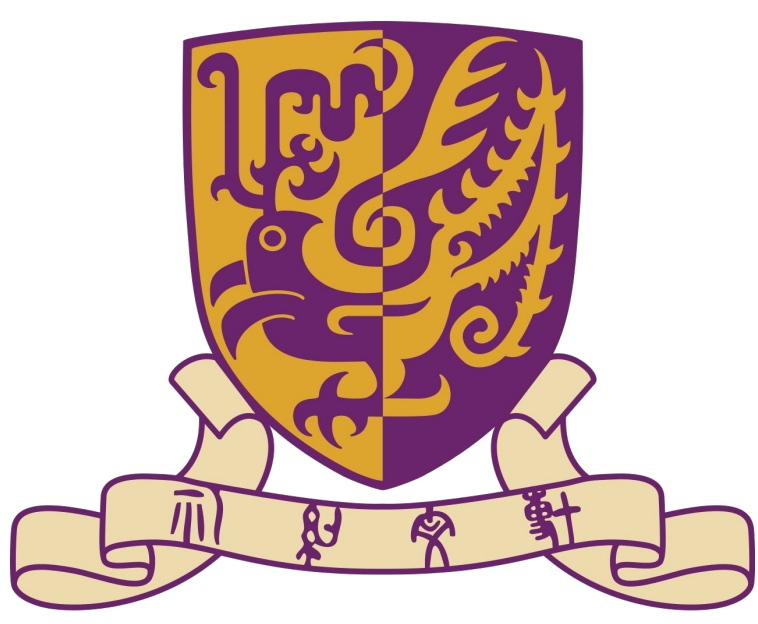




Validation of SYBIL in a Lung Cancer Screening study targeting high-risk Asian never smokers



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INTRODUCTION

Incidence of **lung cancer in never-smokers (LCNS)** is **rising**, with East Asians presenting two-times higher incidence rates compared to the West (Zhou & Zhou, 2018). LDCT screening improves early-stage lung cancer detection, and SYBIL functions to personalise screening intervals based on predicted risk of lung cancer development (Graham et al., 2024).

What is SYBIL?

- A deep learning model that predicts lung cancer risk up to six years from a single baseline LDCT scan (Mikhael, 2023)
- Strong discriminative performance demonstrated in prior studies
- Data on clinical application in never-smokers remains limited

METHODS

Hong Kong Lung Cancer screening study
Enrollment (18/7/2024 - 3/10/2025)

- Never smokers
- Age 50-75 years
- First degree relatives with lung cancer

Baseline Low-dose CT (LDCT)

SYBIL analysis – prediction of lung cancer risk at Years 1-6

For histopathologically confirmed lung cancer diagnoses,
variables collected: Demographics, Nodule size, Nodule type, Lung-RADS, Pathological stage

Primary Endpoint:

Area under the curve receiver operating characteristic curve (AUC) to assess model performance

Secondary Endpoints:

- Cancer vs non-cancer
- Solid/part-solid vs GGN
- Risk score distributions

RESULTS

Data Cutoff Date: 11/06/2026

Study Cohort

1,800 participants enrolled in the Hong Kong Lung Cancer Screening Study. Final analysis cohort: **1,788** participants

- Median age: **62 years**
- Female: **1,165 (65.2%)**
- Simplex family history: **1,463 (81.7%)**
- **12 participants excluded** following study withdrawal
- Histopathologically confirmed lung cancer: **36 (2.0%)**

Sybil demonstrated excellent discrimination for predicting lung cancer.

AUC = 0.951
95% CI: 0.912–0.989
p < 0.001

Participants with confirmed lung cancer had significantly higher Sybil-predicted risk scores than those without lung cancer (median 11.85% [IQR 1.80–36.45] vs. 0.10% [IQR 0.10–0.20]; p < 0.001).

Risk prediction was not significantly associated with:

- Sex ($p = 0.125$)
- Family history (simplex vs. multiplex) ($p = 0.978$)
- Smoking family history ($p = 0.913$)

Age demonstrated a weak positive correlation with predicted risk (Spearman's $\rho = 0.125$, $p < 0.001$).

Sybil 1-year risk scores did not differ significantly according to nodule type. (Mann-Whitney U = 159.5, Z=1.19, p=0.239)

Patients with pure GGO, Mean = 12.49% (SD = 17.06)

Patients with purely Solid or Part-solid Nodules, Mean = 30.71% (SD = 36.79)

*Patients presenting with >1 nodule type were excluded from this analysis (n = 3)

