Lung Cancer Risk Prediction Models for Asian Ever-Smokers

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Nothing to disclose

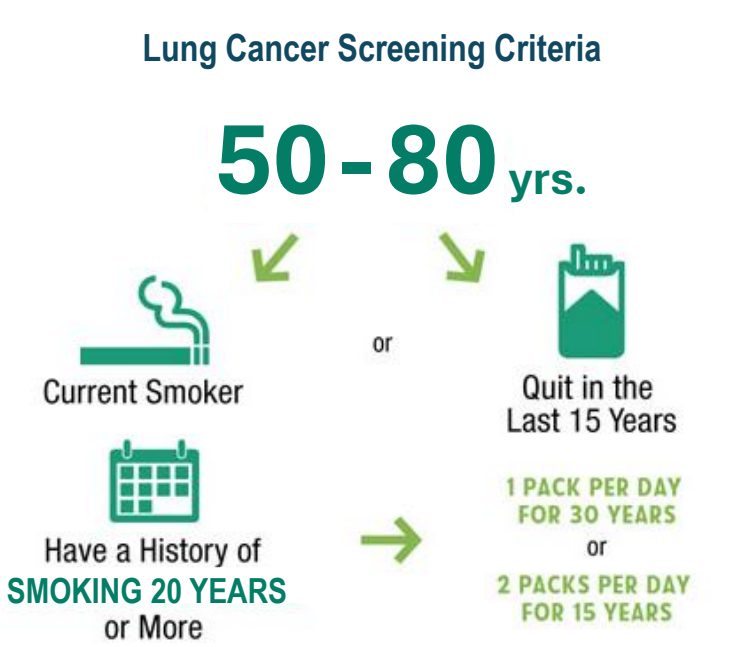
WCE

WORLD CONGRESS OF EPIDEMIOLOGY 2024

Lung Cancer Screening

Implementing Low-Dose Computed Tomography Scan for Early Detection

US Preventive Services Task Force (USPSTF)
Annual Screening for Lung Cancer with
Low-dose computed tomography (LDCT)



The US Preventive Services Task Force (USPSTF) recommendation 2020

- **Benefits**
  : Early detection at the curable stage
  : Lower the chances of dying from lung cancer among high-risk individuals (smokers)

- **Concerns**
  : Uncertainty on the benefit-to-harm ratio
  : Possibility of false-positive results leading to unnecessary invasive procedures/complications

- How to ***better select the LDCT screening candidates*** who would benefit most?

- **Personalized lung cancer risk assessment**
  : To determine screening eligibility incorporating a more comprehensive smoking history and other potential risk factors

Lung Cancer Risk Prediction Models

Selection of Ever-Smokers for Computed Tomography Lung Cancer Screening

Model	Targeted Outcome	Time Frame	Risk Factors Incorporated in Models
Bach (2003)	LC Incidence	1-10 y	age, gender, smoking duration, cigarettes smoked per day, years since cessation, asbestos exposure
Spitz (2007)	LC Incidence	1 y	age, gender, history of COPD, family history of any cancer (2 or more), family history of smoking related-cancer (1 or more), age at quitting, pack-years, asbestos exposure, dust exposure, history of hay fever
LLP V1, V2, V3 (2008)	LC Incidence	5 y	age, gender, smoking duration, history of cancer and pneumonia, family history of lung cancer (early/late onset), asbestos exposure
Hoggart (2012)	LC Incidence	1 y	smoking status, smoking duration, age at staring smoking, cigarettes smoked per day
$PLCO_{M2012}$ (2013)	LC Incidence	6 y	age, race, education, BMI, history of cancer and COPD, family history of lung cancer, smoking status, smoking duration, cigarettes smoked per day, years since cessation
LLPi (2015)	LC Incidence	8.7 y	age, gender, smoking duration, history of cancer and COPD, family history of lung cancer (early/late onset)
Pittsburgh (2015)	LC Incidence	6 y	age, smoking status, smoking duration, cigarettes smoked per day
LCRAT (2016)	LC Incidence	5 y	age, gender, race, education, BMI, pack-years, smoking duration, years since cessation, cigarettes smoked per day, history of COPD, family history of lung cancer (none, early, late onset)
LCDRAT (2016)	LC Mortality	5 y	age, gender, race, education, BMI, pack-years, smoking duration, years since cessation, cigarettes smoked per day, history of COPD, family history of lung cancer (none, early, late onset)

