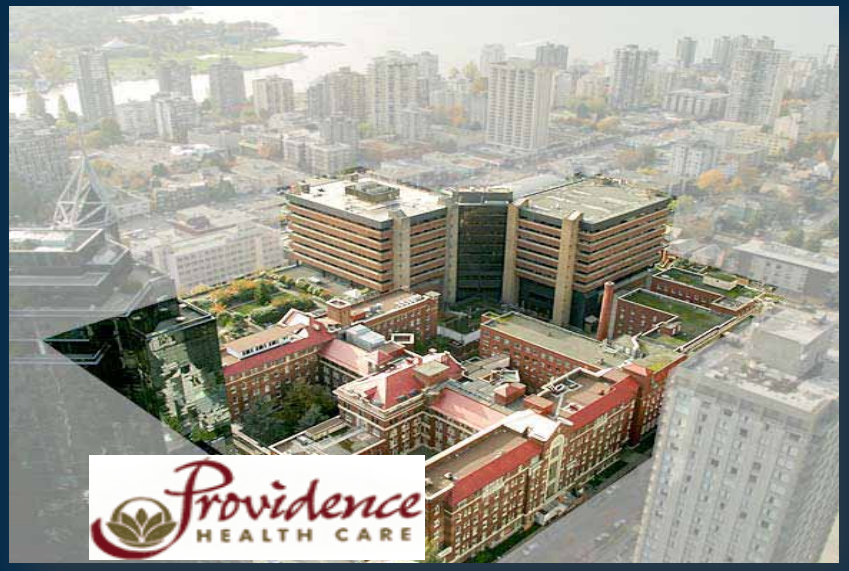
Colorectal Cancer – Follow Up After Curative Resection

