Why do people remain at (high) risk for colorectal neoplasia after polyp excision?

WEO

The voice of world endoscopy

WEO CRC Screening Committee
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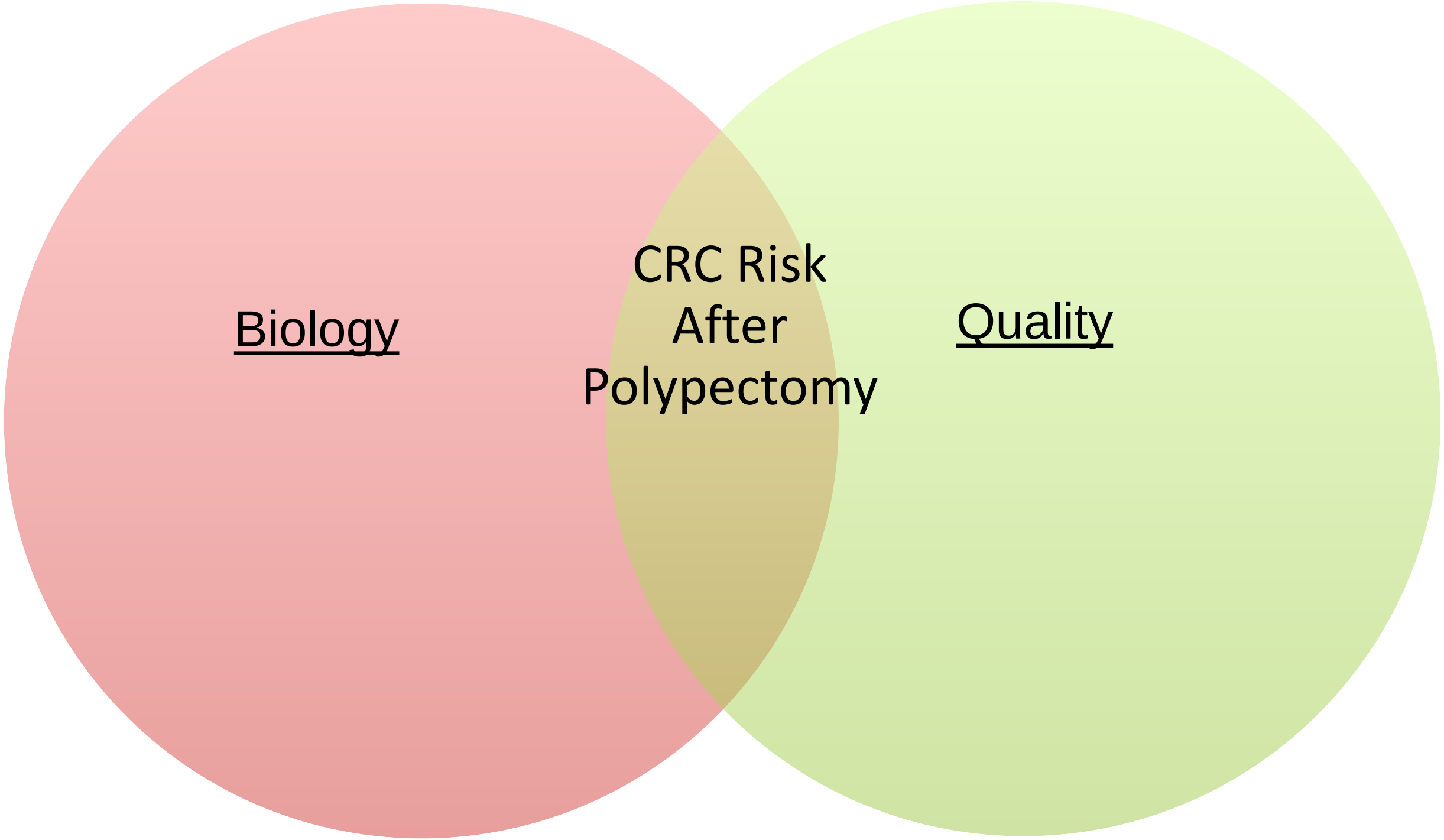
Cumulative CRC risk after polypectomy