- Focused on Western populations (USA & Europe)
- Developed and validated using cohorts with >90% whites
- Post validation studies: limited to Western (White) populations
- Performance in Asian populations?

Asian Smokers

- Low smoking intensity
- Late-onset smoking
- Low rates of smoking cessation
- Very low prevalence of smoking in women
- High prevalence of never-smoking lung cancer

Study Aims

Asia: the major epicenter of lung cancer with more than 50% of lung cancers worldwide

- **Aim1:** To evaluate the statistical performance, *i.e.*, calibration and discrimination, of 11 lung cancer risk models in multiple Asia populations (using 19 prospective cohorts)
- **Aim2:** To better refine risk models for Asians by developing new prediction models incorporating Asian-specific risk estimates based on two well-characterized prospective cohorts (SMHS/SWHS)

The Asia Cohort Consortium

- 19 prospective cohorts in Asia
  - : 4 cohorts from China
  - : 7 cohorts from Japan
  - : 5 cohorts from South Korea
  - : 1 cohort from Taiwan
  - : 1 cohort from Mumbai
  - : 1 cohort from Iran
- Final analytic sample
  - : 186,458 Asian smokers
  - : ~6,800 incident lung cancer

https://www.asiacohort.org/

Methods

- **Study Populations**

  : 186,458 Asian ever-smokers (aged ≥50) from 19 ACC cohorts

- **Evaluation of 11 Western Lung Cancer Risk Prediction Models**

  : Calibration (E/O ratios) and discrimination (AUC)

  : Based on the two-stage random-effects meta-analysis method

  : Using the publicly available R package

- **Development of Shanghai Lung Cancer Risk Prediction Models**

  : Using data on ever-smokers aged 40-75 years at baseline within the SMHS and SWHS

  : Two cause-specific proportional hazards models, considering the competing mortality hazard

    - Shanghai lung cancer incidence (Shanghai-LCM) and death model (Shanghai-LCDM)

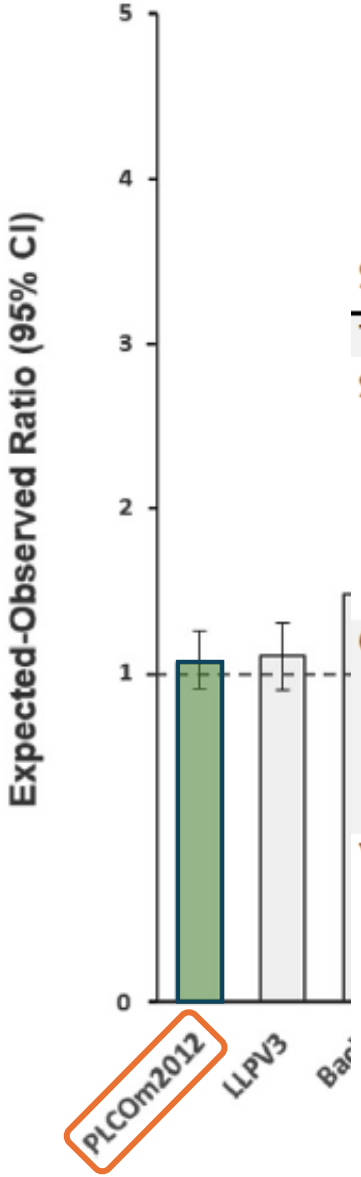
  : External validation using individual participant data from 17 ACC cohorts

