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Risk Stratification for Surveillance Colonoscopy

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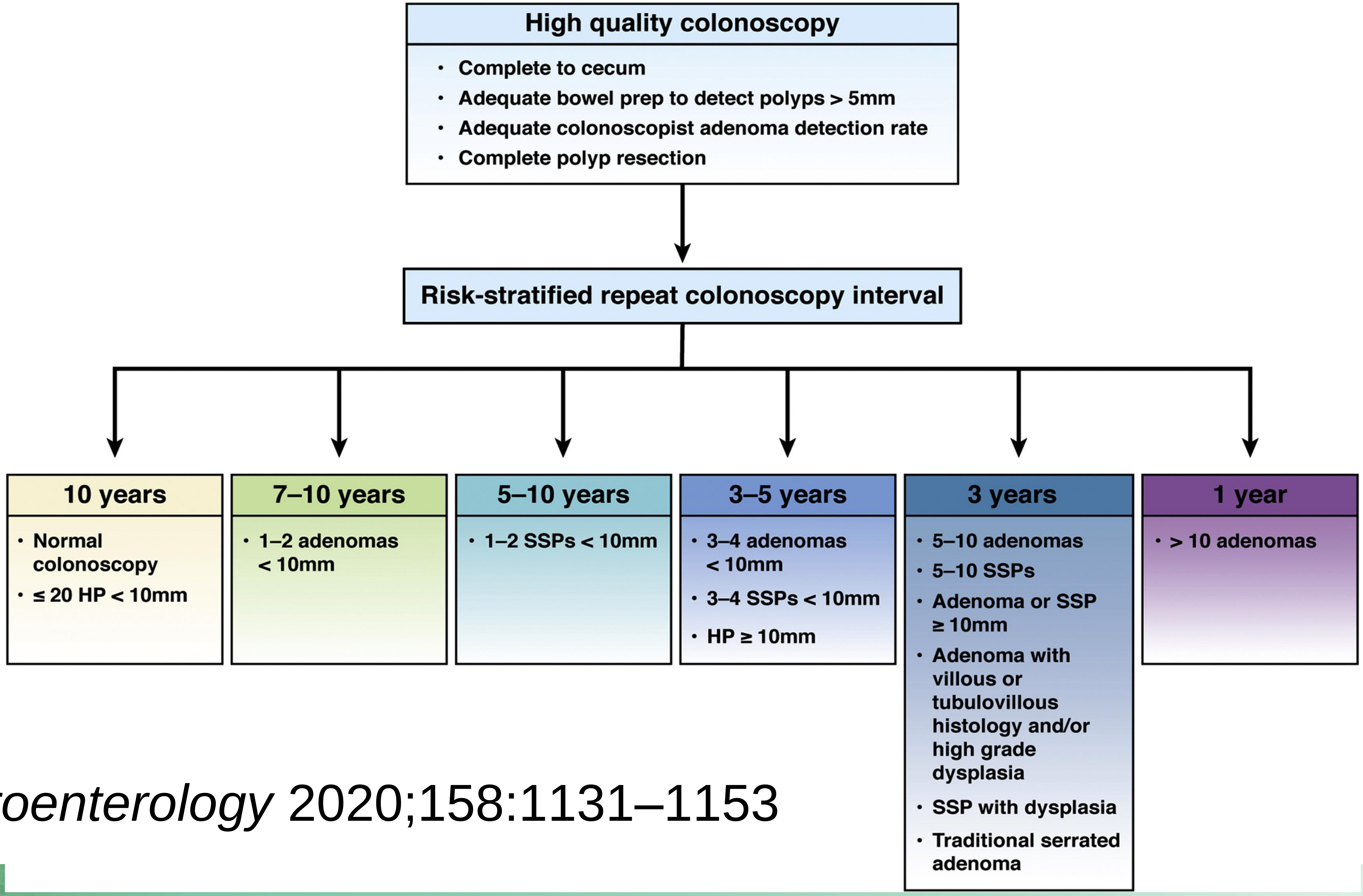
Agenda

3 recently published studies

1. Lee, **Predicting Risk of Colorectal Cancer After Adenoma Removal in a Large Community-Based Setting** Am J Gastro 2024; E pub
2. Levin, Jensen, **Development and external validation of a prediction model for colorectal cancer among patients awaiting surveillance colonoscopy following polypectomy** *Gastro Hep Advances* (2024), doi: https://doi.org/10.1016/j.gastha.2024.03.008
3. Lee, **Surveillance Colonoscopy Findings in Older Adults With a History of Colorectal Adenomas**

   Jama Network Open. 2024 Apr 1;7(4):e244611

Surveillance in the US



Gupta, *Gastroenterology* 2020;158:1131–1153

Background

Lee, AJG 2024

- US guidelines for surveillance are primarily based on polyp characteristics
- Does not take into account potential clinical variables that could explain risk for cancer or advanced adenomas at colonoscopy

Methods

Lee, AJG 2024,

- Large retrospective cohort
- Inclusion:
  - KPNC members
  - Aged 40-85
  - Baseline first colonoscopy 2004-2016
  - Findings: TA, TVA, VA, HGD
  - $\geq$ 1 year membership pre/post
- Exclusion
  - Hx CRC
  - Hereditary Syndrome
  - IBD
  - Prior adenoma
  - Colectomy
- Follow up through 2020