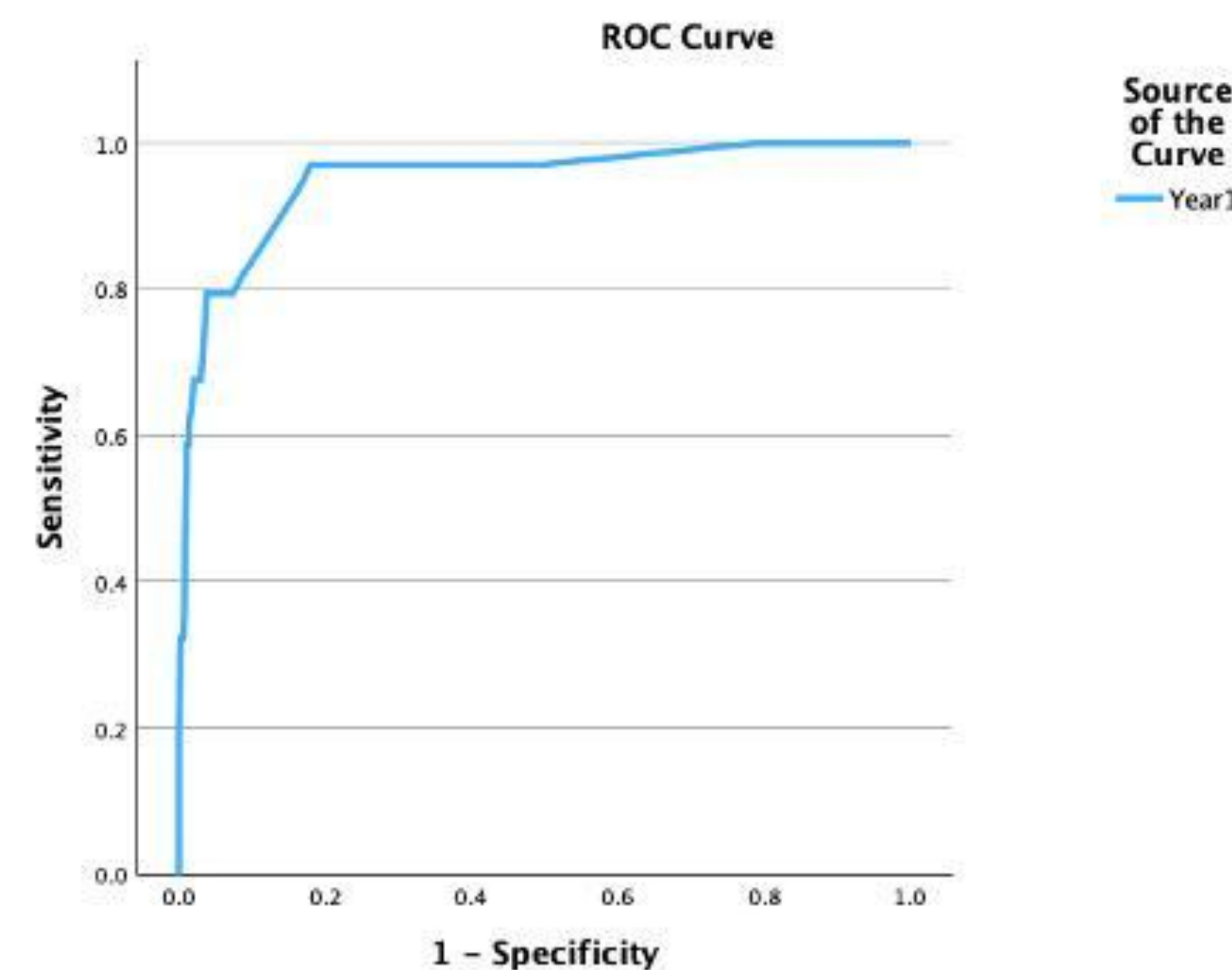


Figure 1. ROC curve for Sybil-predicted 1-year lung cancer risk.

	Value
Total Lung Cancers identified, n	36
Median Age (range)	62 (51–75)
Female, n (%)	28 (77.8)
Multifocal Lung cancers, n (%)	9 (26.5)
Tumour nodules =2, n (%)	5 (55.6)
Tumour nodules >=3, n (%)	4 (44.4)
Total tumour nodules identified, n	53*
Solid, n (%)	14 (26.4)
Part-solid, n (%)	11 (20.8)
Pure GGN,, n (%)	28 (52.8)

Stages of Lung Cancer

Stage I Disease, n (%)	30 (88.2)
Stage III Disease, n (%)	3 (8.8)
Pending	1

Table 1. Clinicopathological characteristics and Sybil-predicted lung cancer risk scores of the 34 participants with histopathologically confirmed lung cancer.

*1 patient presented with pleural effusion and 1 patient presented with lung collapse, instead of nodules

DISCUSSION AND CONCLUSION

Sybil demonstrates high discriminatory performance for short-term lung cancer risk prediction within this high-risk never-smoker cohort, highlighting its potential as a post-LDCT risk-stratification tool. Risk predictions did not differ significantly according to radiological nodule phenotype. However, exploratory analysis identified lower mean predicted risk among lung cancers presenting as pure GGNs compared with solid or part-solid nodules, warranting further investigation in larger cohorts.

Future Direction

- **Prospectively validate Sybil** in larger, multi-centre cohorts of never-smokers across diverse Asian populations.
- **Evaluate the integration of Sybil into LDCT screening programmes** to determine its impact on early cancer detection, risk stratification, and clinical decision-making.

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