



S.S. FORMAZIONE PERMANENTE E RAPPORTI CON L'UNIVERSITA'

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**CRPT - PROGRAMMA REGIONALE DI SCREENING COLORETTALE  
PREVENZIONE SERENA – WORKSHOP 2022**

# La sorveglianza post-polipectomia: nuove evidenze dal programma di screening del Veneto



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## **Il sottoscritto Manuel Zorzi**

ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

# Introduzione

- I programmi di screening colorettaie basati sul FIT riducono l'incidenza e la mortalità da CRC
- L'ADR è inversamente correlato con l'insorgenza di CRC post-colonscopia (PCCRC)
  - Setting «opportunistico»
  - Setting di screening basato sulla colonscopia

Kaminski et al. NEJM 2010

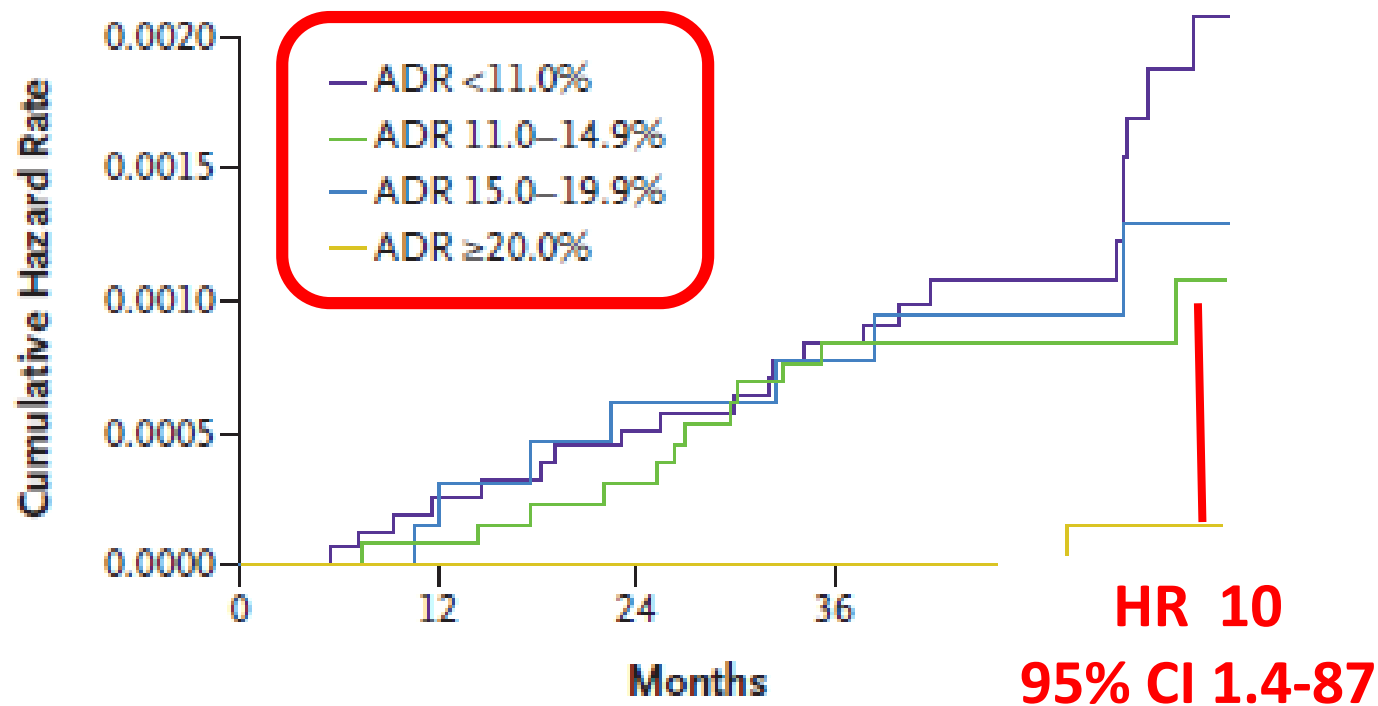
Corley et al. NEJM 2014

Zorzi et al. Gut 2015

Senore et al. Gut 2019

# Quality Indicators for Colonoscopy and the Risk of Interval Cancer

Michal F. Kaminski, M.D., Jaroslaw Regula, M.D., Ewa Ki  
 Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joan  
 Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P.  
 and Eugeniusz Butruk, M.D.



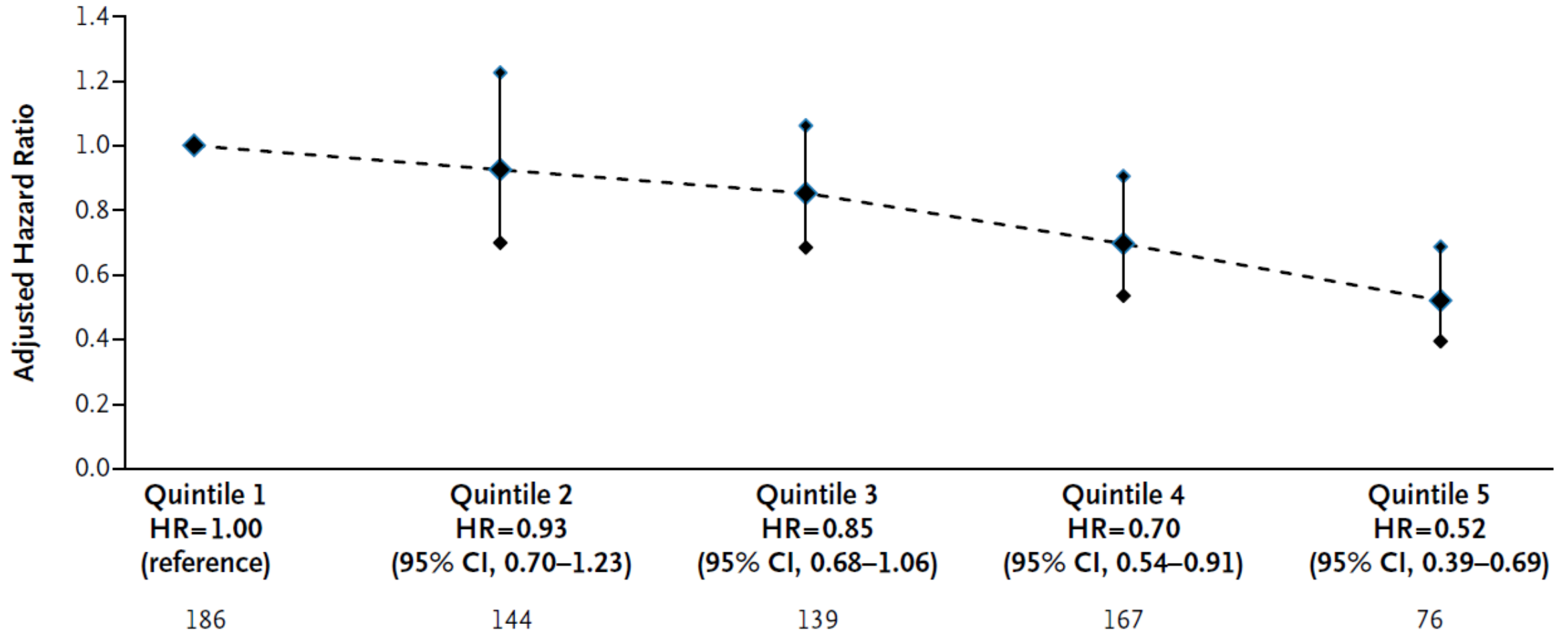
No. at Risk						
ADR <11.0%	15,883	15,805	15,744	15,669	9355	4717
ADR 11.0–14.9%	13,281	13,223	13,182	13,120	7571	4003
ADR 15.0–19.9%	6,607	6,582	6,562	6,539	4022	2529
ADR ≥20.0%	9,255	9,235	9,202	9,166	7155	5548

