



# **CTC vs. Colonoscopy for Surveillance After CRC ?**

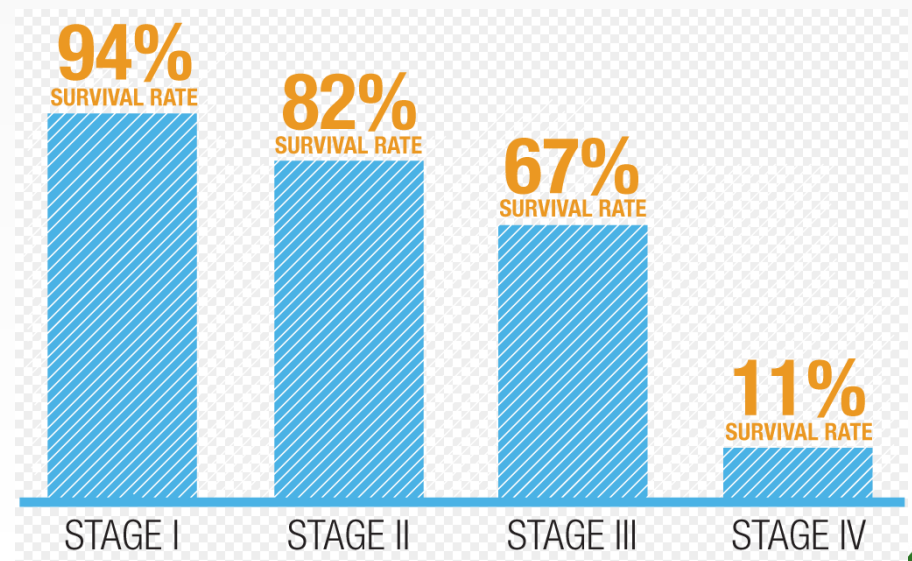
**David Weinberg, MD, MSc**

**June 1, 2018**



# Goals of Post-operative CRC surveillance: Prevention or early detection of metachronous disease

- 30%-50% will suffer post-operative recurrence, mostly extra-intestinal metastasis
- 80% recurrences by year 3, nearly 100% by year 5.
- Expected survival with recurrence <2 years



# Post-Operative Surveillance: Intensive versus Standard

**Intensive:** usually means q 3-6 month follow-up, periodic CEA, imaging, endoscopy

**Standard:** no regular testing or consultation

At least 8 completed RCTs and 2 meta-analyses comparing “intensive” surveillance to “standard”

No trial defines “intensive” the same way!



# Is Intensive Surveillance Effective?

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with conventional follow-up	Risk with intensive follow-up				
Overall survival (OS) Follow-up: range = 24 months to 105 months (median)	Study population		HR 0.92 (0.77 to 1.09)	4786 (12 RCTs)	⊕⊕⊕⊕ HIGH <sup>1, 2</sup>	17 fewer deaths per 1000 (between 50 fewer and 18 more)
	242 per 1000	225 per 1,000 (192 to 260)				
Colorectal cancer-specific survival (CC-SS) Follow-up: range = 24 months to 105 months (median)	Study population		HR 0.93 (0.78 to 1.12)	3822 (7 RCTs)	⊕⊕⊕○ MODERATE <sup>1, 2, 3</sup>	10 fewer death per 1000 (between 30 fewer and 16 more)
	143 per 1000	133 per 1,000 (113 to 158)				
Interval recurrences (IR) assessed with: recurrent CRC diagnosed between scheduled follow-up visits Follow-up: range = 43 months to 79 months (median)	Study population		RR 0.59 (0.41 to 0.86)	3933 (6 RCTs)	⊕⊕⊕○ MODERATE <sup>1, 4</sup>	52 fewer interval recurrences (between 18 fewer and 75 fewer)
	127 per 1000	75 per 1,000 (52 to 109)				



