

# Long Term Risk of Colorectal Cancer after Detection of Adenomatous Polyps

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# Background

- Adenomatous polyps are common (30% screening)
- Randomized trials: removal adenoma prevents carcinoma
- Individuals with adenomas are presumed to have ongoing risk of CRC
- Hence, advised to undergo surveillance CS

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. N Engl J Med 2014.  
Schoen RE, Pinsky PF, Weissfeld JL, et al. N Engl J Med. 2012.

# Background

- Surveillance guidelines based on presumption of CRC risk
- Limited data describing long-term CRC risk based on adenomatous findings at colonoscopy
- Current U.S. surveillance guidelines
  - AA: 3 years
  - $\geq 3$  NAA: 3 years
  - 1-2 NAA: 5-10 years
  - NA: 10 years

# Aims

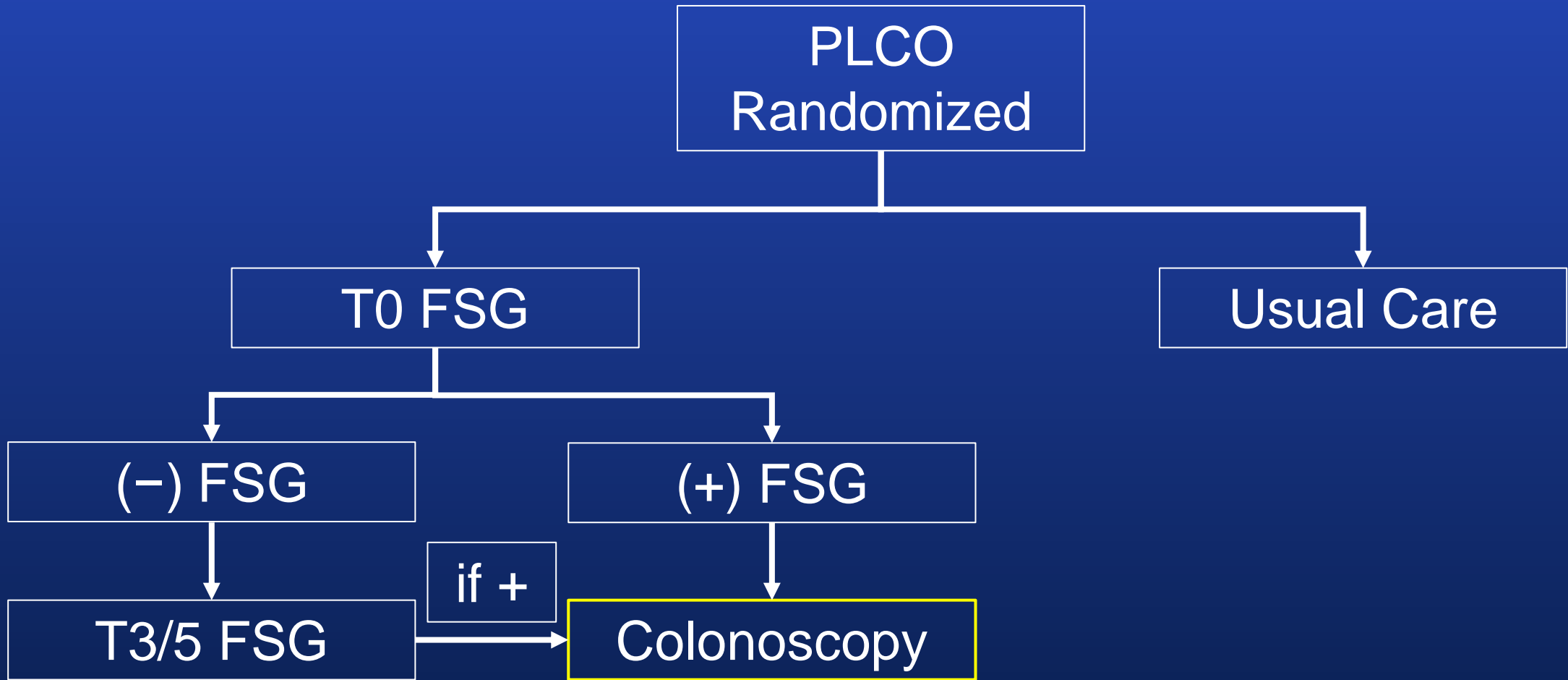
- To examine the relationship between adenoma findings on colonoscopy and long-term, subsequent CRC incidence