	Incidence @ 10 years			Mortality @ 10 years	
Baseline Finding	He (n=122,899)	Lee (n=64,422)	Wieszczy (n=236,089)	Lee	Wieszczy
Normal	0.4%	0.39%	0.24%*	0.07%	0.10%*
Low-risk adenoma	0.3%	0.44%	0.39%	0.03%	0.14%
Hazard Ratio (95% CI)	1.23 (0.65-2.31)	1.29 (0.89-1.88)	1.49 (1.13-1.98)	0.65 (0.19-2.18)	1.48 (0.88-2.46)
High-risk adenoma	1.7%	1.24%	0.74%*	0.25%	0.26%
Hazard Ratio (95% CI)	4.07 (2.89–5.72)	2.61 (1.87-3.63)	2.94 (2.28-3.81)	3.94 (1.90–6.56)	2.16 (1.29-3.62)

He Gastro 2020; Lee JK Gastro 2020; Wieszczy Gastro 2020
*cumulative hazard; **data retrieved through personal correspondence


Biology
CRC Risk
After
Polypectomy
Quality

Biology

Age

Sex

Genetic predisposition

Comorbidity (metabolic syndrome)

Exposures

- Medications (aspirin)
- Smoking
- Exercise
- Diet*

References

Age/Sex: Martinez ME Gastro 2009

Genetics: Guo F Clin Gastro Hep 2022; Jacobs ET Am J Gastro 2018

Met Syndrome: Kim MC Int J Obes 2012; Kim NH Medicine 2016; Kim J Gastro 2017

Diet: Kunzmann AT Int J Cancer 2016; Sardo Molmenti CL Nutr Cancer 2017; Lanza CEBP 2007; Schatzkin NEJM 2000

Smoking: Figueiredo JC Canc Caus Control 2015; Kim MC Int J Obes 2012

Exercise: Molmenti CL Canc Caus Contr 2014

Aspirin: Dulai PS BMJ 2016

Quality

Colonoscopist skill
- Adenoma detection
- Complete polyp excision

Extent of exam

Bowel preparation

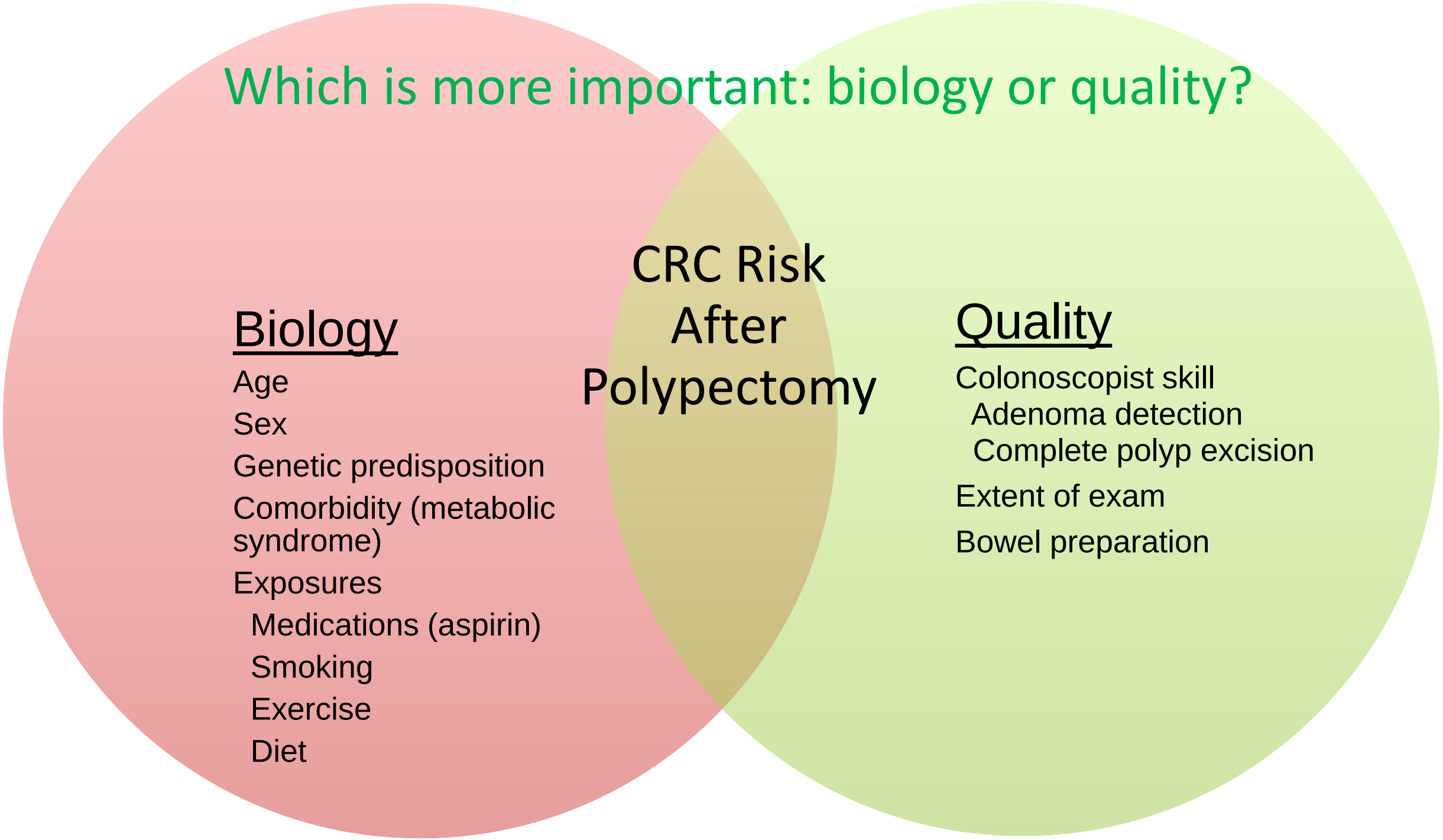
References:

ADR: Wieszczy P, Waldman E Gastro 2021

Polyp excision: Pohl H Gastro 2013

Extent of exam and bowel preparation: Atkin W Lancet Oncol 2017

Which is more important: biology or quality?



Biology vs. Quality: Lessons from post-colonoscopy CRC (PCCRC) analyses using WEO criteria Rutter MD Gastro 2008

Study	# PCCRC cases	Likely new CRC	Incomplete resection	Detected, not resected	Missed, prior exam adequate	Missed, prior exam negative but inadequate
Beaton Endoscopy 2022	48	33%	0%	6%	44%	17%
Lee JK DDW 2021	189	40%	10.6%	5.3%	42%	2%

- Analyses were not restricted to post-polypectomy patients
- Suggest that post-colonoscopy colorectal cancers are driven substantially by both biologic and quality factors

Biology vs. Quality: Studies examining longitudinal risk

- VA Colonoscopy Cohort
- Polish National Colorectal Cancer Screening Program and Australian Colonoscopy Screening Program

Biology vs. Quality: Studies examining longitudinal risk

- VA Colonoscopy Cohort 2004-2016
  - Subset of 30,897 US Veterans who underwent baseline colonoscopy and one surveillance exam
  - Assessed risk for metachronous advanced neoplasia by patient (including polyp) characteristics and colonoscopist ADR
    - Polyp factors serve as a biomarker of aggregate biologic risk driven by exposures, genetics, and other patient characteristics
    - Allows us to examine potential relative importance of biology vs. quality on risk
  - Primary goal: develop a prediction model for metachronous advanced neoplasia
    - Data were split 2:1 into a prediction model development and validation set
    - Findings from development set presented