Candidate Predictors

- Patient Factors
  - Age, Race, BMI, tobacco use (from the EMR)
- Clinical Factors
  - DM, any fam hx CRC, Charlson comorbidity
- Colonoscopy Factors
  - Indication, endoscopist screening ADR ($\leq$ 25 %, > 25%), polyp size, histology, $\geq$ 3 containers, TSA/SSA, proximal HP

Model Development

- Population split 70/30 development/internal validation
- Cox proportional hazards regression:
  - *Polyp model* only included the polyp characteristics
  - *Comprehensive model* included polyp characteristics plus predictors significantly associated with CRC outcome and then simplified for practical utility
- Calibrated using Hosmer-Lemeshow

Variables Not Found to be Significant

- Sex
- Race (Hispanic race was modestly protective)
- BMI
- Smoking
- Proximal HP
- More than 3 containers with adenoma

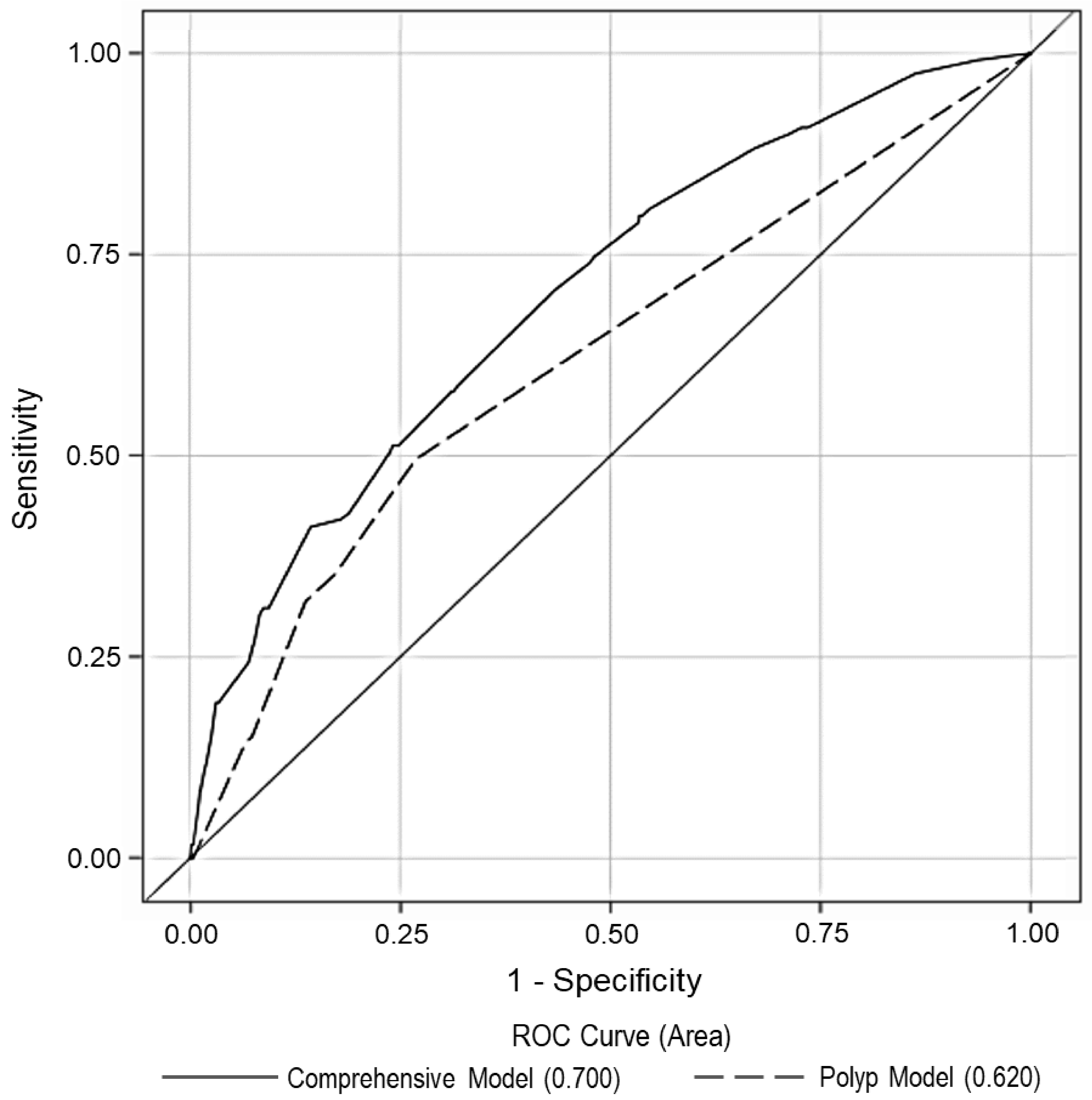
Significant predictors

Predictor	Category	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI)
Age, years	40-54	(REF)	(REF)
	55-69	1.96 (1.40 - 2.74)	1.78 (1.27 - 2.50)
	70-85	3.76 (2.65 - 5.32)	3.08 (2.14 - 4.42)
Fam hx CRC	Yes	1.28 (0.98 - 1.67)	1.79 (1.36 - 2.36)
Diabetes diagnosis	Yes	1.70 (1.33 - 2.17)	1.41 (1.04 - 1.93)
Charlson comorbidity score			
	0	(REF)	(REF)
	1	1.39 (1.06 - 1.83)	1.17 (0.87 - 1.58)
	≥ 2	1.88 (1.47 - 2.40)	1.30 (0.95 - 1.77)
Colonoscopy indication			
	Screening or surveillance	(REF)	(REF)
	Diagnostic	1.65 (1.21 - 2.24)	1.59 (1.16 - 2.18)
