

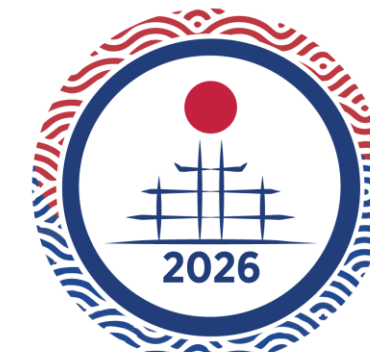


P1.025: Toward Personalized Lung Cancer Screening

Integrating Sex, PRS, Family History, Age and Sybil Risk Prediction

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INTRODUCTION

- PRS** (polygenic risk score) may enhance the effectiveness of lung cancer screening in Taiwan beyond smoking and family history¹.
- Sybil** is an AI (artificial intelligence) model that predicts lung cancer risk from low-dose CT (LDCT)².
- We aimed to integrate sex, PRS, family history, age, and Sybil to:
 - Determine the appropriate age to **initiate** LDCT screening
 - Develop an individualized **follow-up** framework

METHODS

- We conducted a retrospective cohort study including **2,214 individuals who underwent LDCT screening** between November 2008 and August 2021 at a tertiary hospital in Taiwan.
- Genetic data were obtained from the Taiwan Precision Medicine Initiative.
- Polygenic risk scores (PRS)** were calculated using **25 susceptibility loci** associated with non-small cell lung cancer (NSCLC)³.
- Participants were followed for the **1-year NSCLC incidence after LDCT**.
- A **1-year incidence exceeding 1.5%** was used to define the recommended age for screening initiation.
- Sex-specific risk factors were identified to construct risk factor-defined subgroups.
- Sybil generated a 1-year lung cancer risk score from a single LDCT scan.
- Within each subgroup, subgroup-specific Sybil thresholds were derived to classify individuals into low-, intermediate-, and high-risk groups.
- These thresholds were selected to achieve a **false-negative rate <10%** for low risk and a **positive predictive value ≥30%** for high risk.

RESULTS

- Invasive NSCLC:** 25 men (2.2%) and 38 women (3.6%). (Figure 1)
- Risk factors for NSCLC:**
 - Male (Figure 2A): age (AUC 0.664)
 - Female (Figure 2B): family history of lung cancer (ACU 0.683), age (AUC 0.634), PRS (AUC 0.645)
- Sybil's ability to predict NSCLC within 1 year:**
 - Male (Figure 2A): AUC 0.903
 - Female (Figure 2B): AUC 0.888
- Recommended screening age** (Figure 3)
 - Male: ≥50 years
 - Female: based on (1) family history and (2) top 10% PRS
 - No factors: ≥60 years
 - ≥1 factor (family history or top 10% PRS): <50 years
- Subgroup stratification** according to lung cancer risk
 - Male: (1) < 60 years, (2) ≥ 60 years
 - Female: (1) 0 factor, <60 years; (2) 0 factor, ≥60 years; (3) 1 factor; (4) 2 factors

*Factor = lung cancer family history or top 10% of PRS
- Sybil score thresholds** for low-, intermediate and high-risk stratification across different subgroups
 - Male (Figure 4), Female (Figure 5)
- Recommended Follow-up Intervals**
 - Low risk: >1 year
 - Intermediate risk: 3–12 months
 - High risk: ≤3 months or immediate biopsy