# Various Societal Surveillance Guidelines

Society	Year	Colonoscopy	CEA	History and Physical	Imaging
NCCN	2013	@ 1yr. If AA, repeat in 1 year. If not then 3 yrs, then 5 yrs.	q3-6 mos. X2 yrs, then q6mos. X3 yrs.	q3-6 mos. X2 yrs, then q6mos. X3 yrs.	CT C/A/P: q1yr x5 if high risk of recurrence*
ASCO	2005	Assuming "cleared" colon, 2-3 yrs. then q5 if normal.	q3 mos. x3 yrs for stage II/III disease	q3-6 mos. X3 yrs, then q6 mos. X2 yrs.	CT C/A: q 1 yr x3 yrs. Add pelvis for rectal cancer.
NICE	2011	@ 1yr. If normal, repeat in 5 yrs. If not, interval determined by findings.	@ least q6 mos. X 3 yrs.	Regular follow up starting 4-6 weeks post-operatively.	CT C/A/P: at least 2 in the first 3 yrs.
AGA	2006	@1 yr. If normal repeat in 3 then 5 yrs.	Not addressed	Not addressed	Not addressed
ESMO	2012	@ 1 yr, then q5 yrs.	q3-6 mo x3 yrs, then q6-12 months x2 yrs	q3-6 mo x3 yrs, then q6-12 months x2 yrs	CT C/A q 6-12 mo x 3 yrs if high risk. Consider q3-6 mos. Liver ultrasound.
ASCRS	2004	@ 1 yr, then q3 yrs.	Minimum of 4 months x 2 years then q 6 months x 2 years, then annually	Minimum of 4 months x 2 years then q 6 months x 2 years, then annually	Routine hepatic imaging should not be performed; Insufficient data to support or refute CXR; Consider EUS for rectal cancer

NCCN: National Cancer Care Network; yrs: years;

ASCO: American Society of Clinical Oncologists; mos: months

NICE: National Institute for Health and Care Excellence; EUS: endorectal ultrasound

AGA: American Gastroenterological Association; CXR: chest x-ray

ESMO: European Society for Medical Oncology C/A/P: chest/abdomen/pelvis

ASCRS: American Society of Colon & Rectal Surgeons

\*Tumor with lymphatic or vascular invasion or poor differentiation

# Is Optical Colonoscopy Effective for Post-Operative Surveillance?

- Similar to other post-op surveillance: intensive colonoscopy use possibly associated with improved overall 5 year mortality, more asymptomatic disease detection, more surgery, but no change in disease specific outcomes
- No surprise perhaps, since intra-luminal recurrence without extra-luminal disease is unusual



# Is Surveillance the Right Setting to Substitute CTC for OC?

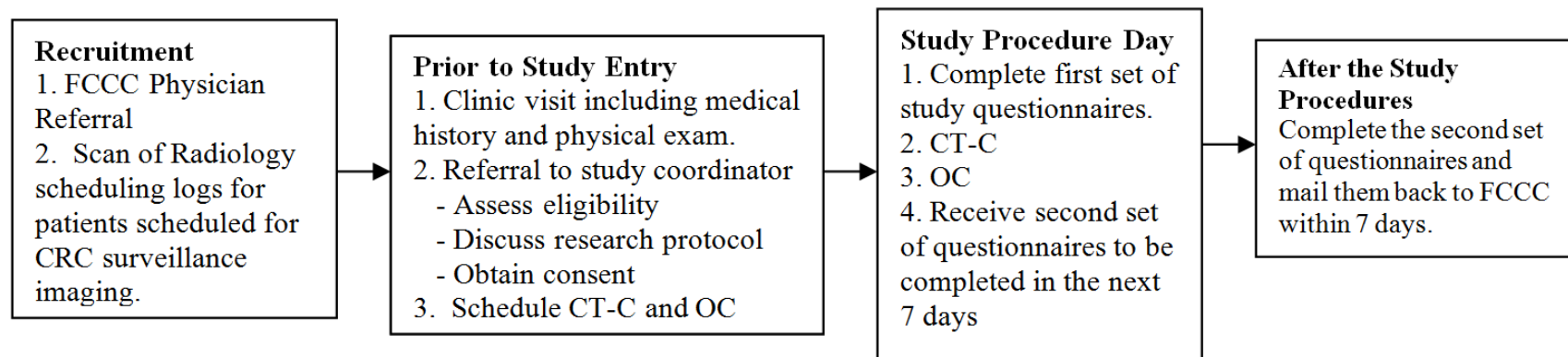
**Screening:** CTC for could be cost-effective if it cost less and/or enticed more people to be screened

**Surveillance:** OC is expensive, has risk and finds relatively few lesions (may also miss lesions). If CTC works well, costs less and/or increases compliance it could be an attractive alternative



# Comparative Effectiveness of Virtual and Optical Colonoscopy for CRC Surveillance

Participating Sites: Fox Chase Cancer Center, Mayo Clinic (Rochester), University of Chicago, University of Wisconsin, Memorial Sloan Kettering, University of Minnesota (modeling only)