Participating cohorts in the Asia Cohort Consortium

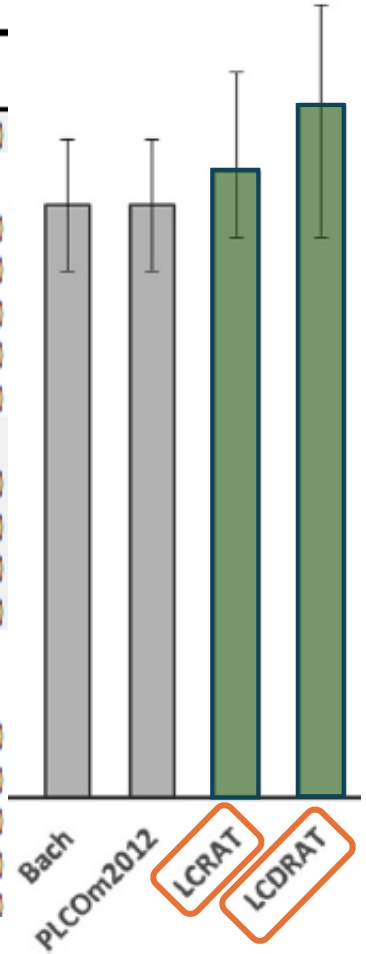
Participating Cohorts	No. of Participants[a]	Baseline Survey	Follow-up Years[b]	Age at Baseline[c]	Men (%)	Current Smokers (%)	Smoking Pack-Years[c]		Eligible USPSTF[d]		No. of Lung Cancer	
							Men	Women	2013 (%)	2021 (%)	Cases[e] (N)	Deaths (N)
Chinese												
SMHS	24,069	2002-2006	11.5	60.0	100.0	84.2	27.7	N.A.	27.1	59.4	845	695
SWHS	1584	1997-2000	15.4	63.6	0.0	81.6	N.A.	14.7	14.4	25.3	85	76
SCHS	15,816	1994-2005	11.5	64.4	82.7	53.7	31.4	15.0	35.1	52.7	906	791
SCS	8485	1986-1989	20.4	57.9	100.0	89.2	26.9	N.A.	32.0	61.0	823	801
CBCSP	3451	1991-1992	14.0	57.6	98.9	85.0	24.5	6.8	28.3	68.9	N.A.	92
Japanese												
JACC	22,699	1988-1990	14.5	62.1	90.8	64.2	28.7	14.4	34.7	54.9	1021	910
Miyagi	11,414	1990-1990	19.5	57.5	91.3	72.4	34.7	17.1	37.9	70.2	811	445
Ohsaki	16,026	1996-1996	10.3	64.2	90.0	63.9	34.8	15.4	45.6	67.3	722	486
3Pref Miyagi	6610	1984-1984	7.4	62.0	83.3	67.7	36.6	18.5	38.6	67.3	125	94
3Pref Aichi	10,374	1985-1985	11.1	61.8	81.7	64.0	38.3	18.4	37.5	66.0	317	283
LSS (RERF)	12,255	1963-1993	16.3	60.6	78.8	88.1	30.2	12.1	47.2	74.2	N.A.	574
Takayama	8369	1992-1992	12.5	63.3	83.3	58.4	25.1	11.8	23.1	40.4	302	N.A.
Korean												
KMCC	5218	1993-2004	12.1	63.5	82.0	68.7	33.4	13.7	41.7	63.7	307	257
Seoul	4818	1992-1993	15.4	54.0	100.0	62.3	24.6	N.A.	16.3	56.8	N.A.	65
KNCC	8278	2002-	8.9	57.3	94.0	39.2	24.4	9.6	20.5	48.8	155	43
Namwon	3356	2004-2007	11.6	64.2	90.2	85.5	31.7	15.8	42.0	64.2	172	127
KCS	3101	1985-1985	12.5	67.4	71.1	91.0	40.5	15.2	49.9	63.3	124	103
Indian												
Mumbai	16,093	1991-1997	4.8	60.0	99.0	73.7	12.9	5.9	7.0	15.8	52	52
Iranian												
GCS	4442	2003-2008	11.1	59.5	93.5	54.7	20.7	7.8	18.5	37.1	54	47
Total	186,458	1963-2008	12.7	61.1	89.7	68.8	28.3	14.5	31.8	55.8	6821	5941