Figure 1. Flowchart of study participant enrollment

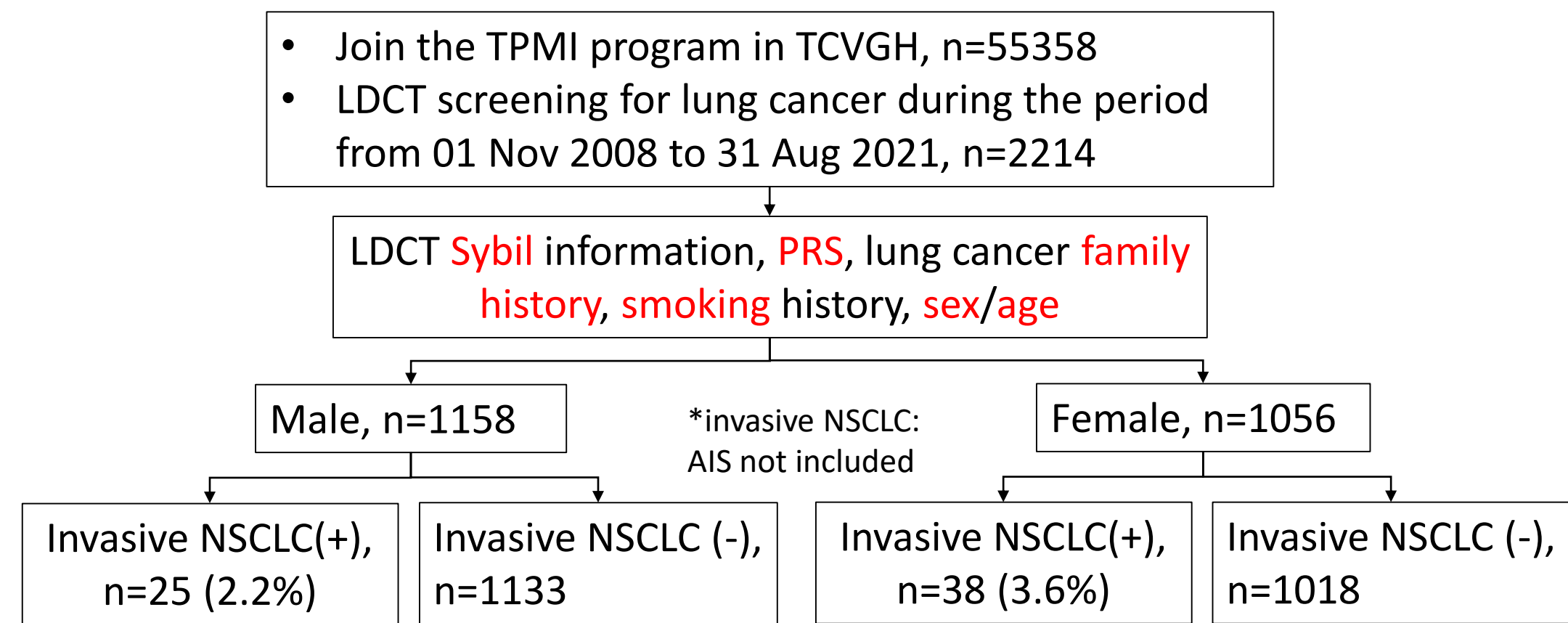


Figure 2. ROC curves for different factors in predicting 1-year NSCLC incidence

