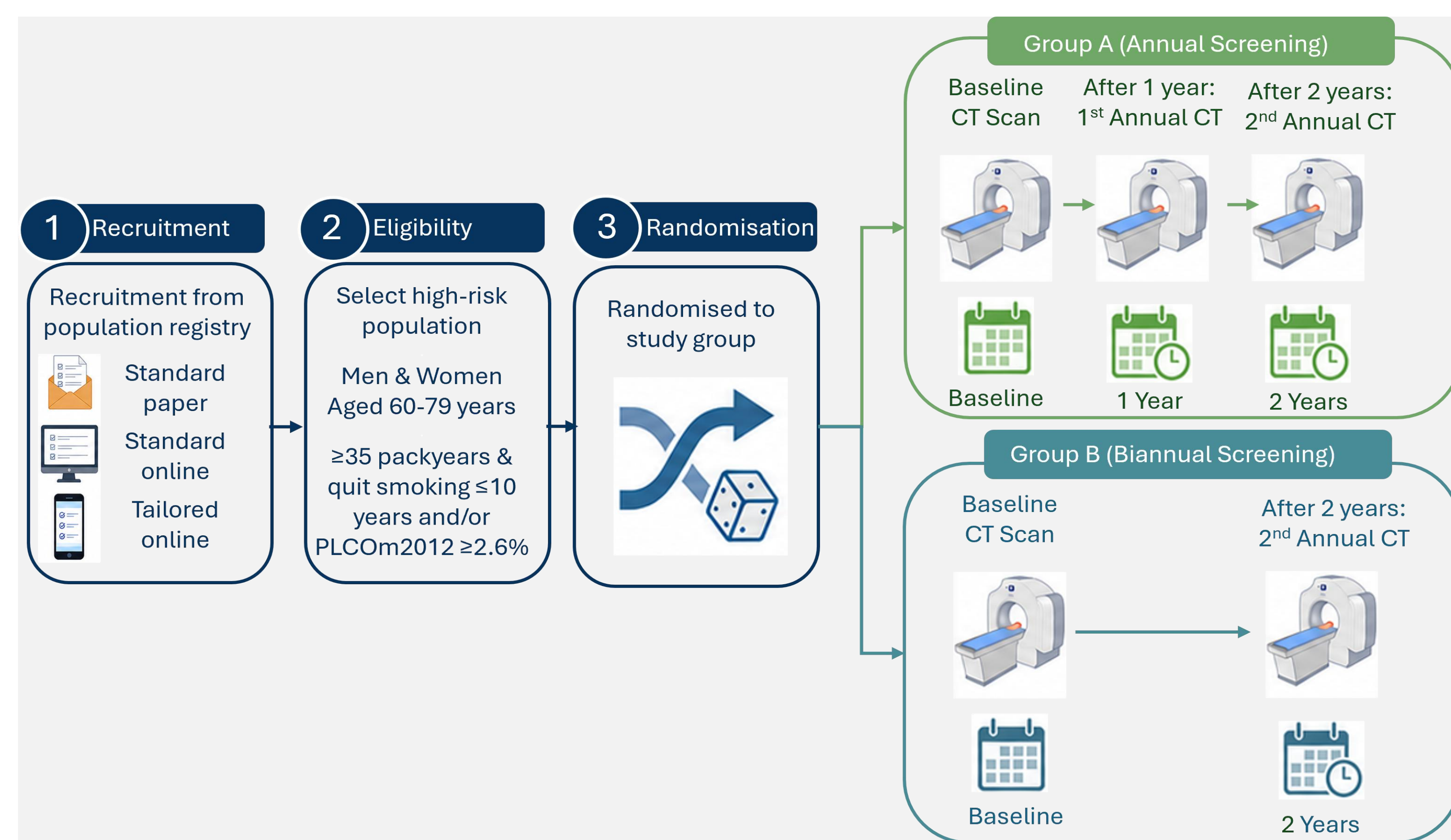


Figure 2 – Lung cancer stage distribution (preliminary results baseline round 5 screening centres 4-ITLR)