ADR and longitudinal CRC risk

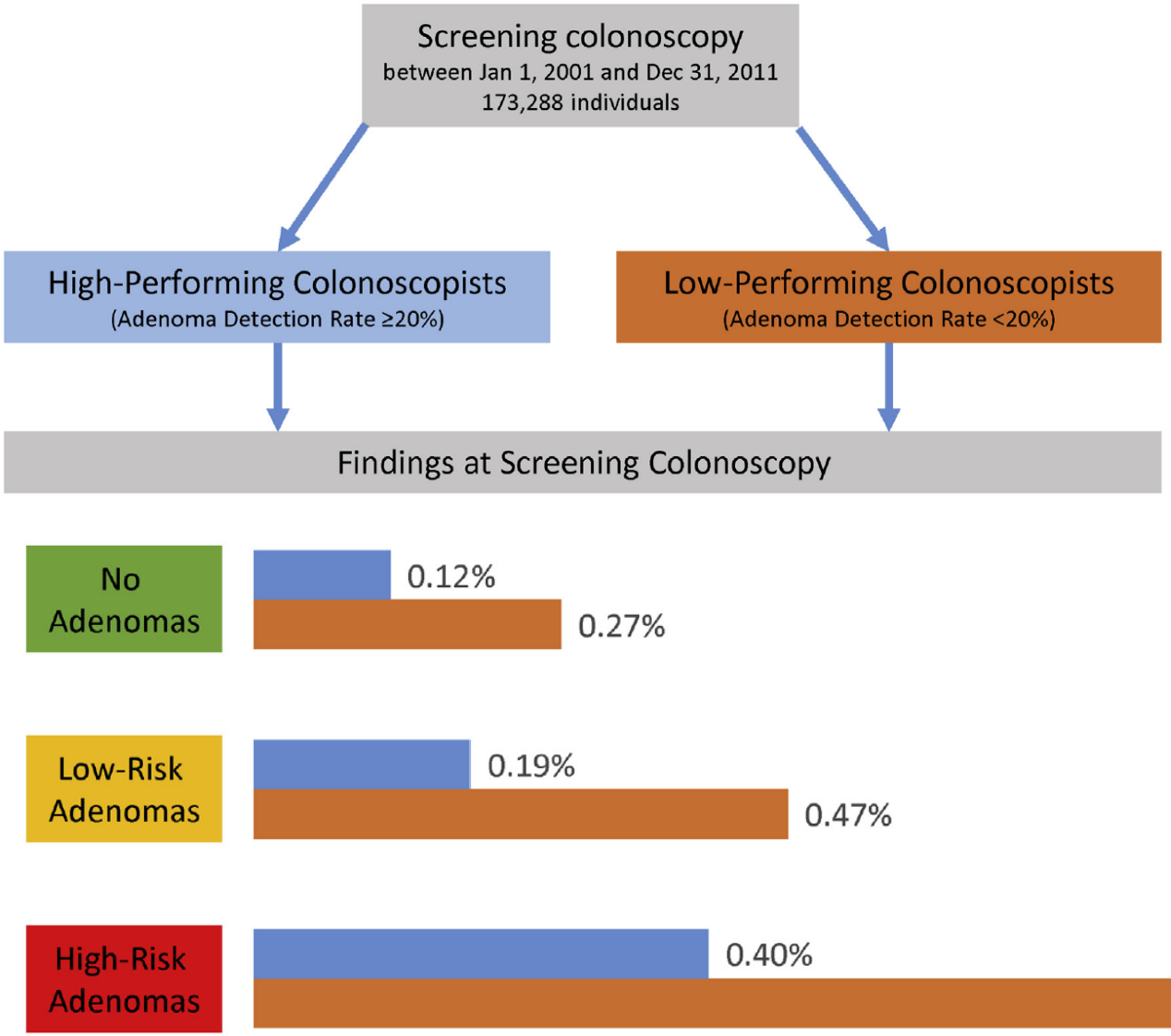


Figure 2. Kaplan-Meier cumulative 10-year risk of colorectal cancer after screening colonoscopy by colonoscopist adenoma detection rates and characteristics of removed adenomas.

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CLINICAL—ALIMENTARY TRACT

Colonoscopist Performance and Colorectal Cancer Risk After Adenoma Removal to Stratify Surveillance: Two Nationwide Observational Studies

Paulina Wieszczy,[1,2,3,*] **Elisabeth Waldmann**,[4,5,6,7,*] Magnus Løberg,[3,8] Jaroslaw Regula,[1,2] Maciej Rupinski,[1,2] Marek Bugajski,[1,2] Kathryn Gray,[7] Mette Kalager,[3,8] Monika Ferlitsch,[4,5] Michal F. Kaminski,[1,2,3,8,§] and Michael Bretthauer[3,7,8,§]

- Examined 10-year cumulative CRC risk by baseline colonoscopy findings
- Baseline risk group associated with cumulative CRC incidence
- Within each risk group, higher performance associated with lower cumulative CRC risk
- Cumulative risk for patients with high-risk adenoma diagnosed by a higher-performing colonoscopist similar to risk for patients with low-risk adenoma diagnosed by a lower performer
- Implies quality may be a major driver of outcomes

Conclusions

- Quality and biology both play a role in persistent risk for CRC after polypectomy
  - Quality may be easier to modify than biology
    - Candidate for ongoing immediate intervention
  - More knowledge on biology is needed to guide:
    - Interventions
      - E.g. biomarkers of response to aspirin
    - Prediction models for improved risk stratification and surveillance

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