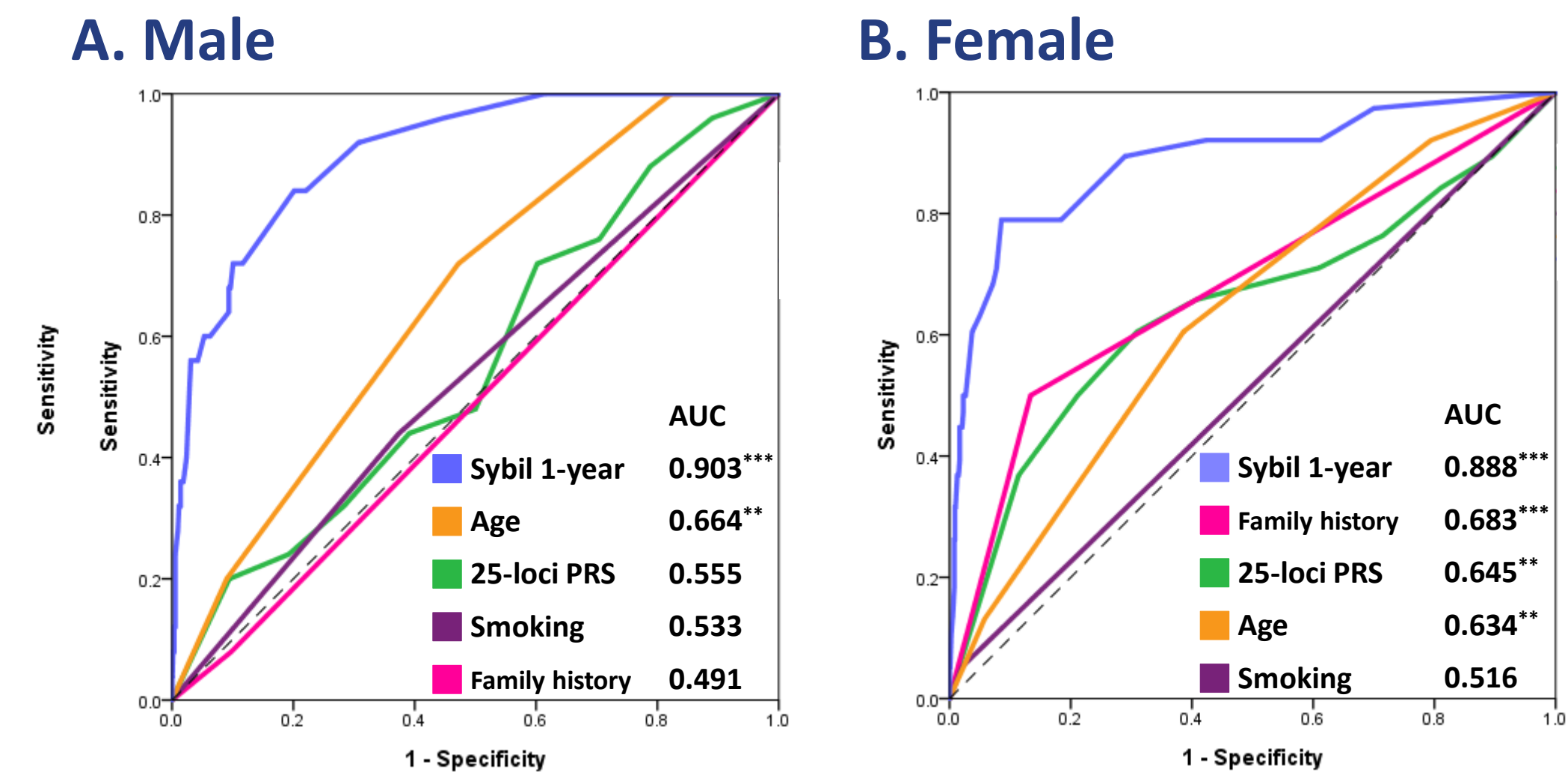


Figure 3. Cumulative incidence of NSCLC among different subgroups. Factors for female: (1) family history, and (2) top 10% of PRS