Clinical Trials.gov Registration Number: NCT02143115

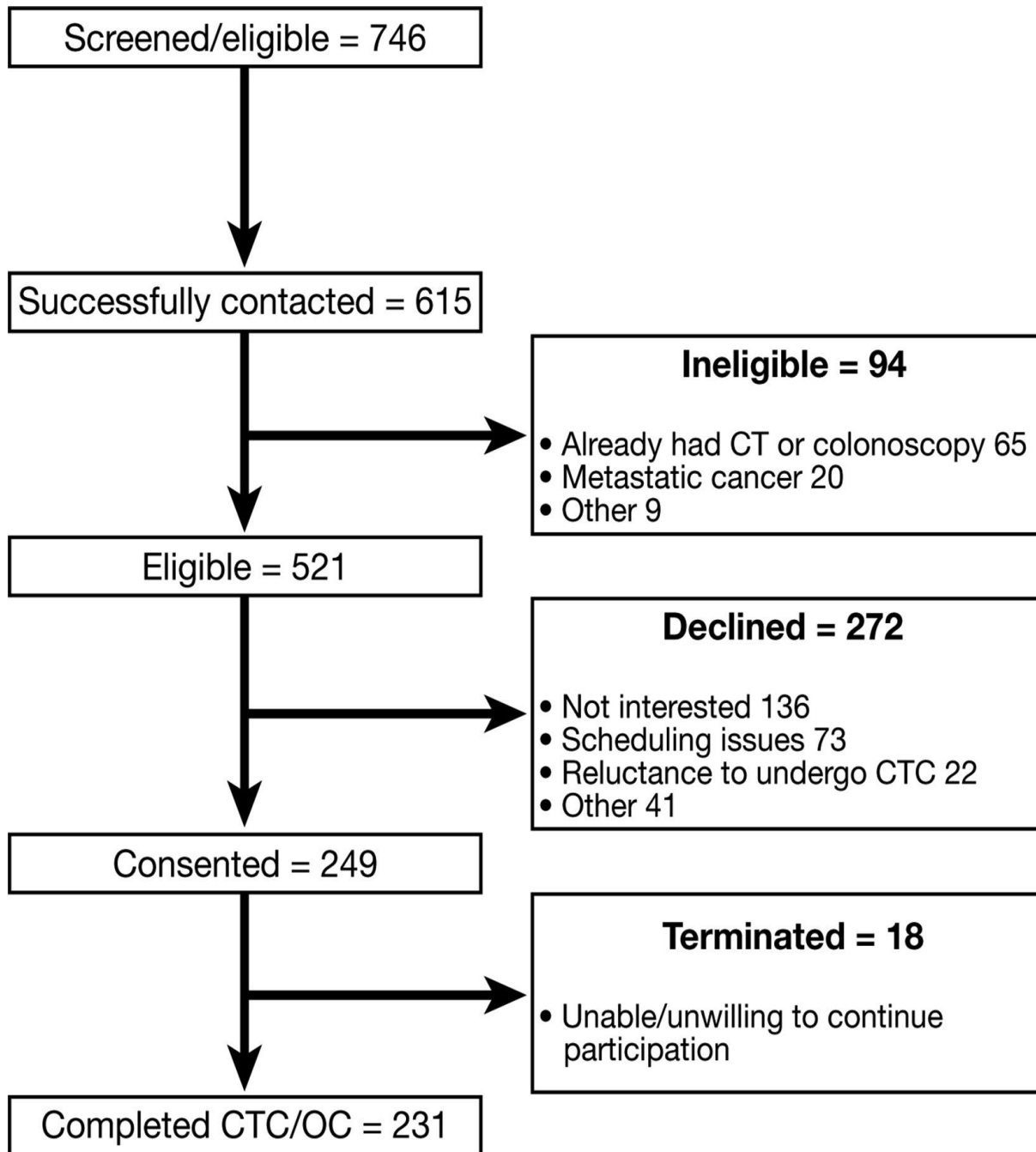




# Specific Aims

1. To evaluate the **test characteristics** (sensitivity, specificity, positive and negative predictive value) of CT colonography (CTC) for detecting colorectal polyps and cancers in the post-CRC resection surveillance setting, using optical colonoscopy (OC) as the reference standard.
2. To compare the **costs and outcomes**, from a societal perspective, of CTC versus independent OC plus CT for post CRC resection surveillance, using standard methods of cost-effectiveness analysis.