	FIT positive	2.83 (2.13 - 3.75)	2.50 (1.86 - 3.37)
Endoscopist screening ADR, %			
	< 25	(REF)	(REF)
	≥ 25	0.63 (0.50 - 0.78)	0.69 (0.55 - 0.86)
	Unknown	0.83 (0.56 - 1.23)	0.86 (0.58 - 1.28)
Adenoma with advanced histology			
	Yes	2.47 (1.96 - 3.10)	1.83 (1.43 - 2.35)
Polyp size ≥10 mm			
	Yes	2.08 (1.66 - 2.61)	1.40 (1.09 - 1.79)
SSA or TSA			
	Yes	1.84 (1.15 - 2.93)	2.05 (1.28 - 3.28)

Simplified Comprehensive Model vs Polyp Model

Predictors	HR (95% CI)	β-coefficient†	Weight^	Risk Score Points#
Comprehensive model				
Adenoma with advanced histology	1.89 (1.47 - 2.43)	0.638	10.00	10
Polyp size ≥10 mm	2.02 (1.27 - 3.23)	0.704	11.03	11
SSA or TSA	1.46 (1.14 - 1.87)	0.379	5.94	6
Age category (years):				
55-69	1.83 (1.31 - 2.56)	0.605	9.48	9
70-85	3.30 (2.32 - 4.68)	1.192	18.69	19
Colonoscopy indication:				
FIT Positive	2.25 (1.69 - 3.00)	0.810	12.70	13
Diagnostic	1.47 (1.08 - 2.00)	0.384	6.02	6
Diabetes diagnosis	1.51 (1.18 - 1.93)	0.409	6.41	6
Polyp model				
Adenoma with advanced histology	2.07 (1.61 - 2.67)	0.730	10.00	10
Polyp size ≥10 mm	1.59 (1.24 - 2.03)	0.463	6.35	6
SSA or TSA	1.90 (1.19 - 3.03)	0.641	8.78	9

Model Comparison



Model	AUC (95% CI)	AIC	Hosmer-Lemeshow goodness-of-fit test
Comprehensive Model	0.700 (0.653 - 0.747)	1475.3	3.346 (p=0.911)
Polyp Model	0.620 (0.573 - 0.667)	1521.0	4.115 (p=0.128)

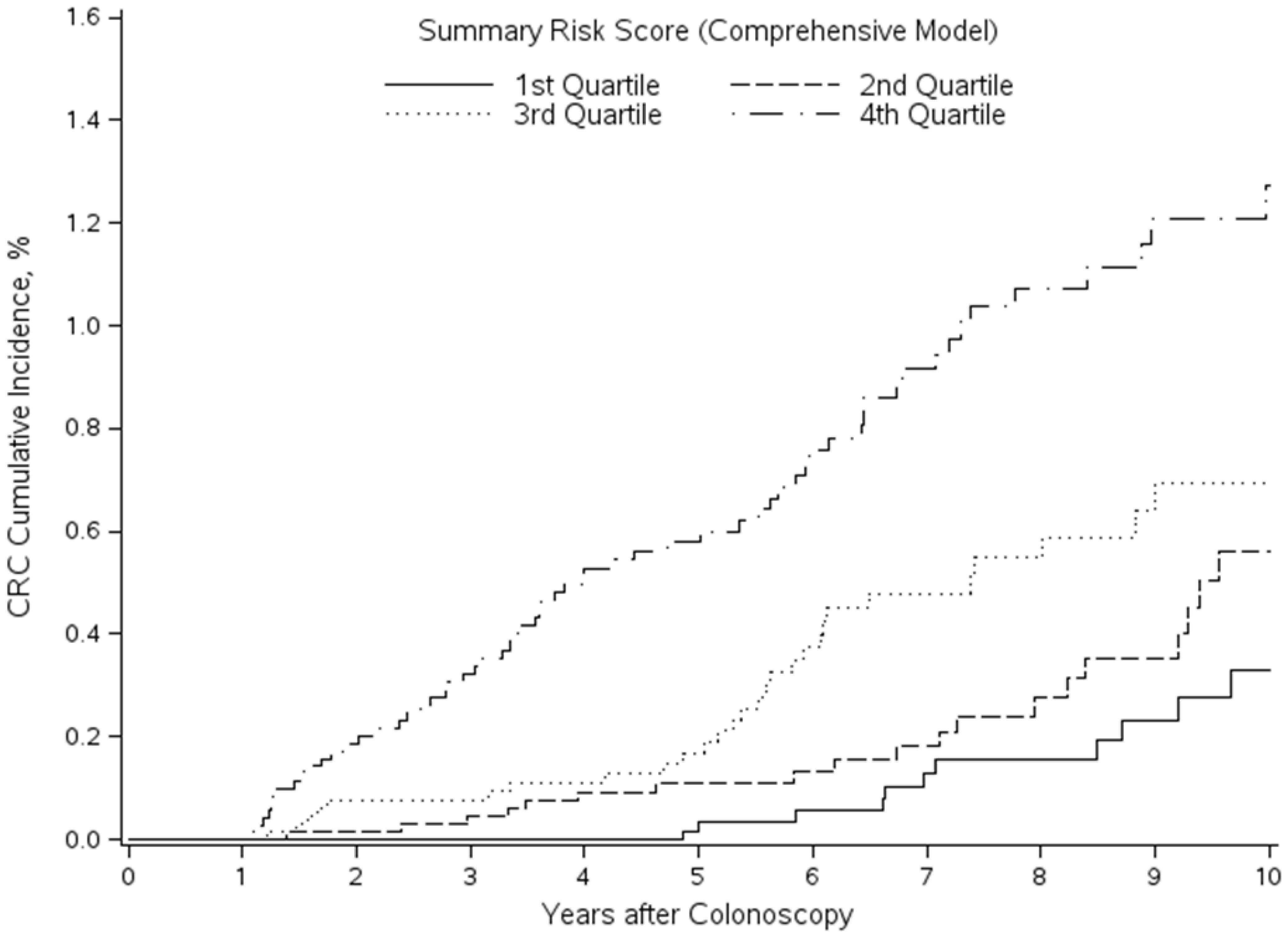
Comprehensive model:

- Patient age category
- Diabetes diagnosis
- Colonoscopy indication
- Polyp characteristics

Polyp Model:

- Polyp Characteristics only

Risk Score Prediction



Summary Risk Score (Comprehensive Model) Quartile	Range	Number of colonoscopies	Person-years of follow-up	CRC cases	CRC crude rate per 10000 person-years	CRC Hazard ratio (95% CI)
1st	0 - 9	7546	56006.3	15	2.68	(REF)
2nd	10 - 19	7197	52490.3	23	4.38	1.71 (0.89-3.29)
3rd	20 - 25	6653	47305.3	33	6.98	2.78 (1.50-5.13)
4th	26 - 65	7105	50705.8	70	13.81	5.54 (3.16-9.72)

70 of 141 CRC cases (49.6%) were found in 4th quartile of risk score.

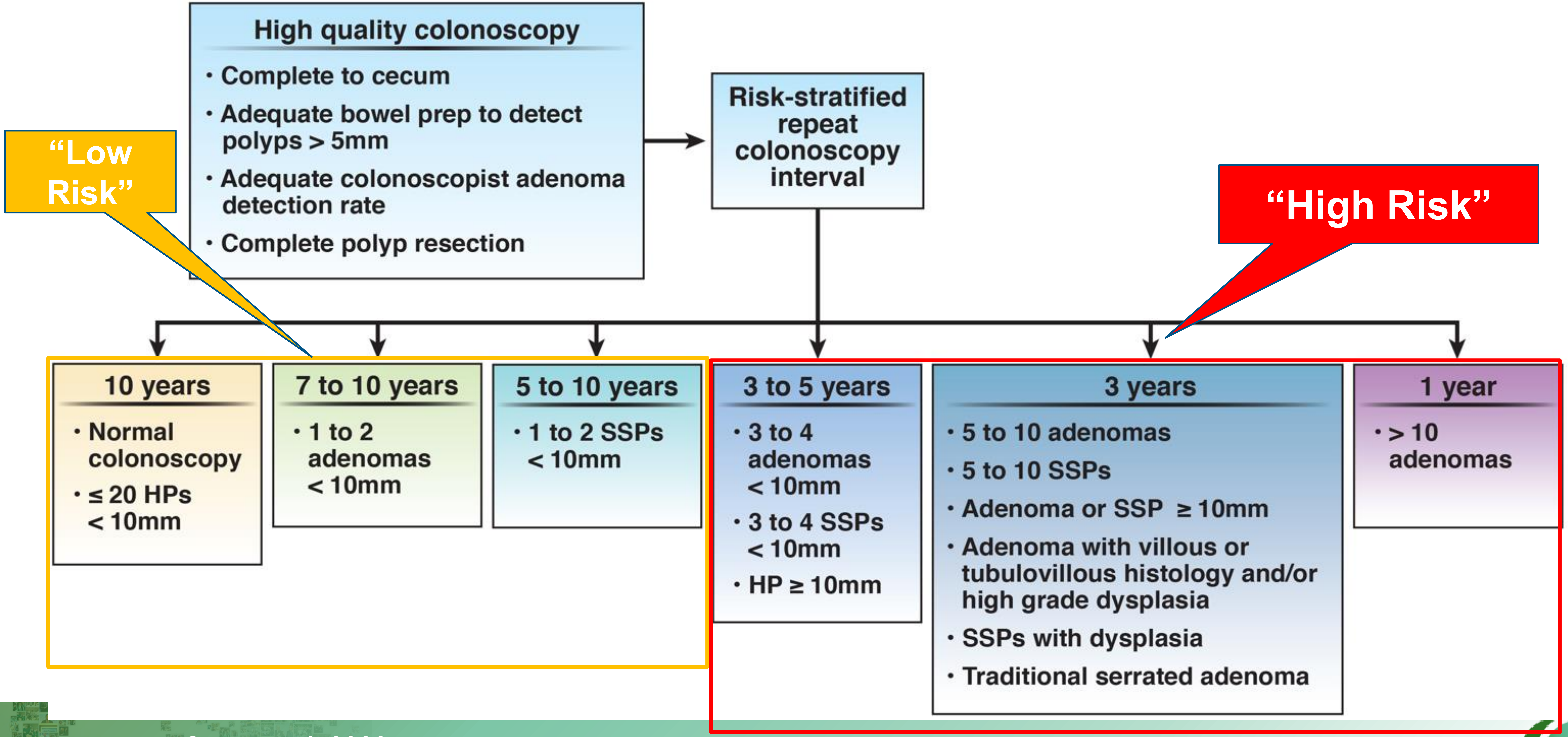
103 of 141 cases (73.0%) were found in the 3rd and 4th quartiles of risk score.