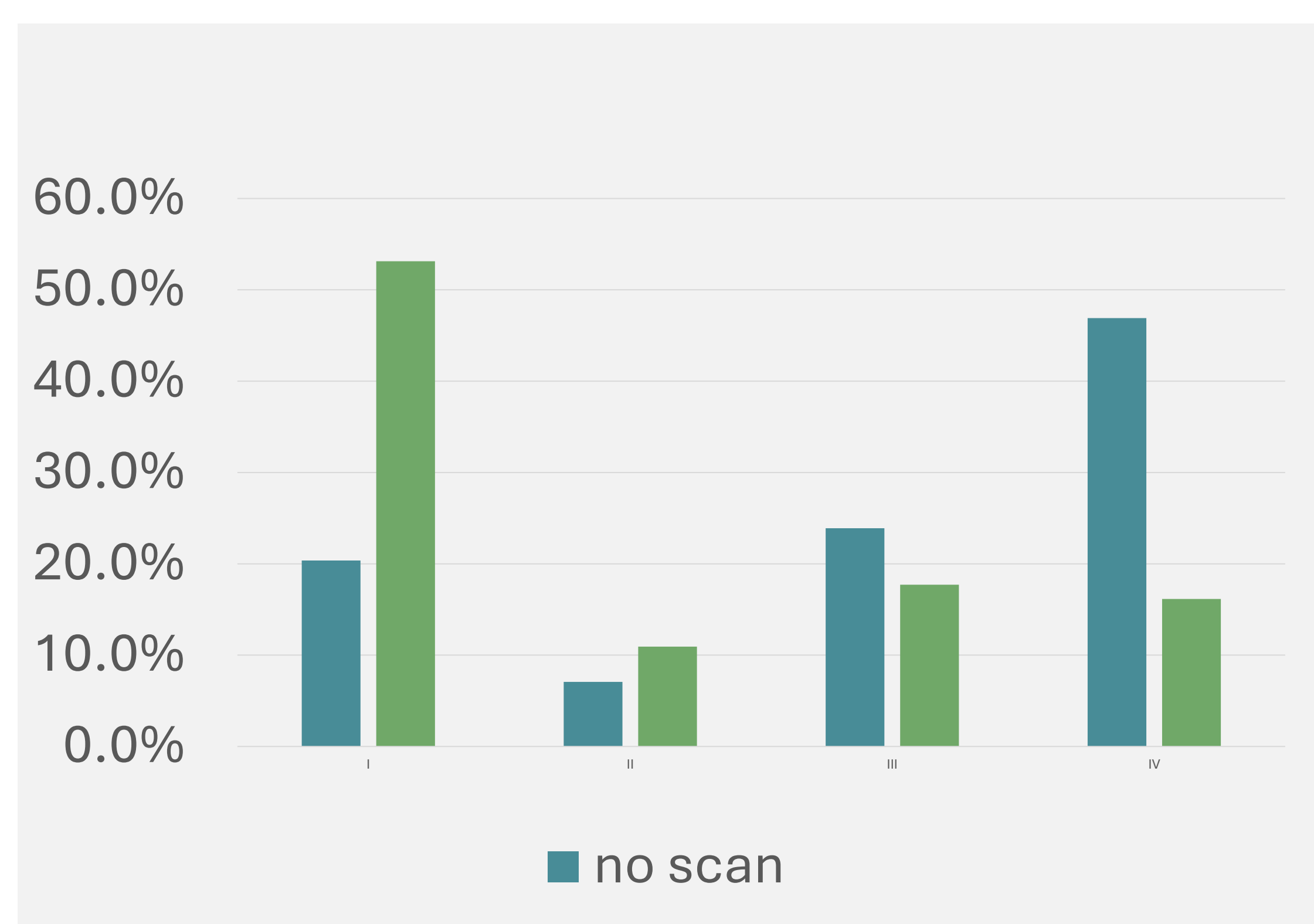
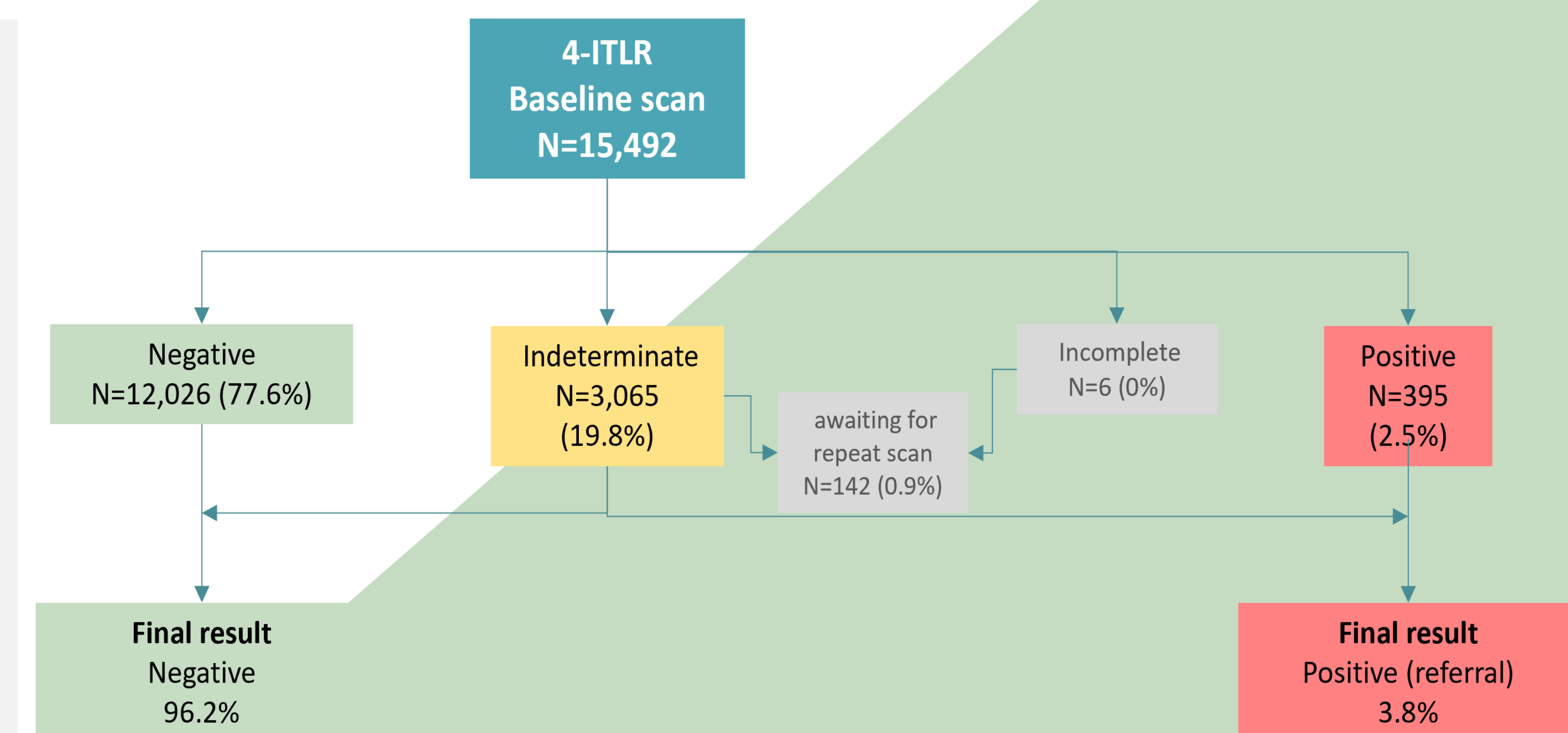