### Inclusion Criteria

1. Age 18y and older
2. CRC Stage 0-III at diagnosis
3. Completed therapy

### Exclusion Criteria

1. Diverting ileostomy
2. IBD
3. FAP
4. Pregnancy
5. Acute GI symptoms



# Results: Detection of any Polyp

**Table 3. Performance Characteristics of CT Colonography relative to Optical Colonoscopy for detecting lesions of all types<sup>1,2</sup>**

Performance Characteristic	Lesion Size Category from Optical Colonoscopy	
	≥6mm	≥10mm
<b>Patient-Level Analyses<sup>3</sup></b>		
<b>Sensitivity</b>	22/50 44.0 (30.2-57.8)*	10/13 76.9 (54.0-99.8)
<b>Specificity</b>	169/181 93.4 (89.7-97.0)	194/218 89.0 (84.8-93.1)
<b>Negative Predictive Value</b>	169/197 85.8 (80.9-90.7)	194/197 98.5 (96.8-100)
<b>Positive Predictive Value</b>	22/34 64.7 (48.6-80.8)*	10/34 29.4 (14.1-44.7)*

1-Cell values include number/total number, performance characteristic estimate and two-sided 95% confidence intervals

2-Optical colonoscopy results are from initial pass before CTC results were revealed to gastroenterologist. CTC is defined as positive for a patient if at least one ≥6mm lesion as measured by CTC is detected.

3-Lesion size category represents maximum lesion size per patient as determined by optical colonoscopy.

\*-operating characteristics significantly less than 90% (p<.05).



# Results: Detection of Adenomas

**Table 4. Performance Characteristics of CT Colonography relative to Optical Colonoscopy for detecting adenomas<sup>1,2,3</sup>**

Performance Characteristic	Adenoma Size Category from Optical Colonoscopy	
	≥6mm	≥10mm
<b>Patient-Level Analyses<sup>4</sup></b>		
<b>Sensitivity</b>	16/36 44.4 (28.2-60.7)*	7/10 70.0 (41.6-98.4)
<b>Specificity</b>	193/195 98.9 (97.6-100)	210/221 95.0 (92.2-97.9)
<b>Negative Predictive Value</b>	193/213 90.7 (86.7-94.5)	210/213 98.6 (97.0-100)
<b>Positive Predictive Value</b>	16/18 88.9 (74.4-100)	7/18 38.9 (16.4-61.4)*

1-Cell values include number/total number, performance characteristic estimate and two-sided 95% confidence intervals

2-Optical colonoscopy results are from initial pass before results from virtual colonoscopy were revealed to gastroenterologist. CTC is defined as positive for a patient if at least one ≥6mm lesion as measured by CTC is detected.

3-Adenomas include serrated polyps also

4-Adenoma size category represents maximum adenoma size per patient as determined by optical colonoscopy.

\*-operating characteristics significantly less than 90% (p<.05).



# Translated into Practical Numbers

- Universal application of CTC at year 1 post-resection:
  - Reduce OC use by 92.2% (patients with nothing or a polyp <6mm in size)
- For a population of 1000 persons
  - 78 OCs → 69 patients with  $\geq 6\text{mm}$  polyp
    - 30 patients with  $\geq 10\text{mm}$  polyp
  - Miss 87 patients with  $\geq 6\text{mm}$  and 13 patients with  $\geq 10\text{mm}$  polyp



# Our cost data applied to other studies

Study	Setting	sens	spec	prev	Cost/adenoma	Missed/10K
6mm					Detected by OC	
Weinberg	Surveillance	0.500	0.918	0.156	\$5,725	779
Cotton	Diagnosis	0.452	0.931	0.173	\$12,560	855
Pickhardt	Screening	0.887	0.796	0.136	\$45,595	176
Mulhall	Meta-Analysis	0.700	0.930	0.156	\$21,570	468
Kim	Surveillance	0.800	0.931	0.144	\$34,657	287
Study	Setting	sens	spec	prev	MCE	Missed/10K
10mm						
Weinberg	Surveillance	0.600	0.973	0.156	\$28,350	173
Cotton	Diagnosis	0.595	0.980	0.173	\$67,323	174
Pickhardt	Screening	0.938	0.960	0.136	\$420,313	27
Mulhall	Meta-Analysis	0.850	0.970	0.156	\$175,517	65
DeHaan	Screening	0.833	0.987	0.156	\$160,929	72



# Broad Conclusions

- CTC is a sub-optimal clinical substitute for OC
- Adenomas and cancer are relatively rare (i.e. pretest probability is low), so a negative CTC has very high predictive value
- OC directly (versus CTC→OC) strategy costs XYZ for each additional  $\geq 6\text{mm}$  polyp and XYZ for each additional  $\geq 10\text{mm}$  polyp.