Calibration & Discrimination of Western Models in Asian Populations

Extremely unstable among Asian
"low-intensity smokers" and
"long-term abstainers"



Stratification	Expected-to-Observed Ratio (95% CI)			AUC (95% CI)		
	$PLCO_{m2012}$	LCRAT	LCDRAT	$PLCO_{m2012}$	LCRAT	LCDRAT
Total study population	1.06 (0.90-1.25)	1.55 (1.30-1.86)	1.67 (1.39-2.00)	0.68 (0.66-0.70)	0.69 (0.67-0.72)	0.71 (0.67-0.74)
Smoking pack-years						
<10	0.19 (0.14-0.26)	1.26 (0.84-1.88)	1.38 (0.83-2.28)	0.58 (0.54-0.63)	0.65 (0.59-0.71)	0.72 (0.66-0.78)
10-19	0.62 (0.49-0.77)	1.33 (1.02-1.75)	1.45 (1.10-1.90)	0.62 (0.58-0.67)	0.65 (0.60-0.71)	0.69 (0.61-0.78)
20-29	1.05 (0.84-1.31)	1.16 (0.97-1.39)	1.05 (0.84-1.31)	0.67 (0.63-0.72)	0.69 (0.63-0.76)	0.71 (0.65-0.77)
30-39	1.12 (0.89-1.41)	1.49 (1.19-1.86)	1.57 (1.23-2.01)	0.64 (0.60-0.69)	0.65 (0.58-0.72)	0.64 (0.58-0.72)
≥40	1.34 (1.11-1.63)	1.67 (1.38-2.02)	1.68 (1.36-2.08)	0.61 (0.58-0.65)	0.63 (0.59-0.67)	0.62 (0.56-0.68)
Cigarettes smoked/d						
<10	0.24 (0.18-0.33)	1.59 (1.18-2.15)	1.90 (1.30-2.76)	0.63 (0.58-0.69)	0.72 (0.64-0.80)	0.81 (0.76-0.86)
10-19	1.00 (0.80-1.24)	1.35 (1.11-1.64)	1.39 (1.16-1.67)	0.70 (0.66-0.73)	0.69 (0.65-0.73)	0.68 (0.63-0.72)
20-29	1.22 (1.03-1.46)	1.46 (1.23-1.73)	1.55 (1.28-1.88)	0.68 (0.64-0.72)	0.69 (0.65-0.73)	0.71 (0.66-0.78)
≥30	1.25 (1.02-1.54)	1.56 (1.26-1.94)	1.61 (1.27-2.03)	0.68 (0.60-0.76)	0.69 (0.62-0.76)	0.71 (0.63-0.80)
Years since quitting smoking						
<5	0.98 (0.76-1.27)	1.50 (1.11-2.03)	1.26 (0.91-1.77)	0.70 (0.65-0.75)	0.67 (0.60-0.74)	0.76 (0.69-0.83)
5-9	0.99 (0.78-1.27)	1.08 (0.84-1.40)	0.85 (0.67-1.09)	0.71 (0.63-0.80)	0.67 (0.56-0.81)	0.76 (0.68-0.84)
10-14	0.83 (0.64-1.07)	0.89 (0.66-1.19)	0.93 (0.70-1.24)	0.67 (0.57-0.78)	0.69 (0.55-0.81)	0.62 (0.51-0.76)
15-19	0.63 (0.48-0.83)	0.73 (0.56-0.94)	0.77 (0.51-1.15)	0.67 (0.58-0.78)	0.67 (0.57-0.78)	0.64 (0.52-0.80)
≥20	0.48 (0.34-0.78)	0.55 (0.39-0.76)	0.60 (0.38-0.95)	0.64 (0.55-0.73)	0.71 (0.64-0.79)	0.68 (0.59-0.77)