Measuring Risk for CRC at Colonoscopy

Levin, Jensen: *Gastro Hep Advances* (2024), doi: https://doi.org/10.1016/j.gastha.2024.03.008

- In many settings, due to temporary COVID-related reduced colonoscopy production, there are many patients waiting for surveillance colonoscopy
- Gastroenterologists need a way to stratify their waiting lists, to identify those at highest risk for CRC

One Approach to Risk Stratification



Gupta et al. 2020

Background & Aims

- Surveillance guidelines recommend colonoscopy intervals based on polyp size, histology, and number
- No externally validated prediction models exist to prioritize surveillance based on other colorectal cancer (CRC) risk factors
- We developed a multivariable risk prediction model for CRC at surveillance comparing performance to a model that assigned people to low versus high risk according to their guideline-recommended surveillance interval (<5 or ≥5 years).

Methods

- Stepwise logistic regression was used for model development among patients receiving post polypectomy surveillance colonoscopy in 2014-2019.
- Candidate predictors included index colonoscopy indication, findings, and endoscopist all-indication adenoma detection rate (ADR), and patient and clinical characteristics at surveillance.
- Models were applied to patients randomly divided (70/30) into model development (n=36,994) and internal validation cohorts (n=15,854).
- External validation was performed on 30,015 patients receiving surveillance colonoscopy in 2020-2022, and the multivariable model was then updated and re-tested.

Two Cohorts

Development Cohort 2014-2019

Updated Model 2020-2022

70%
Development

30
Validation

External
Validation

Predictor Variables

Development Model (Development Cohort, 2014-2019)

Characteristic	Unadjusted CRC risk	Multivariable adjusted CRC risk
Age (per 1-year increase)	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)
Ever Smoked		
Yes	2.00 (1.39, 2.89)	1.77 (1.22, 2.57)
No	1.00 (reference)	1.00 reference)
Max polyp size (index)		
≥ 10 mm	2.01 (1.27, 3.18)	2.08 (1.31, 3.29)
< 10 mm or no polyp	1.00 (reference)	1.00 (reference)
ADR, all indications, %		
<32.5 or missing	1.94 (1.34, 2.81)	1.96 (1.35, 2.85)
≥32.5	1.00 (reference)	1.00 (reference)

* Reference for unadjusted model was Screening indication for colonoscopy.

Predictor Variables

Updated Model (Ext Validation Cohort, 2020-2022)

	Unadjusted CRC risk	Multivariable adjusted CRC risk
Age (per 1-year increase)	1.05 (1.02, 1.08)	1.06 (1.03, 1.09)
Index Colonoscopy indication		
Positive fecal test	4.72 (2.26, 9.87)	2.71 (1.71, 4.28)
All other indications	1.00 (reference)*	1.00 (reference)
Adenoma with advanced histology		
Yes	2.40 (1.30, 4.45)	2.16 (1.15, 4.09)
No	1.00 (reference)	1.00 (reference)
ADR, all indications, %		
<37.5 or missing	2.54 (1.65, 3.91)	2.68 (1.73, 4.14)
≥37.5	1.00 (reference)	1.00 (reference)

* Reference for unadjusted model was Screening indication for colonoscopy.

	Development: multivariable model		Internal validation: multivariable model		External validation: multivariable model		External validation: updated model	
Risk Score Decile	Colo, n	CRC, n (%)	Colo, n	CRC n (%)	Colo, n	CRC n (%)	Colo, n	CRC n (%)
1st	3,571	2 (1.8)	1,502	2 (4.7)	4,437	2 (2.4)	3,900	1 (1.2)
2nd	3,891	3 (2.6)	1,610	1 (2.3)	4,874	9 (11.0)	3,950	5 (6.1)
3rd	3,534	5 (4.4)	1,454	0 (0.0)	3,775	6 (7.3)	3,885	2 (2.4)
4th	3,842	6 (5.3)	1,688	3 (7.0)	4,144	8 (9.8)	3,349	3 (3.7)
5th	3,620	8 (7.0)	1,606	1 (2.2)	3,724	7 (8.5)	3,827	4 (4.9)
6th	3,740	11 (9.6)	1,674	5 (11.6)	4,186	10 (12.2)	4,376	7 (8.5)
7th	3,867	11 (9.6)	1,752	4 (9.3)	4,002	7 (8.5)	3,794	13 (15.9)
8th	3,398	10 (8.8)	1,470	5 (11.6)	3,327	16 (19.5)	3,606	9 (11.0)
9th	3,989	29 (25.0)	1,644	6 (14.0)	3,248	7 (8.5)	3,870	14 (17.1)
10th	3,542	29 (25.0)	1,454	16 (37.2)	2,525	10 (12.2)	3,685	24 (29.3)
Total	36,994	114 (100)	15,854	43 (100)	38,242	82 (100)	38,242	82 (100)