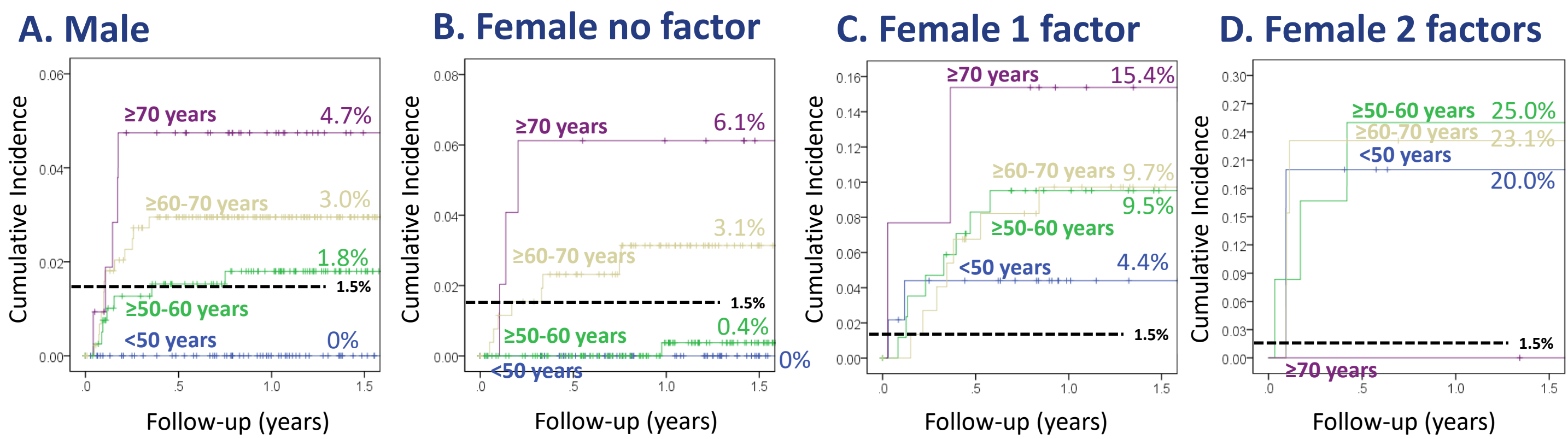
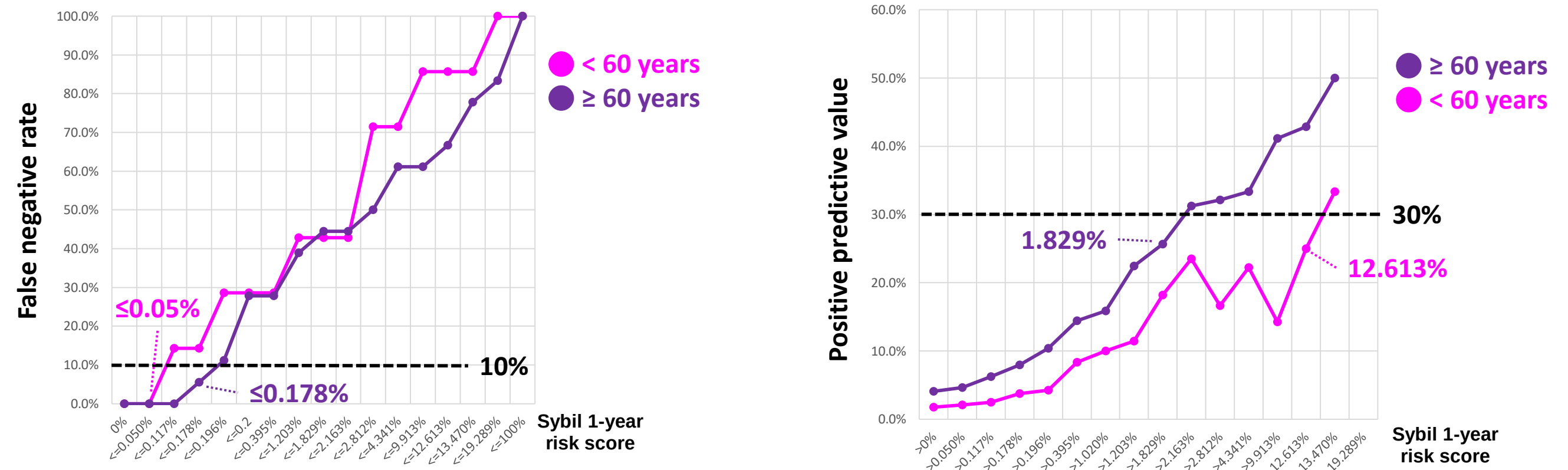


Figure 4. Identification of the Sybil threshold for stratifying males into high-, intermediate-, and low-risk groups.