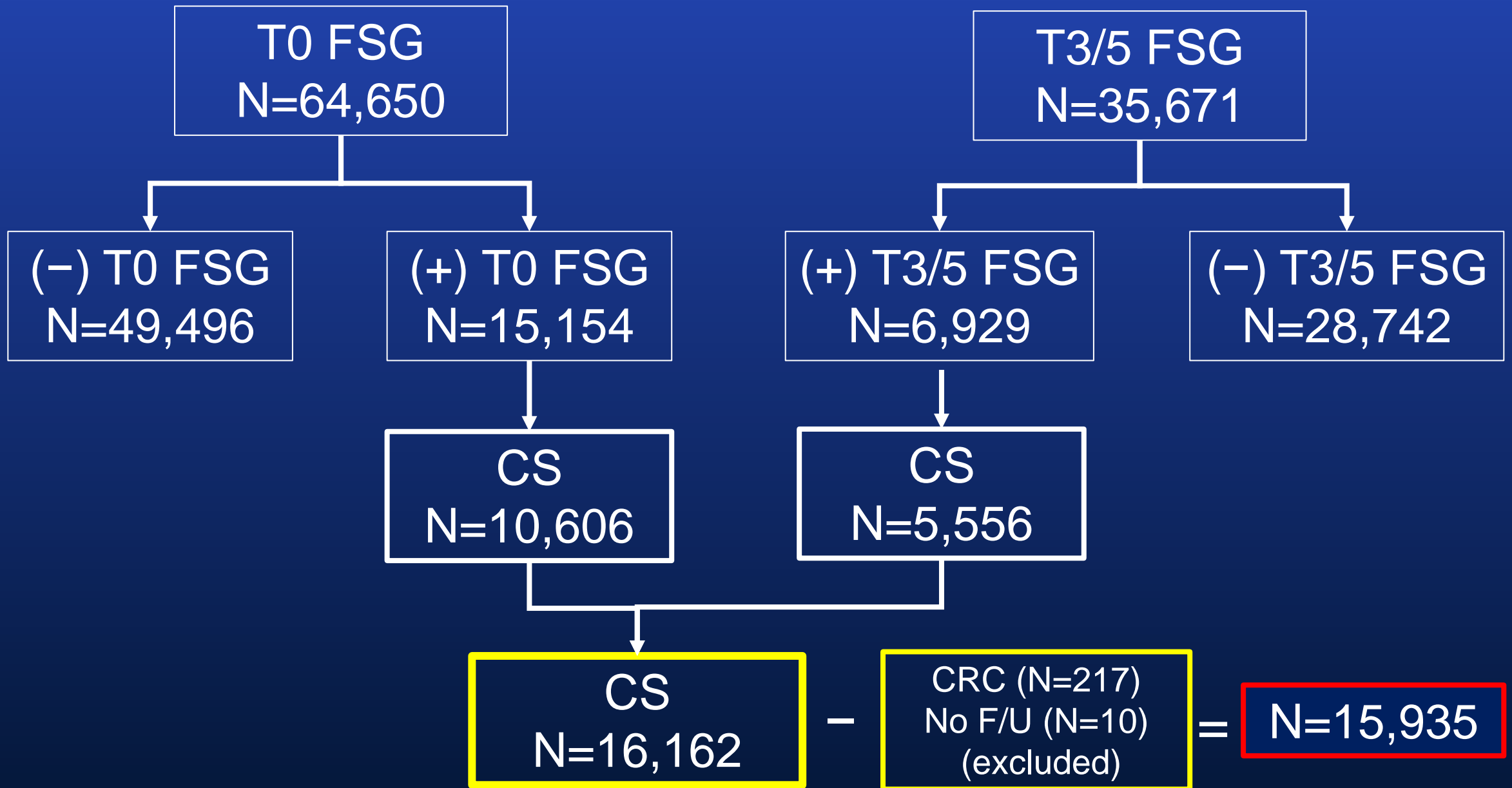
# Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial

- Multicenter, randomized trial of FSG
- Screening FSG baseline at 0 yrs, then again 3/5 yrs
- Enrollment 154,900 men and women
  - Age 55-74
- Follow-up: 13 yrs, death, or loss to FU

# Methods

- In general, if (+) FSG → Colonoscopy
- CS results categorized hierarchically
  - AA:  $\geq 1$  cm, or tubulovillous, or villous or HGD
  - NAA:  $< 1$  cm, #1-2 or  $\geq 3$
  - No Adenoma
- Compared CRC incidence in AA and NAA to No Adenoma







# Statistical Analysis

- Incidence rates per 10,000 PYO
- Risk ratios (95% CI)
- Multivariate Cox proportional hazards
- Kaplan-Meier

CS  
N=15,935

AA  
N=2,882

NAA  
N=5,068

NA  
N=7,985

$\geq 1$  cm  
N= 2,178

$< 1$  cm  
N= 704

1-2  
N= 4,496

$\geq 3$   
N= 572

	<b>All</b> N=15,935	<b>AA</b> N=2,882	<b>NAA</b> N=5,068	<b>NA</b> N=7,985
<b>Age</b>	64	65	64	64
<b>Male, %</b>	59.7	67.2	65.3	53.4*
<b>Race, %</b>				
<b>White</b>	90.7	90.5	89.8	91.3
<b>Black</b>	4.8	4.9	4.0	5.2
<b>Hispanic</b>	1.6	1.3	1.8	1.5
<b>Asian</b>	1.8	2.0	3.1	1.0
<b>Other</b>	1.2	1.4	1.4	1.0
<b>BMI</b>	27.3	27.2	27.3	27.1

	<b>All</b> N=15,935	<b>AA</b> N=2,882	<b>NAA</b> N=5,068	<b>NA</b> N=7,985
<b>Smoking, %</b>				
<b>Never</b>	37.8	36.2	37.9	38.3
<b>Current</b>	14.8	15.9	14.8	14.5
<b>Former</b>	46.7	47.3	46.5	46.5
<b>Unknown</b>	0.7	0.6	0.8	0.6
<b>1<sup>st</sup> Degree FHx CRC, %</b>	11.1	12.3	11.0	10.7
<b>ASA/IBU*, %</b>	42.8	39.4	42.8	44.1
<b>Follow-up, yr</b>	9.7	10.3	9.8	9.4