58.8

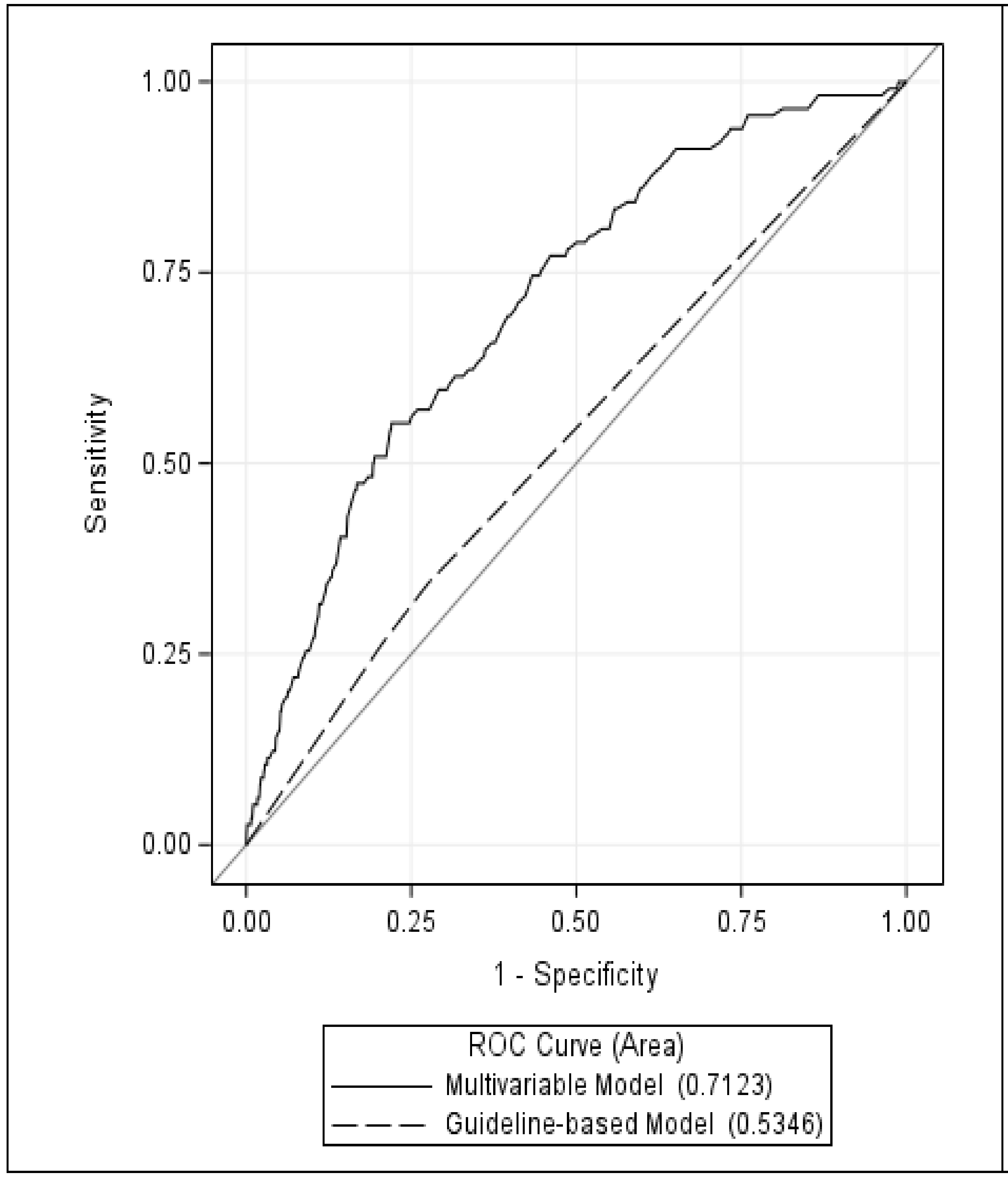
62.8

40.2

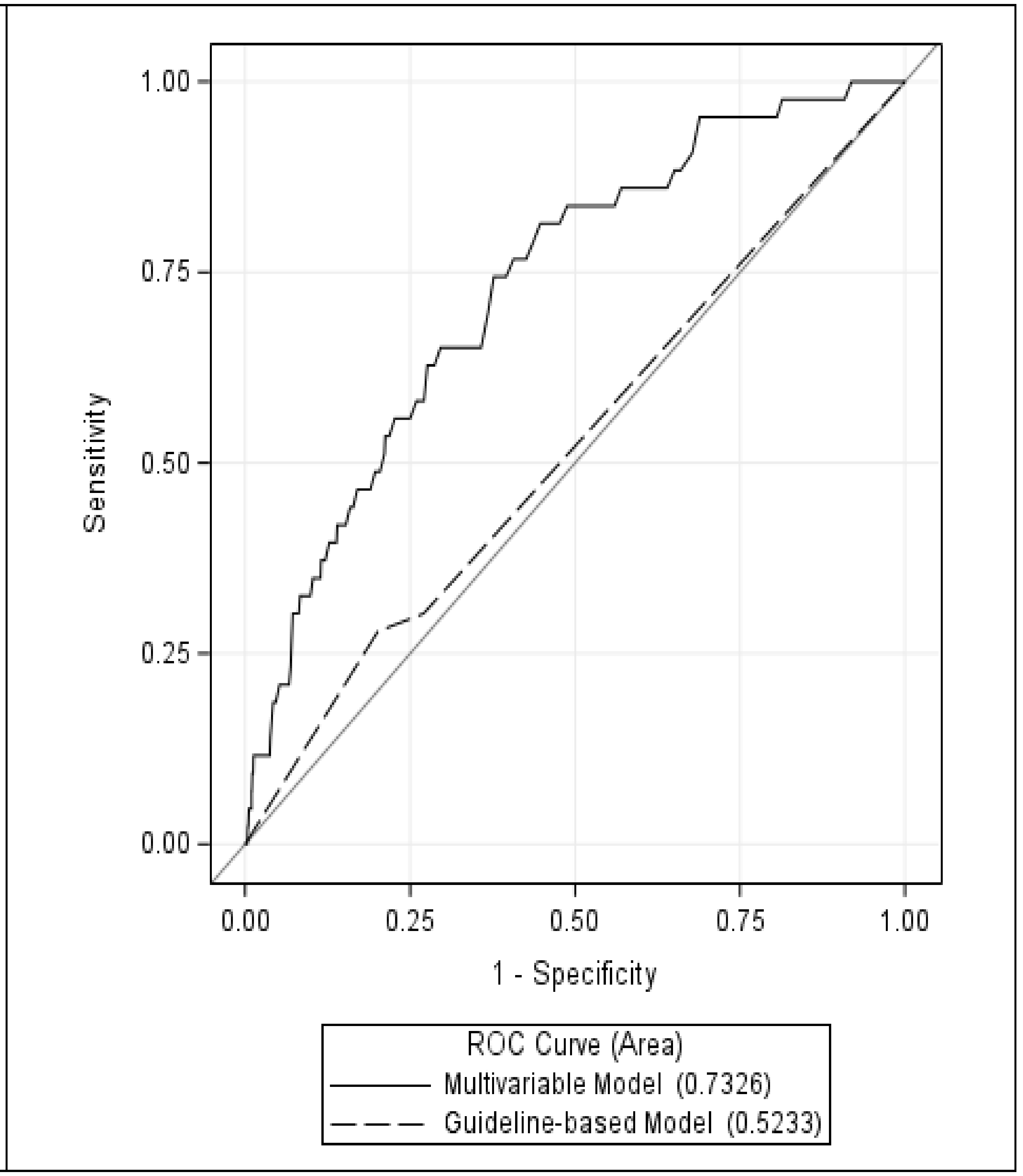