**Table 2.** Adenoma Detection Rate and Risk of an Interval Colorectal Cancer among All Patients.

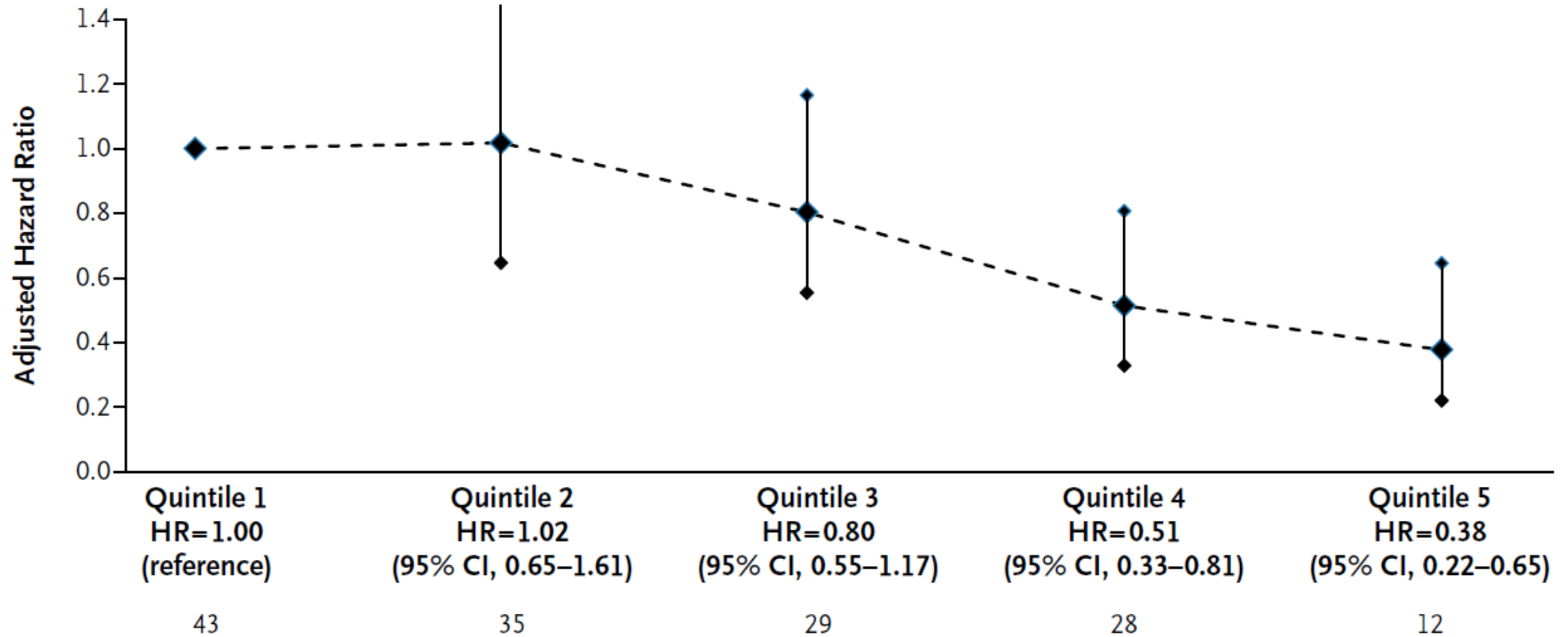
Adenoma Detection Rate	Interval Cancer <i>no. of cases</i>	Hazard Ratio (95% CI)*	Unadjusted Risk <i>no. of cases/ 10,000 person-yr</i>
Continuous rate	712	0.97 (0.96–0.98)	7.7
Rate quintile			
Quintile 1: 7.35–19.05%	186	1.00 (reference)	9.8
Quintile 2: 19.06–23.85%	144	0.93 (0.70–1.23)	8.6
Quintile 3: 23.86–28.40%	139	0.85 (0.68–1.06)	8.0
Quintile 4: 28.41–33.50%	167	0.70 (0.54–0.91)	7.0
Quintile 5: 33.51–52.51%	76	0.52 (0.39–0.69)	4.8

314,872 colonoscopies performed by 136 gastroenterologists; the adenoma detection rates ranged from 7.4 to 52.5%.

# Rischio di PCCRC



# Rischio di decesso per PCCRC



## Relationship Between Detection of Adenomas by Flexible Sigmoidoscopy and Interval Distal Colorectal Cancer

SHARI S. ROGAL,\* PAUL F. PINSKY,<sup>‡</sup> and ROBERT E. SCHOEN\*

\*Division of Gastroenterology, Hepatology, and Nutrition, University of Pittsburgh, Pittsburgh, Pennsylvania; and <sup>‡</sup>Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland

**Table 3.** Relationship Between Adjusted Adenoma and Polyp Detection Rates and Interval Cancer

Quartile of examiners' rates (% detected)	Number of cancers	Number of examinations among eligible subjects <sup>a</sup>	Interval cancer rate (per 10,000 examinations)
Quartile of adjusted ADR			
1st (3.6–9.3)	13	17,361	<u>7.5</u>
2nd (9.4–12.1)	8	23,957	3.3
3rd (12.2–14.3)	8	13,947	5.7
4th (14.4–24.5)	3	11,446	<u>2.6</u>

<sup>a</sup>The number of examinations are not equal across quartiles because quartiles reflect the distribution of adenoma and polyp detection rates among examiners, and examiners performed varying numbers of examinations.