\* Defined as  $\geq 3$  times a week in prior 12 months

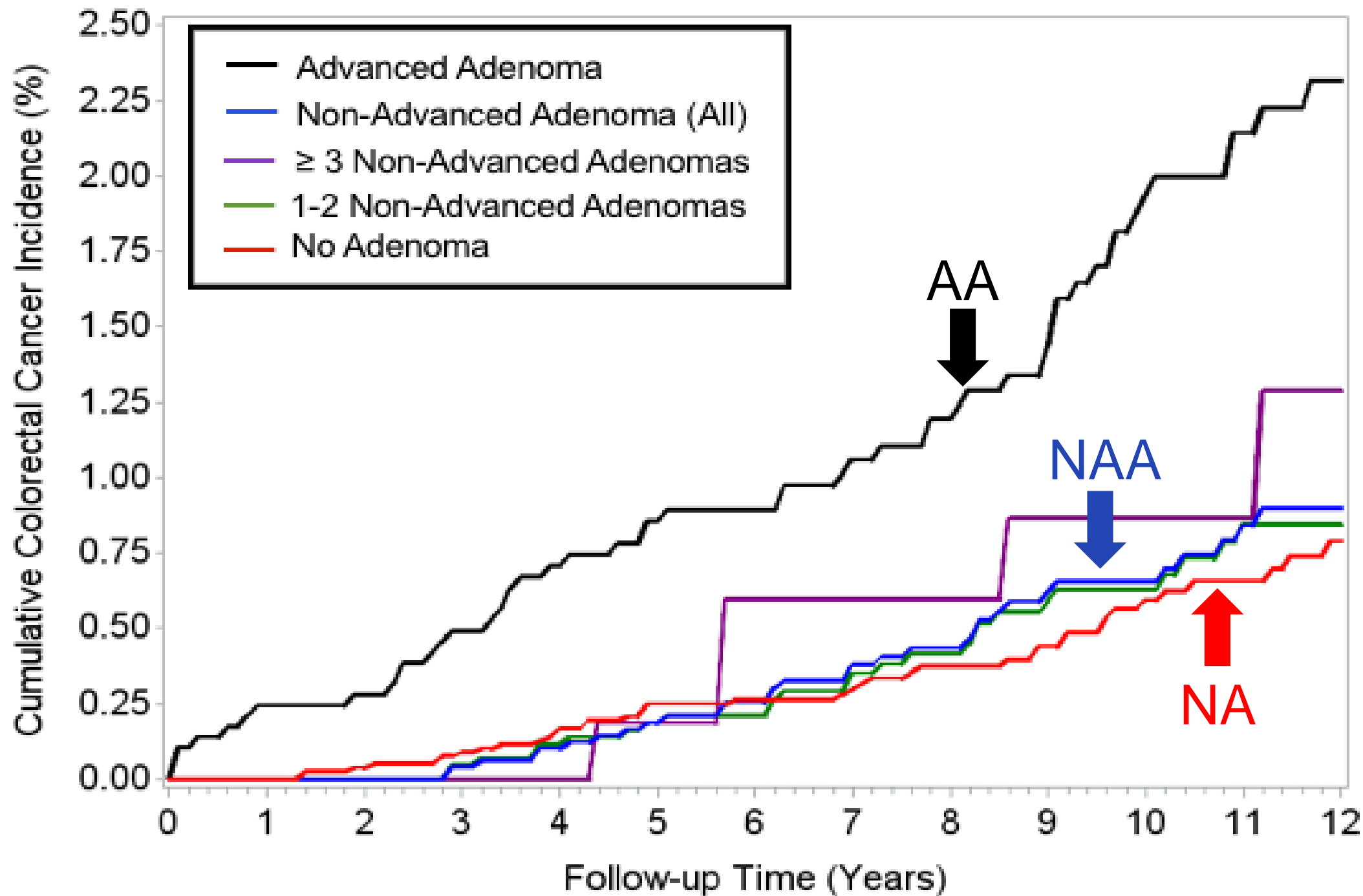
# CRC Incidence: Cancers/10,000 PYO

	AA			NAA			NA
	All N=2882	≥ 1 cm N=2178	< 1 cm N=704	All N=5068	≥ 3 N=572	1-2 N=4496	All N=7985
#CAs	51	37	14	32	6	26	41
Rate	18.3	17.5	20.8	6.8	11.1	6.3	5.7

# Univariate RR CRC Incidence

	AA			NAA			NA
	All	≥ 1 cm	< 1 cm	All	≥ 3	1-2	All
RR (95%CI)	3.18 (2.1-4.8)	3.1 (2.0- 4.8)	3.6 (2.0- 6.6)	1.2 (0.7-1.9)	1.9 (0.8-4.6)	1.1 (0.7-1.8)	Ref
p value	<0.001	<0.001	<0.001	0.46	0.13	0.72	--

AA: Years 5-10 vs. 0-5  
 RR 1.2 (0.6-2.1); p=0.60



# Multivariate Cox Proportional Hazards

	<b>AHR</b>	<b>95% CI</b>	<b>P-value</b>
<b>No adenoma</b>	Ref	--	--
<b>NAA</b>	1.21	0.8-1.9	0.4
<b>1-2 NAA</b>	1.11	0.7-1.8	0.66
<b>≥3 NAA</b>	1.93	0.8-4.7	0.14
<b>AA</b>	3.14	2.1-4.8	<0.0001
<b>≥ 1 cm</b>	3.0	1.9-4.8	<0.0001
<b>&lt; 1 cm</b>	3.6	1.9-6.7	<0.0001
<b>Age ≥ 65</b>	1.6	1.1-2.3	0.01
<b>Male</b>	1.07	0.6-1.6	0.74
<b>ASA Use</b>	1.05	0.7-1.5	0.28
<b>First + screen</b>	0.99	0.6-1.6	0.96



Could surveillance CS  
account for the similarity in  
CRC incidence?