A. False negative rate at each Sybil score threshold B. Positive predictive value at each Sybil score threshold



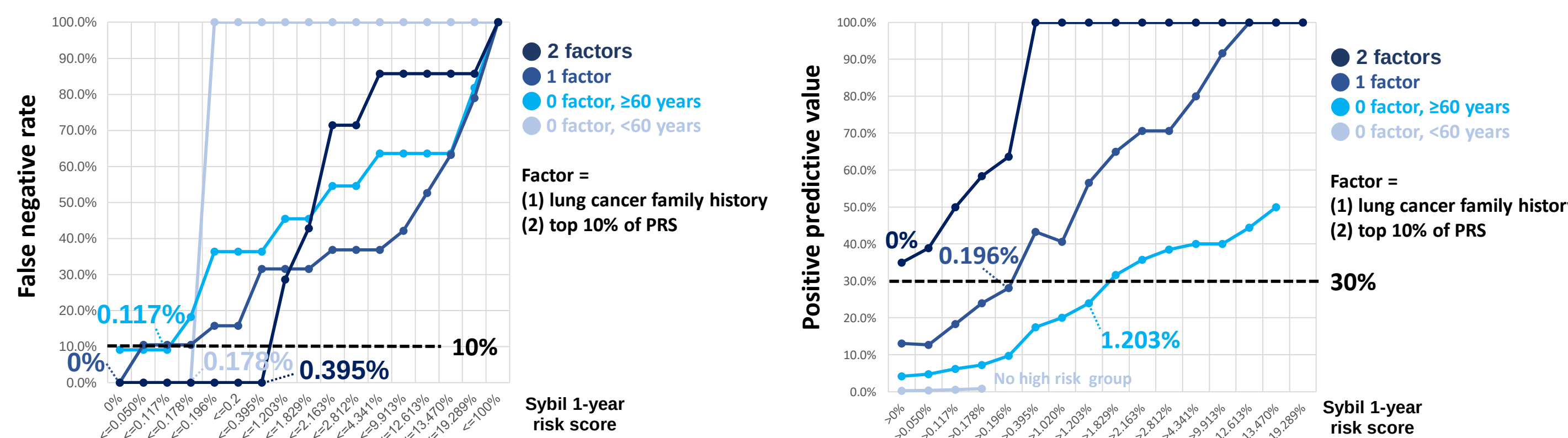
C. Sybil score thresholds for low- and high-risk stratification across different male subgroups.

Sybil 1-year score	0.000%	0.050%	0.117%	0.178%	0.196%	0.395%	1.020%	1.203%	1.829%	2.163%	2.812%	4.341%	9.913%	12.613%	≥13.113%	1-year NSCLC incidence
<60 years																1.2%
≥60 years																3.3%

● Low risk: follow-up CT >1 year ● Intermediate risk: CT 3-12 months ● High risk: <3 months CT or biopsy

Figure 5. Identification of the Sybil threshold for stratifying females into high-, intermediate-, and low-risk groups.

A. False negative rate at each Sybil risk threshold B. Positive predictive value at each Sybil risk threshold



C. Sybil score thresholds for low- and high-risk stratification across different female subgroups.

Sybil 1-year score	0.000%	0.050%	0.117%	0.178%	0.196%	0.395%	1.020%	1.203%	≥1.829%	1-year NSCLC incidence
0 factor, <60 years										0.3%
0 factor, ≥60 years										3.6%
1 factor										8.9%
2 factors										22.0%

Factor = (1) lung cancer family history, or (2) top 10% of PRS

● Low risk: follow-up CT >1 year ● Intermediate risk: CT 3-12 months ● High risk: <3 months CT or biopsy

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The recommended age for LDCT screening initiation varied across subgroups defined by sex, family history, and PRS.
- Within each subgroup, Sybil further refined risk stratification into low-, intermediate-, and high-risk groups using distinct thresholds.
- Low-risk individuals were eligible for extended follow-up intervals (e.g., >1 year), whereas high-risk individuals were recommended to undergo repeat imaging within 3 months or immediate biopsy.

Future Direction for Research

- Prospective** LDCT screening for women with top 10% PRS
- Integrating Sybil with LUNG-RADS** to guide personalized follow-up

REFERENCES & ACKNOWLEDGEMENTS

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