# Introduzione

- Colonscopia dopo FIT+
  - Adenomi avanzati fino a 5 volte più frequenti
  - CRC fino a 30 volte più frequente

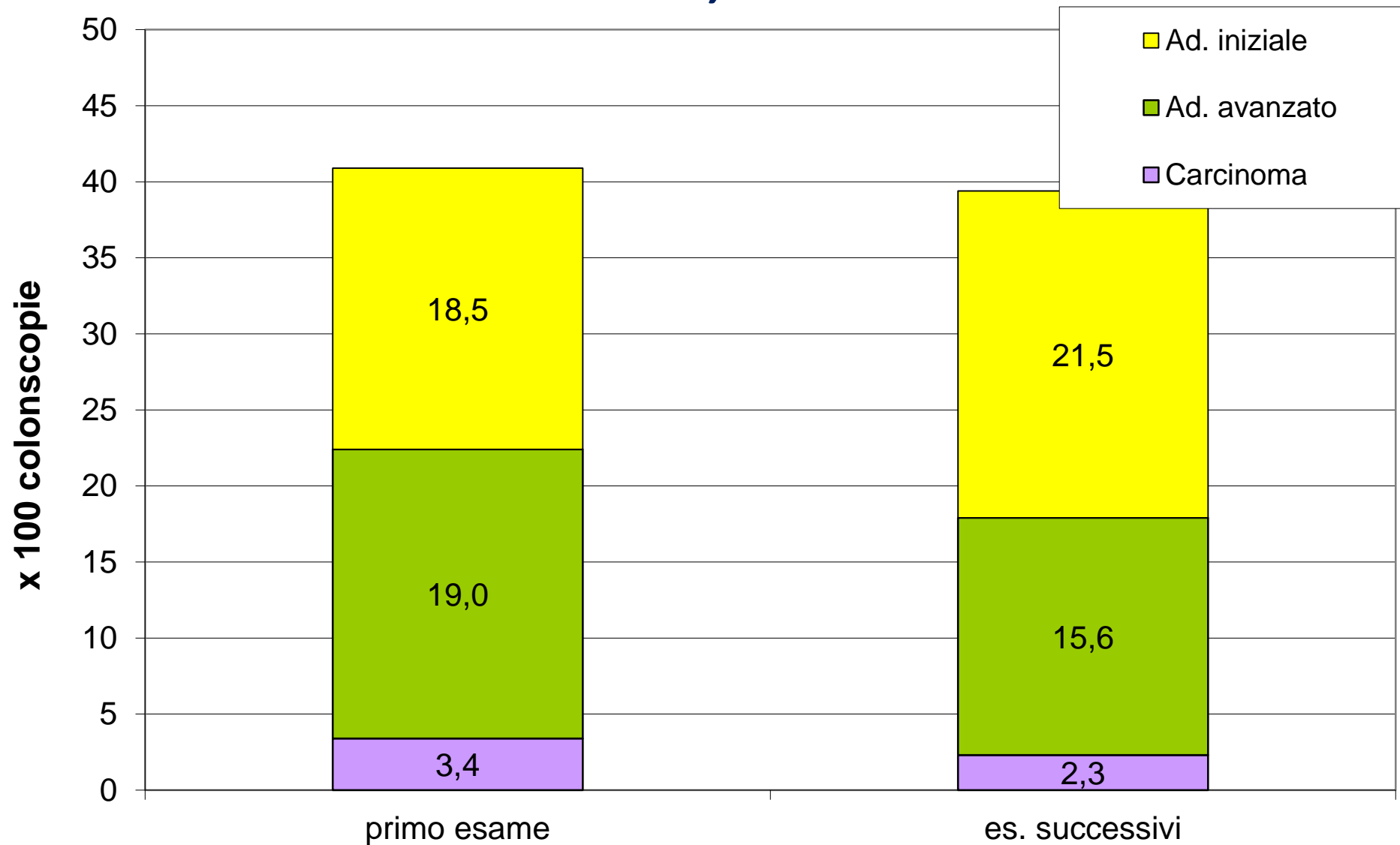
Quintero et al. NEJM 2014

Zorzi et al. Gut 2015

Alsayid et al. Clin Gas Hepatol 2018

Pohl et al. Gastroenterology 2013

# Valore Predittivo Positivo del FIT+ alla colonscopia Italia, 2019



# Introduzione

- Colonscopia dopo FIT+
  - Adenomi avanzati fino a 5 volte più frequenti
  - CRC fino a 30 volte più frequente
- Elevata variabilità dell'ADR
- Variabilità della completezza della polipectomia

Quintero et al. NEJM 2014

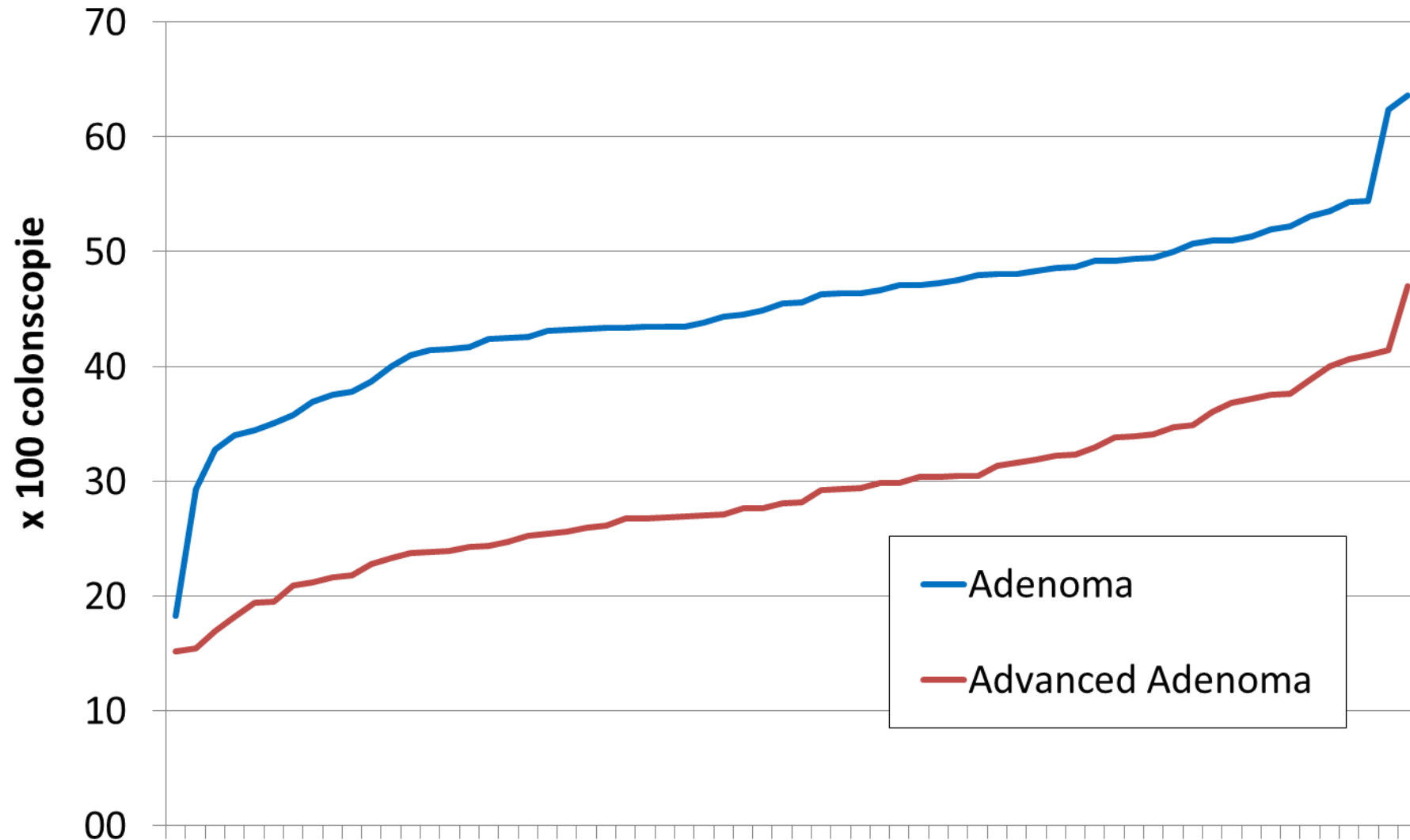
Zorzi et al. Gut 2015

Alsayid et al. Clin Gas Hepatol 2018

Pohl et al. Gastroenterology 2013

# Detection rate individuale. Studio Equipe, 2010

(endoscopisti con almeno 200 colonscopie)