Predictor	Definition	Model
age **agex** **agex2** **log_age** **lage2**	40-75 years at the baseline age-55 agex^2 log(age)-log(55) log_age^2	**Shanghai-LCM** Cox model lung cancer incidence cases: Surv(followed_years, lung_cancer_case) ~ log_age + gender + educatn1 + educatn2 + educatn4 + educatn5 + bmix + bmix2 + smkyrsc1 + smkyrsc2 + smkyrsc4 + smkyrsc5 + log_pkyrs + log_qtyrs + fam_lcnum. **Shanghai-LCDM** Cox model lung cancer deaths: Surv(followed_years, lung_cancer_death) ~ log_age + gender + educatn1 + educatn2 + educatn4 + educatn5 + bmix + bmix2 + smkyrsc1 + smkyrsc2 + smkyrsc4 + smkyrsc5 + log_pkyrs + log_qtyrs + fam_lcnum.
gender	female vs male 0-male (reference) 1-female	
educatn	education levels 1-elementary school or lower 2-middle school 3-high school (reference) 4-some college 5-college or higher	
bmix **bmix2** **log_bmi** **lbmi2**	bmi-25 bmix^2 log(bmi)-log(25) log_bmi^2	
copd	COPD history 0-no (reference) 1-yes	
smoke status	smoking status 1-former smoker (reference) 2-current smoker	
cigar per day **years_smoked** **smkyrsc**	number of cigarettes per day number of smoking years categorized number of smoking years 1-<10 years 2-<20 years 3-<30years (reference) 4-<40 years 5->= 40 years	
packyears **log_pkyrs**	cigar per day*years smoked/20 log(packyears+1)	
years_quitted **log_qtyrs**	duration (years) of smoking cessation log(years_quitted+1)	
fam lcnum (continuous)	number of lung cancer cases in family members 0-None 1-one lung cancer case in family members 2- ≥2 lung cancer cases in family members	

Development of Lung Cancer Risk Models Based on the SMHS & SWHS

To predict 1- to 10-year cumulative risk of developing lung cancer or dying from lung cancer, considering the competing mortality hazard