57.4

ROC curves

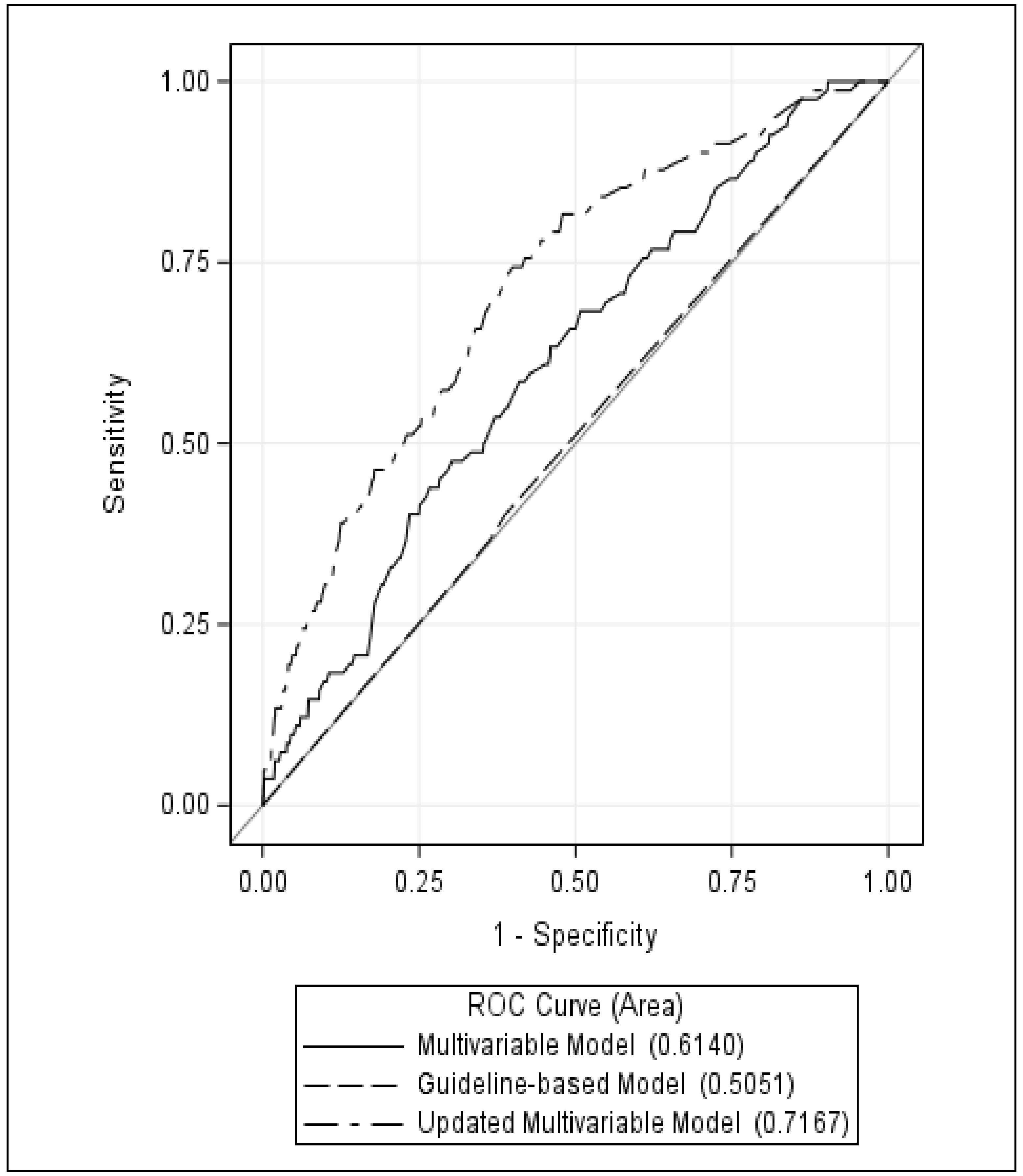
Model Development (2014-2019)