# Introduzione

- Colonscopia dopo FIT+
  - Adenomi avanzati fino a 5 volte più frequenti
  - CRC fino a 30 volte più frequente
- Elevata variabilità dell'ADR
- Variabilità della completezza della polipectomia
- Ruolo dell'ADR post FIT+ ancora inesplorato

Quintero et al. NEJM 2014

Zorzi et al. Gut 2015

Alsayid et al. Clin Gas Hepatol 2018

Pohl et al. Gastroenterology 2013

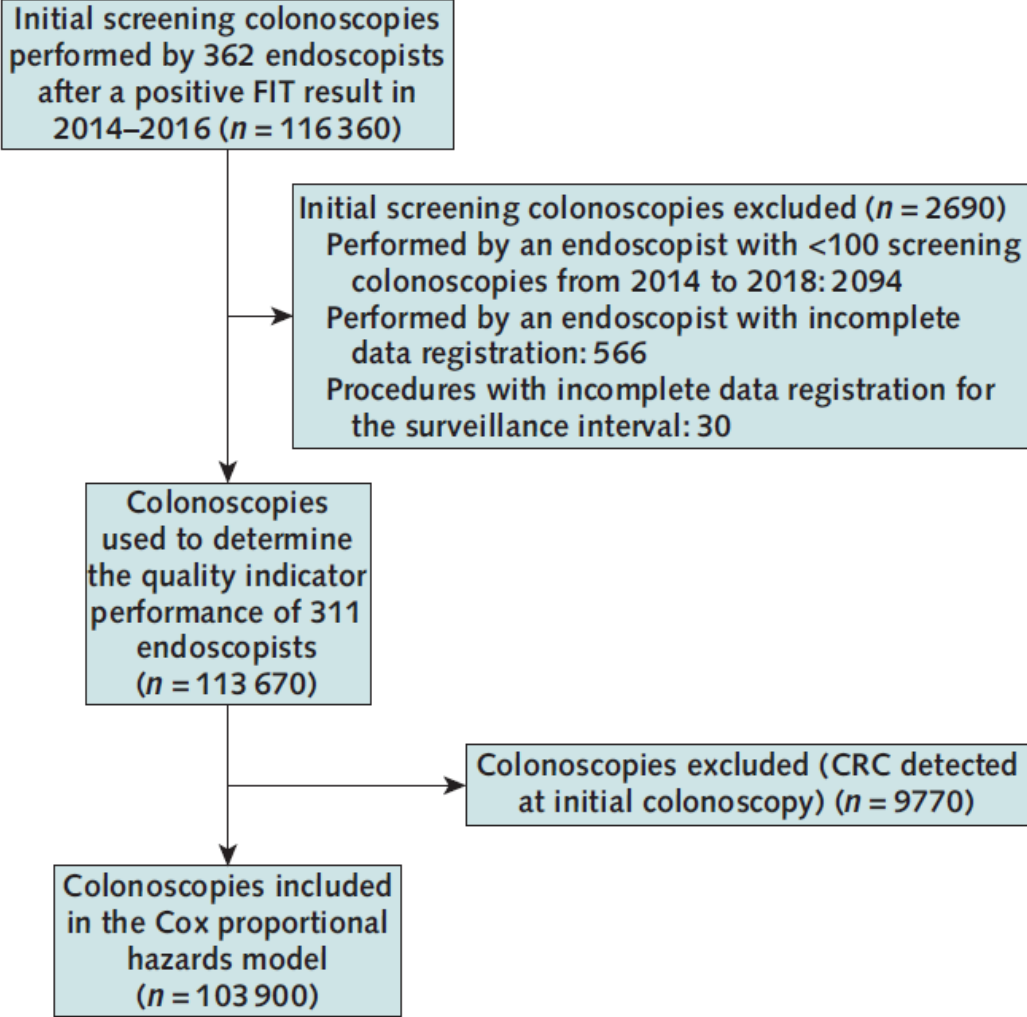
# Adenoma Detection Rate and Risk for Interval Postcolonoscopy Colorectal Cancer in Fecal Immunochemical Test-Based Screening