Stratification	Expected to Observed Ratio (95% CI)		AUC (95% CI)	
	Shanghai-LCM	Shanghai-LCDM	Shanghai-LCM	Shanghai-LCDM
Total study population	1.55 (1.24-1.93)	1.80 (1.44-2.25)	0.70 (0.67-0.72)	0.72 (0.69-0.74)
Ethnicity				
Chinese	0.98 (0.89-1.08)	1.08 (0.85-1.38)	0.70 (0.65-0.76)	0.69 (0.63-0.77)
Japanese	1.70 (1.36-2.13)	1.97 (1.52-2.55)	0.70 (0.66-0.75)	0.71 (0.67-0.75)
Korean	1.20 (0.73-1.99)	1.72 (1.11-2.66)	0.69 (0.66-0.72)	0.75 (0.68-0.81)
Indian	4.24 (3.00-6.00)	4.39 (2.94-6.55)	0.64 (0.55-0.74)	0.65 (0.54-0.76)
Iranian	2.75 (1.71-4.42)	2.31 (1.41-3.77)	0.74 (0.64-0.84)	0.75 (0.65-0.85)
Age, y				
50-59	1.67 (1.27-2.19)	1.79 (1.37-2.33)	0.68 (0.64-0.71)	0.67 (0.64-0.71)
60-69	1.45 (1.15-1.82)	1.64 (1.31-2.05)	0.65 (0.62-0.67)	0.66 (0.64-0.68)
≥70	1.65 (1.27-2.14)	1.89 (1.40-2.54)	0.71 (0.69-0.73)	0.71 (0.68-0.75)
Gender				
Men	1.52 (1.22-1.89)	1.77 (1.43-2.18)	0.69 (0.66-0.71)	0.70 (0.67-0.73)
Women	1.85 (1.21-2.83)	1.78 (1.06-2.98)	0.76 (0.69-0.84)	0.84 (0.78-0.91)
Smoking status				
Current	1.58 (1.25-1.99)	1.88 (1.47-2.40)	0.70 (0.68-0.71)	0.71 (0.68-0.74)
Former	1.40 (1.09-1.79)	1.45 (1.13-1.87)	0.69 (0.65-0.74)	0.70 (0.60-0.81)
Smoking pack-years				
<10	0.88 (0.64-1.22)	1.15 (0.78-1.70)	0.70 (0.63-0.78)	0.77 (0.71-0.83)
10-19	1.36 (1.00-1.86)	1.65 (1.21-2.26)	0.69 (0.64-0.74)	0.72 (0.65-0.80)
20-29	1.52 (1.19-1.93)	1.53 (1.17-2.01)	0.71 (0.65-0.78)	0.72 (0.65-0.79)
30-39	1.45 (1.10-1.91)	1.71 (1.27-2.30)	0.66 (0.63-0.70)	0.67 (0.62-0.71)
≥40	1.64 (1.30-2.06)	1.73 (1.35-2.21)	0.64 (0.60-0.67)	0.67 (0.62-0.71)
Cigarettes smoked/d				
<10	1.15 (0.79-1.67)	1.66 (1.03-2.67)	0.71 (0.63-0.80)	0.81 (0.75-0.87)
10-19	1.52 (1.19-1.94)	1.77 (1.38-2.26)	0.70 (0.66-0.74)	0.69 (0.65-0.74)
20-29	1.48 (1.20-1.82)	1.67 (1.33-2.11)	0.69 (0.66-0.72)	0.70 (0.64-0.77)
≥30	1.53 (1.18-1.99)	1.69 (1.29-2.22)	0.69 (0.62-0.78)	0.73 (0.66-0.82)
Years since quitting smoking				
<5	1.58 (1.12-2.24)	1.55 (1.02-2.35)	0.63 (0.53-0.74)	0.68 (0.58-0.80)
5-9	1.28 (0.95-1.73)	1.01 (0.78-1.32)	0.76 (0.67-0.87)	0.83 (0.76-0.91)
10-14	1.09 (0.83-1.42)	1.11 (0.81-1.52)	0.66 (0.54-0.80)	0.68 (0.55-0.84)
15-19	1.08 (0.79-1.48)	1.02 (0.66-1.59)	0.73 (0.68-0.79)	0.74 (0.64-0.86)
≥20	0.88 (0.65-1.19)	0.94 (0.67-1.32)	0.70 (0.63-0.77)	0.69 (0.63-0.76)