# Surveillance CS

- Study of Colonoscopy Utilization (SCU)
  - Nested study in PLCO
  - Rates and findings of surveillance CS
  - N=3,561
  - 98.1% (N=3,492) of SCU subjects in current study

# Surveillance Colonoscopy Utilization

		% of Pts at Risk		
	No.	5 Yr	7 Yr	9 Yr
AA	1304	62.5	76.3	82.5
NAA	980	53.9	72.2	78.7
≥ 3	123	59.9	77.0	83.0
1-2	857	53.0	71.5	78.1
NA	1208	36.9	59.9	69.9

# % with Adenoma Removal

		% of Pts at Risk		
	No.	5 Yr	7 Yr	9 Yr
AA	1304	26.5	34.1	40.4
NAA	980	18.2	26.6	33.2
≥ 3	123	30.5	42.6	47.4
1-2	857	16.4	24.3	31.1
NA	1208	8.8	15.7	20.3

# Limitations

- CS followed abnormal FSG
- Not all (+) FSG had subsequent CS (75%)
- Surveillance CS data in subset of pts, utilization not standardized
- CS indication and quality
  - Prep
  - ADR

# Strengths

- Real world setting: multicenter, across U.S. variety of practices
  - e.g., the path findings represent U.S. practice
- Few lost to follow up
  - Compliance with annual update (93.8%)
- Large sample, followed nearly 10 years

# Summary

Compared to subjects with No Adenoma on CS:

- AA: 3-fold increased risk of subsequent CRC
- 1-2 NAA: No increased subsequent CRC risk

# Conclusions

- AA: Increased cancer risk supports ongoing surveillance
- 1-2 NAA: Do not appear to be at significantly increased CRC risk compared to No Adenoma
  - Uncertain contribution of small increase in surveillance CS/adenoma removal
- Further evaluation of the benefit of surveillance colonoscopy is needed.
  - EPOS, FORTE



Thank You!

Questions?



# CRC Mortality

	AA			NAA			NA
	All	≥ 1 cm	< 1 cm	All	≥ 3	1-2	All
<b>No.</b>	9	6	3	5	1	4	8
<b>RR</b>	2.9	2.5	4.0	0.95	1.7	0.9	Ref
<b>(95%CI)</b>	(1.1-7.6)	(0.9- 7.4)	(1.04-15.1)	(0.3- 2.9)	(0.2-13.7)	(0.3- 2.9)	
<b>p value</b>	0.03	0.09	0.04	0.93	0.63	0.81	--

# Are NA representative of negative screen?

- Distal CRC incidence (–) T0 FSG vs. (+) T0 FSG but NA
- (–) T0 FSG
  - N= 42,348
  - Incidence: 2.48 (114 cases, 460,310 PYO)
- (+) T0 FSG (No Adenoma)
  - N=4,811
  - Incidence: 2.34 (12 cases, 51,264 PYO)
- RR 1.05 (95% CI 0.6-1.9), p=0.87
- Overall CRC: 8.0 vs. 6.6, RR 1.21 (95% CI 0.9-1.7), p=0.28

# AA Location and CRC

AA location	N	CRC (%)	Distal CRC	Proximal CRC	HR (95% CI) for CRC
Distal	1990	28 (1.4%)	15	13	Ref
Proximal	565	16 (2.8%) <sup>b</sup>	4	11	2.3 (1.2-4.2)
Both	248	6 (2.4%)	3	3	1.8 (0.7-4.3)
Unknown	79	1 (1.3%)	0	1	0.95 (0.1-7.2)

No significant association between initial AA location and subsequent CRC location (p=0.09)