## A Population-Based Cohort Study

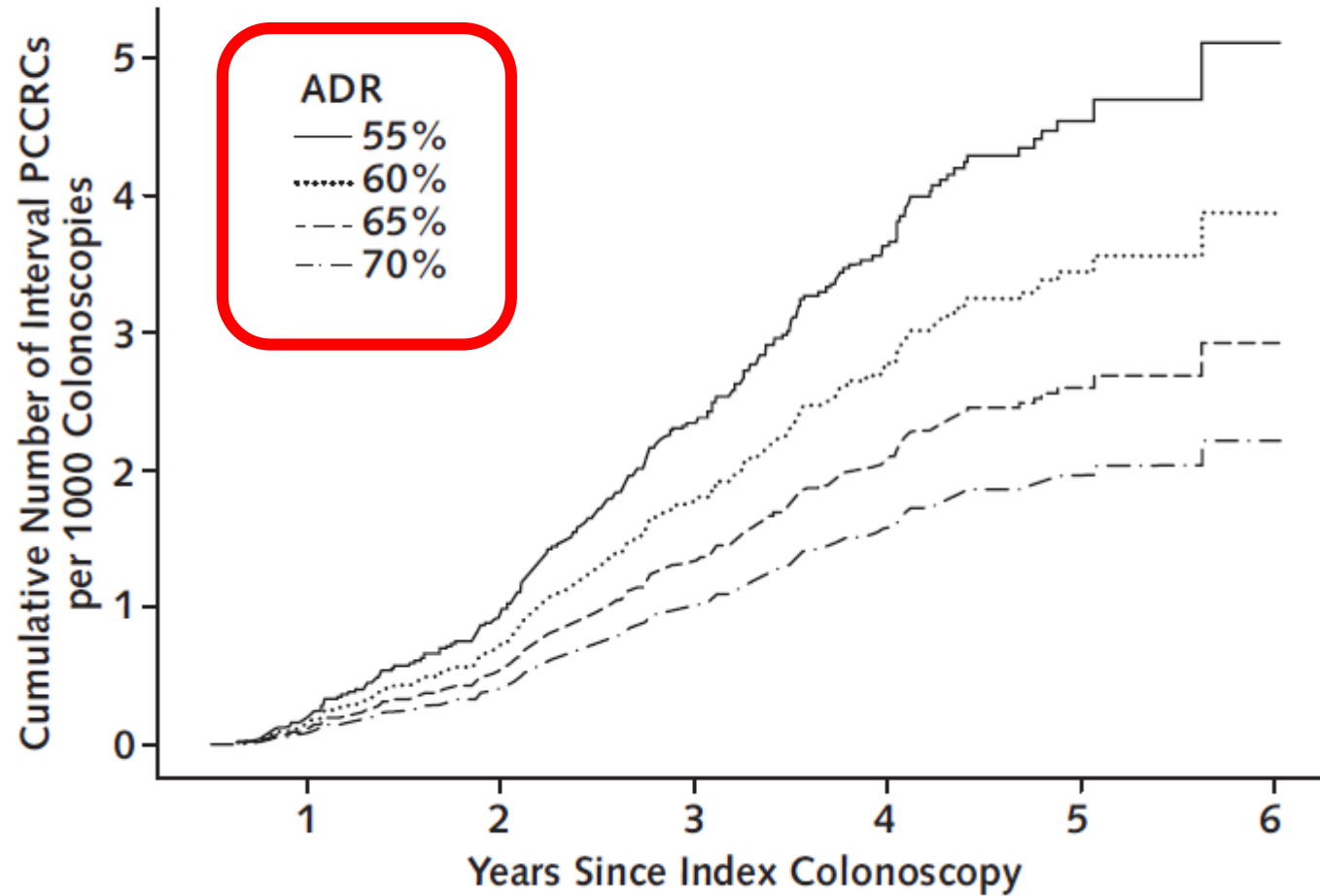
Pieter H.A. Wisse, MD, MSc; Nicole S. Eler, PhD; Sybrand Y. de Boer, MD, PhD; Bert den Hartog, MD, PhD; Marco Oudkerk Pool, MD, PhD; Jochim S. Terhaar sive Droste, MD, PhD; Claudia Verveer, MD; Gerrit A. Meijer, MD, PhD; Iris Lansdorp-Vogelaar, PhD; Ernst J. Kuipers, MD, PhD; Evelien Dekker, MD, PhD\*; and Manon C.W. Spaander, MD, PhD\*

Soglia positività per FIT:  
47 mg Hb / grammo feci

Figure 1. Flow chart of colonoscopies done in the Dutch CRC screening program.



**Figure 4.** Cumulative number of interval PCCRCs diagnosed per 1000 persons after the first colonoscopy done by endoscopists with different ADRs.



**Table 2.** Risk Factors for Interval PCCRC: Multivariable Cox Regression Model\*

Variable	HR	95% CI	P Value
<b>Age, per year increase</b>	1.05	1.03-1.08	<0.001
<b>Sex</b>			
Female is baseline	1.02	0.77-1.36	0.88
<b>Most advanced finding at colonoscopy</b>			
No lesion	Reference	Reference	Reference
Advanced adenoma	0.62	0.35-1.10	0.105
Nonadvanced adenoma	0.82	0.51-1.33	0.43
Serrated polyp	1.23	0.66-2.29	0.51
Other	0.75	0.42-1.34	0.33
<b>Recommended surveillance interval at colonoscopy</b>			
10 y	Reference	Reference	Reference
5 y	0.98	0.63-1.53	0.94
3 y	0.81	0.47-1.42	0.47
<b>Center</b>			
Academic	Reference	Reference	Reference
Nonacademic hospital	3.74	1.31-10.66	0.014
Endoscopy center	3.87	1.31-11.43	0.014
<b>ADR, per 1% increase</b>	0.95	0.92-0.97	<0.001



# Obiettivi

- In un setting di colonscopia dopo FIT+, valutare l'influenza sull'incidenza di PCCRC di:
  - ADR individuale
  - Adv. ADR individuale
- Valutare la rilevanza sui PCCRC delle resezioni incomplete per livello di ADR

# Metodi

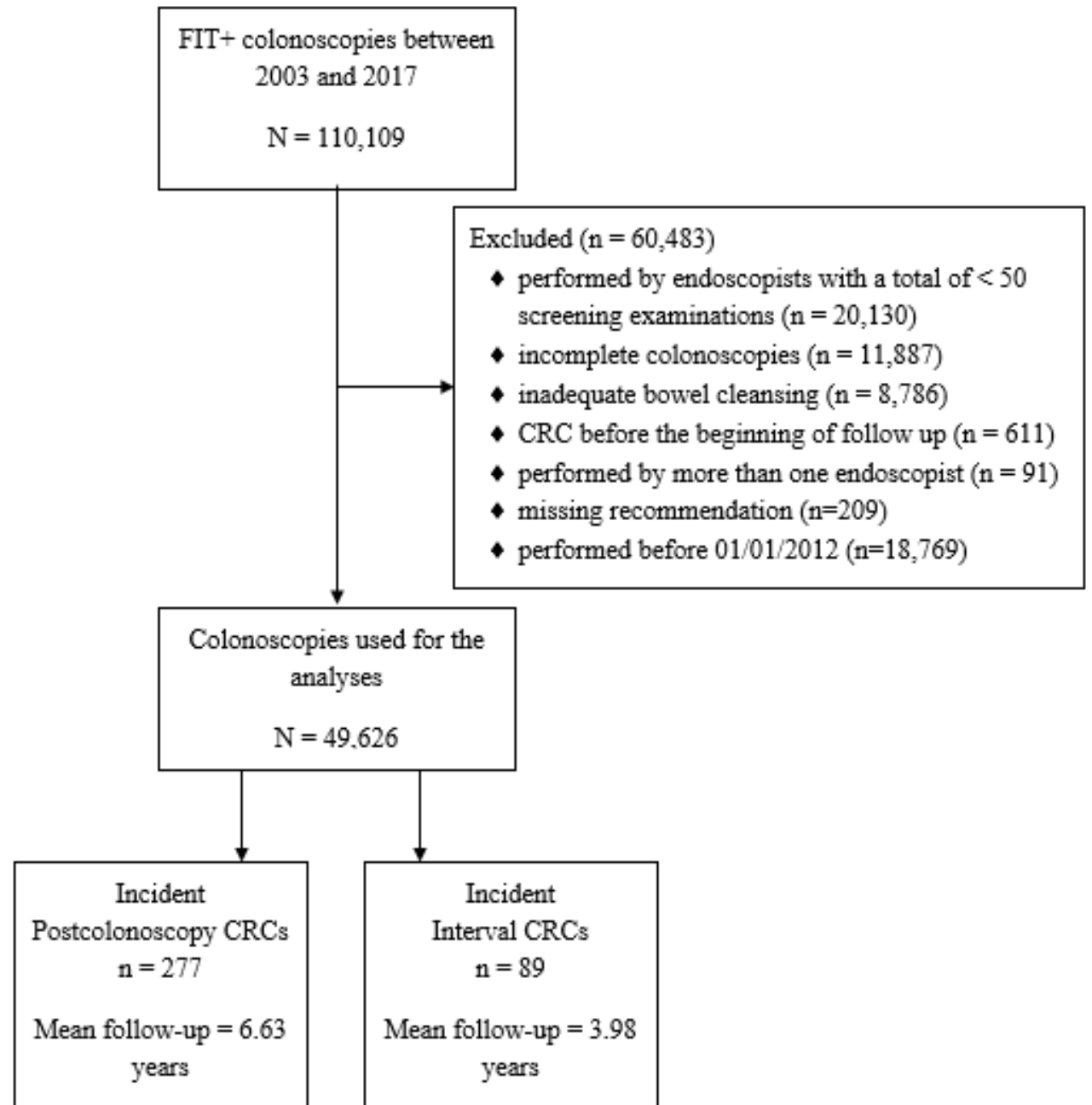
- Programmi di screening della Regione Veneto
  - 50-69 anni
  - FIT biennale
  - Positività: 20 mg Hb / g feci
  - Approfondimento: colonscopia
- Colonscopie post FIT+ dal 2012 al 2017
- Follow up al 31.12.2021 per incidenza di PCCRC\*
  - Registro Tumori
  - SDO, referti AP
  - Registro mortalità