External Validation of Shanghai Models

Good internal validity

= Overall AUCs 0.78-0.80

Conclusion

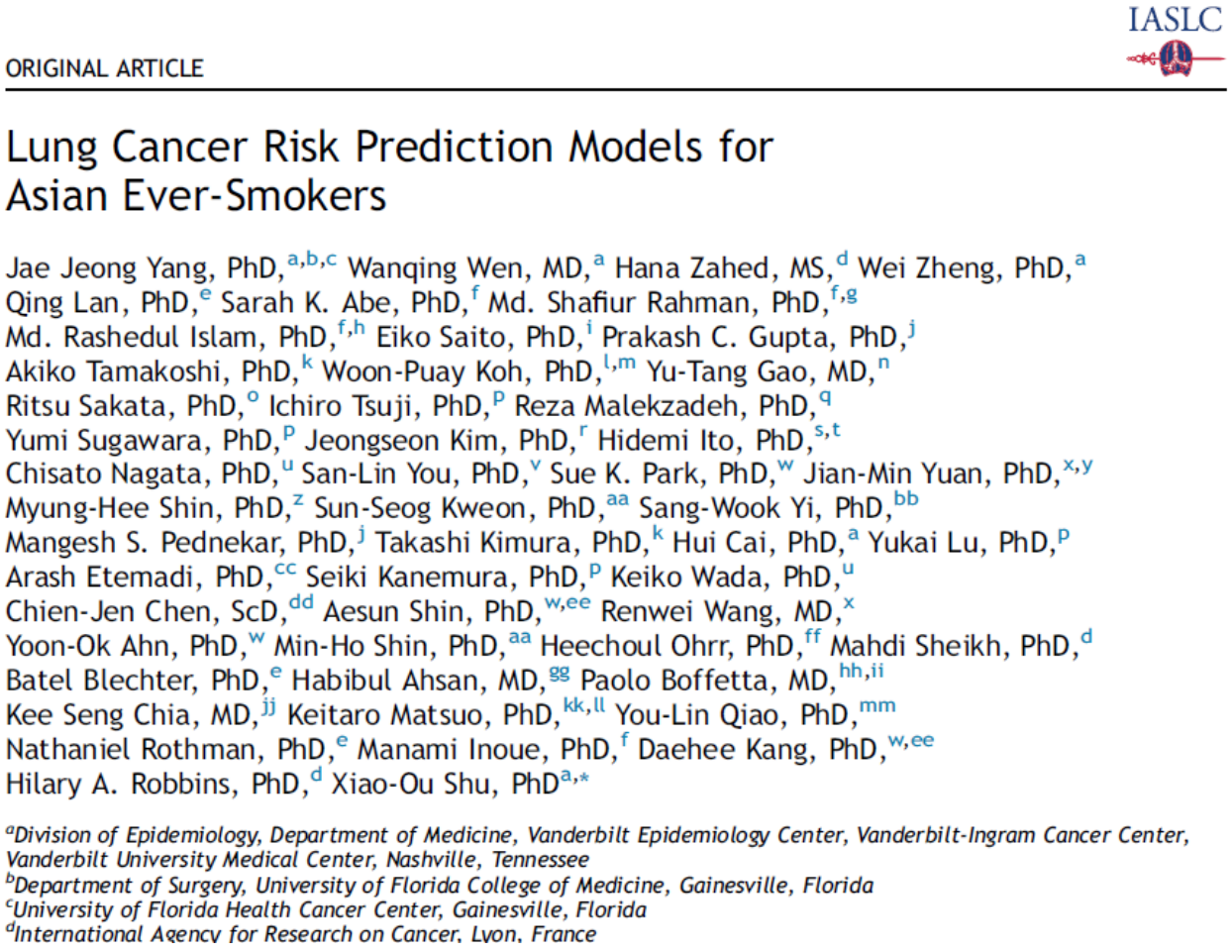
- **Lung cancer risk models developed in the U.S. and Europe**
  - $PLCO_{m2012}$, LCRAT, and LCDRAT had good predictive performance in Asian populations
  - Performed poorly in predicting lung cancer risk among Asians who reported low-intensity smoking or who had quit smoking for prolonged periods

- **Shanghai lung cancer risk prediction models**
  - *Improved predictive performance* for *low-intensity smokers* and *long-term quitters* who were particularly prevalent in Asia but not captured well by Western models
  - Also had room to be refined for universal application to diverse Asian populations

- Importance of incorporating *Asia-specific risk estimates into* ***personalized lung cancer risk assessment*** *to better implement risk-based LDCT screening in Asia*

- Further need for *country-specific adjustment* in identifying at-risk Asians who are most eligible for LDCT screening

Acknowledgement



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ORIGINAL ARTICLE

Lung Cancer Risk Prediction Models for Asian Ever-Smokers

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THANK YOU

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