Internal Validation (2014-2019)



External Validation (2020-2022)



Conclusions

- Including additional patient, clinical or endoscopic variables improves risk prediction

- Layered over existing guideline recommendations
- Ensures highest risk patients are not overlooked
- ADR particularly useful as marker for 'high quality baseline colonoscopy'
- These variables increase model complexity may create implementation challenges

Surveillance Among the Elderly

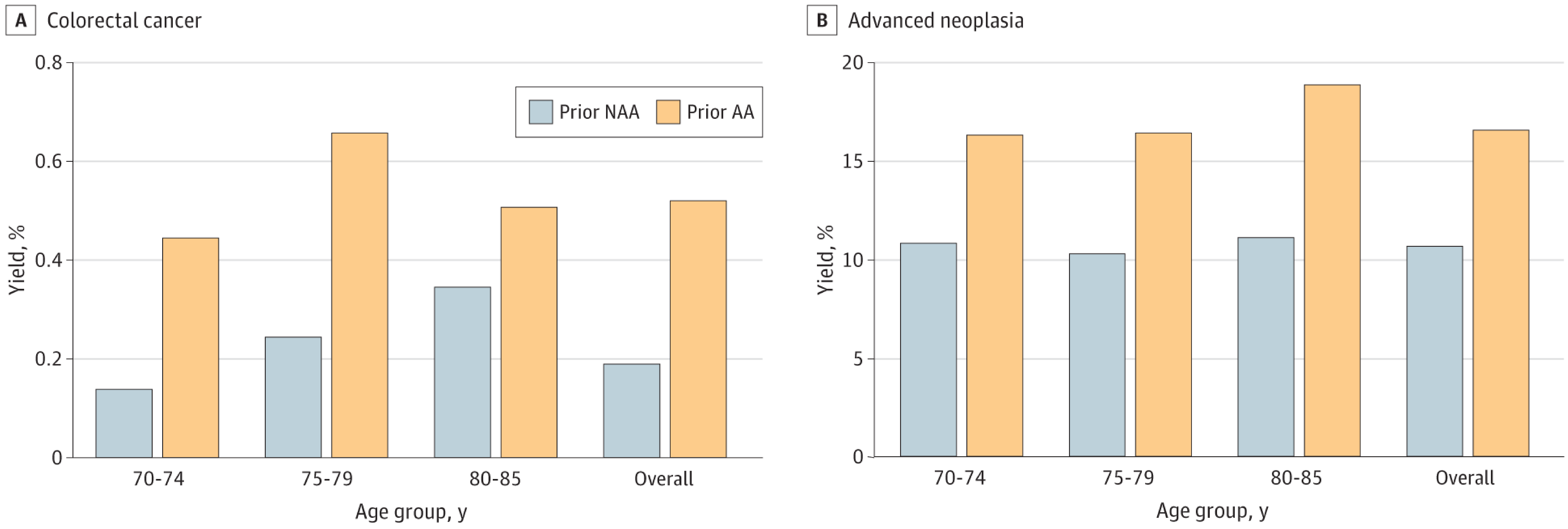
Lee Jama Network Open. 2024 Apr 1;7(4):e244611

- Surveillance guidelines are unclear about when to discontinue colonoscopy for older patients.
- To inform shared decision making between patients and providers, this study sought to evaluate surveillance colonoscopy yields in older patients.

Methods

- Cross sectional evaluation at KPNC
- Surveillance colonoscopies between 2017-2019, with prior h/o adenoma
- Exposures: age (70-74, 75-79, 80-85), prior adenoma findings

Results



Lee Jama Network Open. 2024 Apr 1;7(4):e244611

Conclusions

- CRC detection is rare—much less than 1%
- Advanced neoplasia yield 12% overall
- Yields were higher among those with prior advanced adenoma
- Yields did not increase with age

- Non-invasive tests might be useful to select older patients for colonoscopy

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