\* > 6 mesi da colonscopia  
Interval CRC secondo WEO

# Metodi

- Id unico per ciascun endoscopista
- Calcolo dell'ADR
- Distribuzione degli endoscopisti in 5 gruppi di ADR:
  - 20-39.9%, 40-44.9%, 45-49.9%, 50-54.9%, 55-70%
- Stima del rischio di PCCRC con intervalli di confidenza al 95% (95%CI) tramite modelli di Cox
- Corrispondenza di sede tra PCCRC e adenoma avanzato al baseline

# Study flow-chart



# Characteristics of study patients and endoscopists

<b>Study endoscopists</b>	<b>N = 113</b>
<b>Mean ADR value (SD)</b>	48.3% (9.05)
<b>Total colonoscopies</b>	49,626
<b>Mean age at colonoscopy – years (SD)</b>	59.7 (6.02)
<b>Age group at colonoscopy</b>	
50-59 years	23,815 (48.0%)
60-70 years	25,811 (52.0%)
<b>Sex</b>	
Male	28,180 (56.8%)
Female	21,446 (43.2%)
<b>Follow up recommendations</b>	
FIT	22,395 (45.1%)
1-year colonoscopy	4,327 (8.7%)
3-year colonoscopy	11,033 (22.2%)
5-year colonoscopy	10,478 (21.1%)
Exit from screening	1,393 (2.8%)

# Characteristics of colorectal cancers detected at follow up

Characteristics		N = 277
Age	50-59 years	97 (35.0%)
	60-70 years	180 (65.0%)
Sex	Female	107 (38.6%)
	Male	170 (61.4%)
Time from index colonoscopy		
	6-11 months	5 (1.8%)
	12-35 months	67 (24.2%)
	36-59 months	84 (30.3%)
	≥60 months	121 (43.7%)
ADR category		
	20-39.9%	86 (31.1%)
	40-44.9%	54 (19.5%)
	45-49.9%	53 (19.1%)
	50-54.9%	39 (14.1%)
	55-70%	45 (16.3%)
Interval cancer (WEO)	Yes	89 (32.1%)
	No	188 (67.9%)
Site	Proximal Colon	119 (43.0%)
	Distal Colon	58 (20.9%)
	Rectum	59 (21.3%)
	Missing	41 (14.8%)
Deceased	Total	31
	Female	15 (48.4%)
	Male	16 (51.6%)

## Adenoma Detection Rate for every year of observation

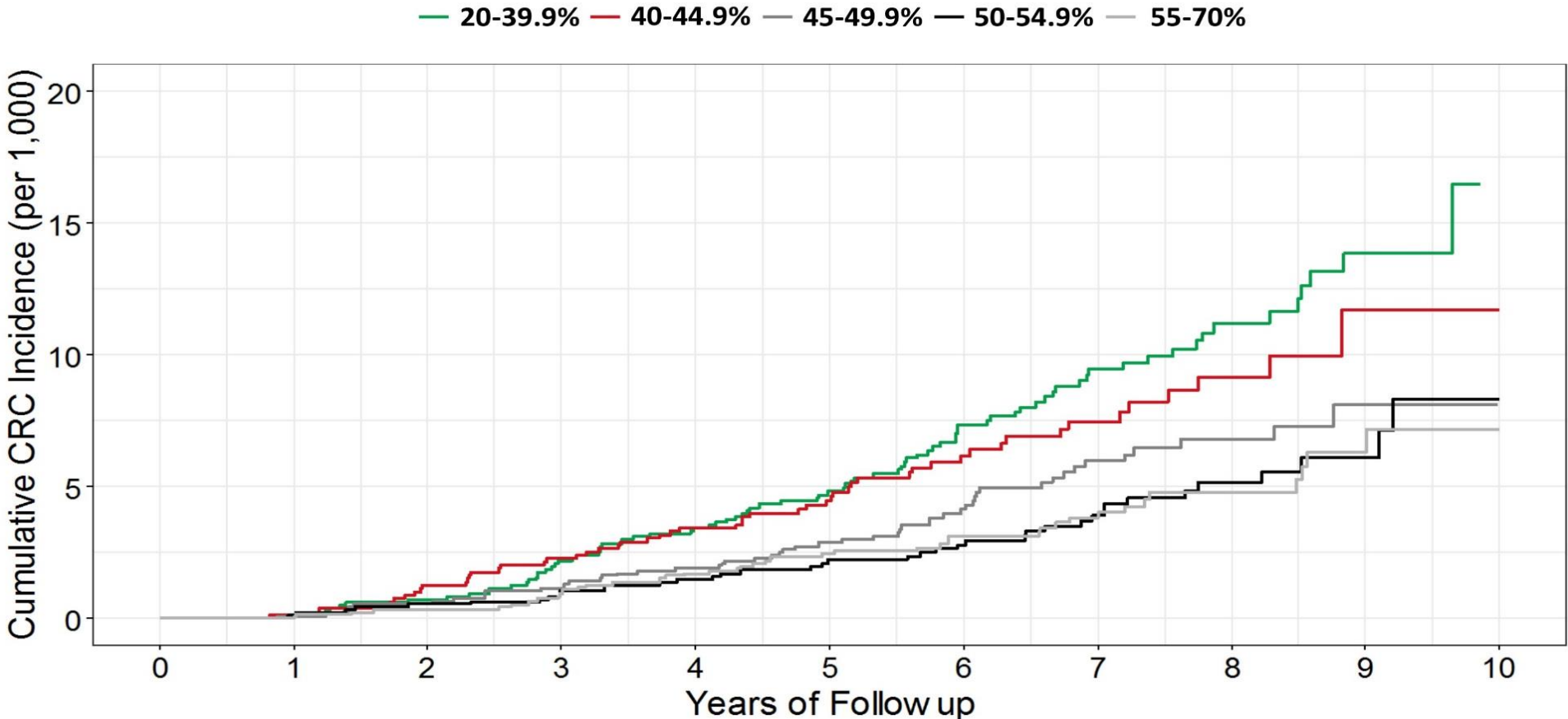
Year	Endosco- pists (N)	Endosco- pies (N)	Mean ADR	20 <sup>th</sup> percentile	40 <sup>th</sup> percentile	60 <sup>th</sup> percentile	80 <sup>th</sup> percentile
2012	77	4,948	48.5%	38.6%	46.8%	50.9%	57.9%
2013	86	8,533	48.0%	40.2%	45.3%	50.7%	55.0%
2014	93	9,149	48.4%	40.2%	45.3%	50.8%	55.4%
2015	91	8,862	48.6%	40.2%	45.3%	50.9%	55.5%
2016	89	8,968	48.7%	40.2%	45.3%	50.9%	56.9%
2017	89	9,166	47.8%	40.2%	45.3%	48.8%	55.4%
Overall	113	49,626	48.3%	40.2%	45.3%	50.8%	55.4%