Figure 3 – Baseline CT screening across 7 screening centers of 4-ITLR



Preliminary Results:

- ✓ > **33,000 CT scans** have been performed (excl. pooling data RISP & SUMMIT)
- ✓ Risk-based recruitment is feasible in a population that is less likely to participate in screening programmes.
- ✓ Acceptable informed-decision making
- ✓ Refined nodule management protocol after NELSON with low radiation doses, CAC scoring, and strict incidental findings management
- ✓ Integration of AI
 - rule out test-negatives
 - outperforms human reading in identification of rapid growth (VDT).
- ✓ Confirmed stage shift towards early-stage screen-detected lung cancers with acceptable referral baseline rate (Figure 2 & Figure 3).
- ✓ Personalized smoking cessation support may enhance smoking abstinence after lung cancer screening.
- ! Evidence regarding the safety of personalize screening intervals is under evaluation.

Why does 4-ITLR matter?

- Adequate risk-based selection real-world high-risk population
- Sufficient screening participation among hard-to-reach populations
- Implementation high-quality screening protocol across countries feasible
- Improved nodule management protocol
- Minimal radiation exposure
- Reduce false-positive findings and related harms as anxiety and unnecessary follow-up procedures
- Integration of AI reading (lung nodules & CAC)
- Increase cost-effectiveness

Conclusion: The 4-ITLR trial will provide evidence for real-world implementation aimed at more **(cost)effective, safer and more accessible lung cancer screening for all European countries.**