# Risk Factors for the incidence of PCCRC based on ADR endoscopist group

				Basic adjustment		Fully adjusted model	
Variable	PCCRC	Person-years	Incidence rate per 10,000 person-years	Hazard Ratio	95% Confidence Interval	Hazard Ratio	95% Confidence Interval
ADR group							
20-39.9%	86	65,475	13.13 (10.63 - 16.23)	2.21	1.54 - 3.17	2.35	1.63 - 3.38
40-44.9%	54	50,895	10.61 (8.13 - 13.85)	1.85	1.25 - 2.75	1.94	1.30 - 2.89
45-49.9%	53	69,721	7.60 (5.81 - 9.95)	1.32	0.89 - 1.97	1.37	0.92 - 2.03
50-54.9%	39	64,884	6.01 (4.39 - 8.23)	1.01	0.66 - 1.55	1.05	0.68 - 1.61
55-70%	45	77,804	5.78 (4.32 - 7.75)	Ref.	–	Ref.	–
ADR - 1% increase	277	328,778	8.43 (7.49 - 9.48)	0.96	0.95 - 0.98	0.96	0.95 - 0.98



# Post-Colonoscopy Colorectal Cancer cumulative incidence per Adenoma Detection Rate group



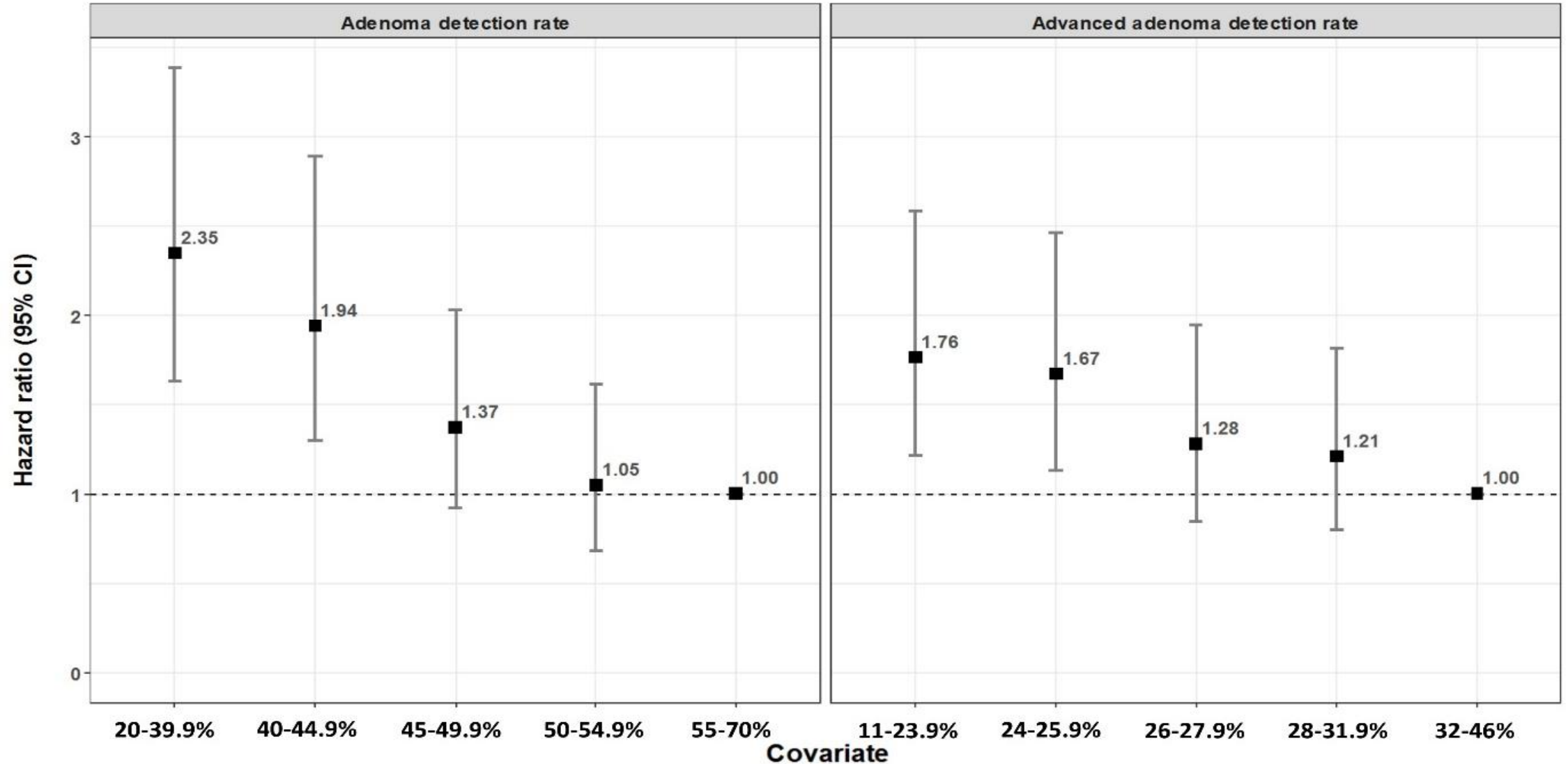
Number at risk

20-39.9%	9700	9668	9627	9553	9470	7786	6161	4480	2730	1149	0
40-44.9%	7997	7960	7898	7826	7750	5921	4403	3039	1639	397	0
45-49.9%	10618	10592	10536	10465	10374	8239	6216	4398	2634	811	0
50-54.9%	9443	9417	9363	9300	9213	7790	6375	4681	2809	1060	0
55-70%	11868	11818	11751	11679	11592	9366	6946	4785	2742	1105	0
	0	1	2	3	4	5	6	7	8	9	10

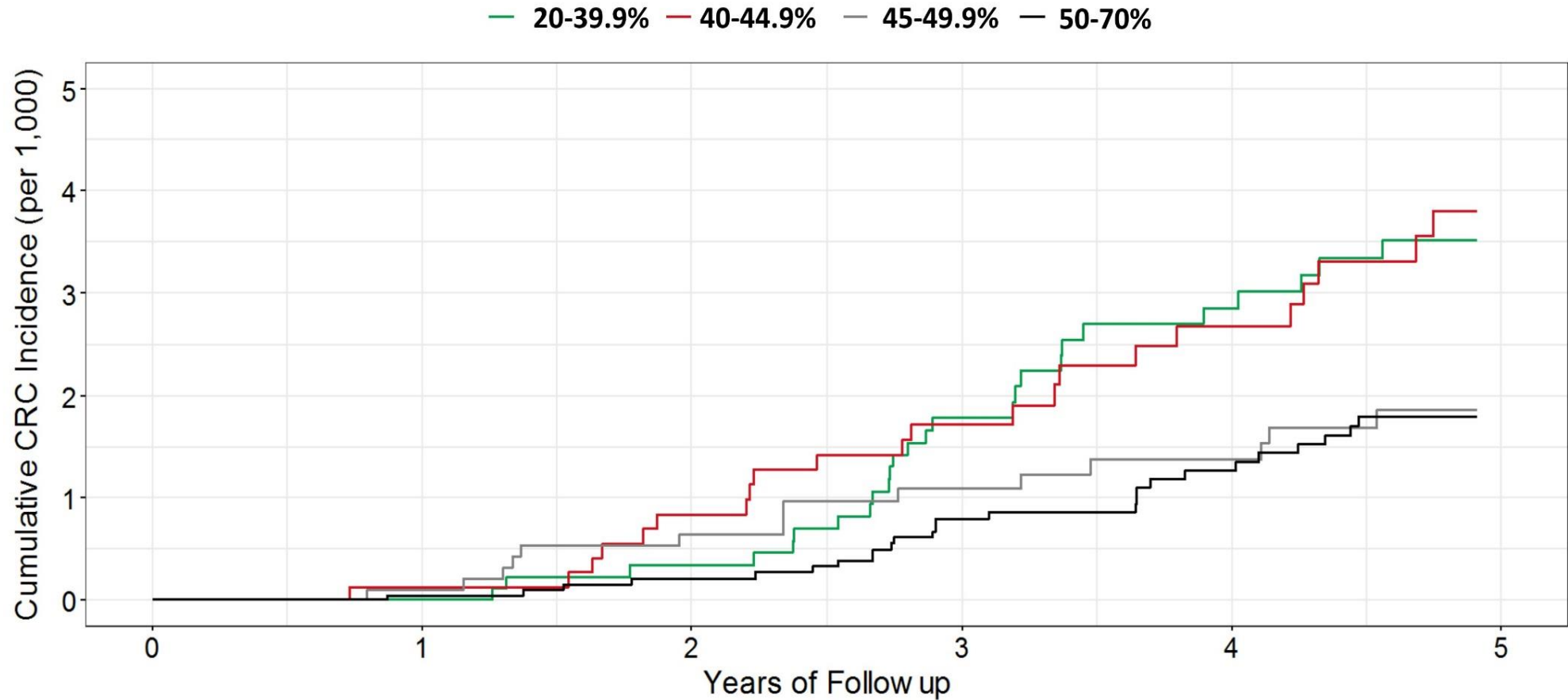
# Risk Factors for the incidence of PCCRC, by Advanced ADR endoscopist group

				Basic adjustment		Fully adjusted model	
Variable	PCCRC	Person-years	Incidence rate per 10,000 person-years	Hazard Ratio	95% Confidence Interval	Hazard Ratio	95% Confidence Interval
Advanced ADR group							
11-23.9%	72	68,342	10.54 (8.36 - 13.27)	1.64	1.13 - 2.39	1.76	1.21 - 2.58
24-25.9%	66	66,355	9.95 (7.81 - 12.66)	1.58	1.08 - 2.31	1.67	1.13 - 2.46
26-27.9%	45	57,569	7.82 (5.84 - 10.47)	1.23	0.81 - 1.86	1.28	0.84 - 1.94
28-31.9%	50	67,099	7.45 (5.65 - 9.83)	1.16	0.77 - 1.74	1.21	0.80 - 1.81
32-46%	44	69,413	6.34 (4.72 - 8.52)	Ref.	–	Ref.	–
AADR - 1% increase	277	328,778	8.43 (7.49 - 9.48)	0.97	0.95 - 0.99	0.96	0.94 - 0.98

# Fully adjusted hazard ratios for PCCRC incidence, by ADR and Advanced ADR



# Cumulative incidence of Interval Colorectal Cancers (WEO), by ADR



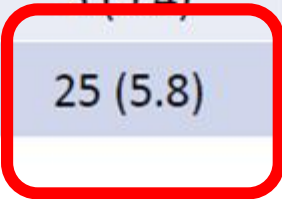
Number at risk

	0	1	2	3	4	5
20-39.9%	9659	8867	8361	6524	6374	0
40-44.9%	7778	7120	6845	5181	5032	0
45-49.9%	10244	9286	9042	6834	6687	0
50-70%	20548	18463	17573	12385	12161	0

Years of Follow up

# Corrispondenza di sede tra PCCRC e adenoma avanzato al baseline

Quintile of endoscopists according to ADR	Findings at FIT+ colonoscopy				Total PCCRC N (%)
	No Advanced Adenoma N (%)	Advanced Adenoma in a different segment than PCCRC N (%)	Advanced Adenoma in an unknown segment N (%)	Advanced Adenoma in the same segment than PCCRC N (%)	
1	62 (75.6)	8 (21.9)	.	2 (2.4)	82 (100)
2	57 (66.2)	11 (22.1)	6 (7.0)	4 (4.5)	86 (100)
3	68 (67.3)	13 (21.8)	3 (3.0)	8 (7.9)	101 (100)
4	62 (57.9)	12 (23.4)	12 (11.2)	8 (7.5)	107 (100)
5	34 (60.7)	12 (30.4)	2 (3.6)	3 (5.4)	56 (100)
<b>Total</b>	283 (65.5)	56 (23.4)	23 (5.3)	25 (5.8)	432 (100)



# Conclusioni

- In un setting di colonscopia dopo FIT+, l'incidenza di PCCRC è inversamente associata sia all'ADR che all'Adv. ADR
- Importanza del monitoraggio dell'ADR
- Re-training specifico se  $ADR < 45\%$
- L'associazione è lineare: per tutti ci sono spazi di miglioramento!
- PCCRC non associato a resezione incompleta

# Grazie a

Cesare Hassan, Giulio Antonelli, Claudio Barbiellini Amidei,  
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