The University of British Columbia

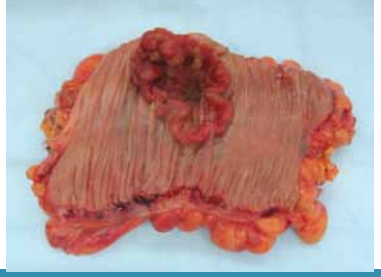
St. Paul's Hospital



October 4, 2012

Carl J. Brown, MD MSc FRCSC

Background

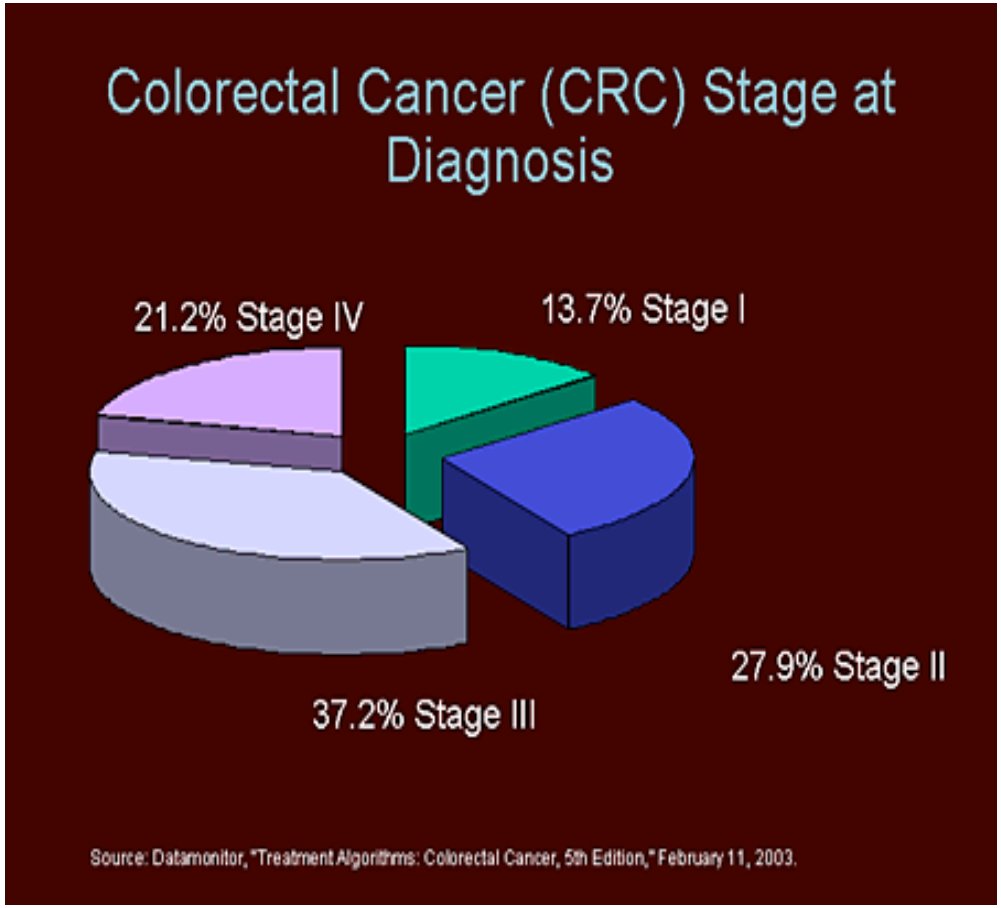


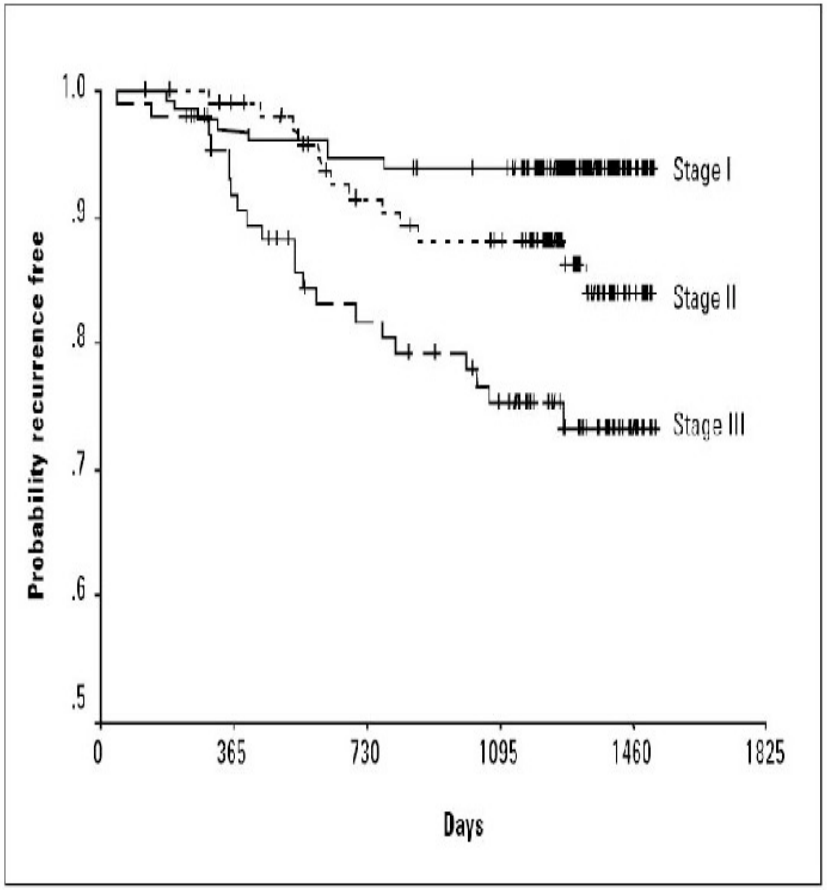
- Lifetime risk of colorectal cancer is 6.5%
  - Rectal cancer 30% of this risk

Estimated New Cases and Deaths for Cancer Sites by Sex, Canada, 2005

	New Cases 2005 Estimates			Deaths 2005 Estimates			Deaths/Cases Ratio 2005 Estimates		
	Total	M	F	Total	M	F	Total	M	F
All Cancers	**149,000**	**76,200**	**72,800**	**69,500**	**36,700**	**32,800**	**0.47**	**0.48**	**0.45**
Lung	22,200	12,000	10,200	19,000	10,700	8,300	0.86	0.89	0.82
Breast	21,800	150	21,600	5,300	45	5,300	0.24	0.30	0.24
Prostate	20,500	20,500	–	4,300	4,300	–	0.21	0.21	–
Colorectal	19,600	10,600	9,000	8,400	4,500	3,900	0.43	0.42	0.43

CRC – Stage and Survival





Why screen for CRC recurrence?

- Principle of Screening
  - Important/Prevalent Condition
  - Acceptable/Safe/Accurate Tests
  - Timeline of Disease and Outcome Modifiable

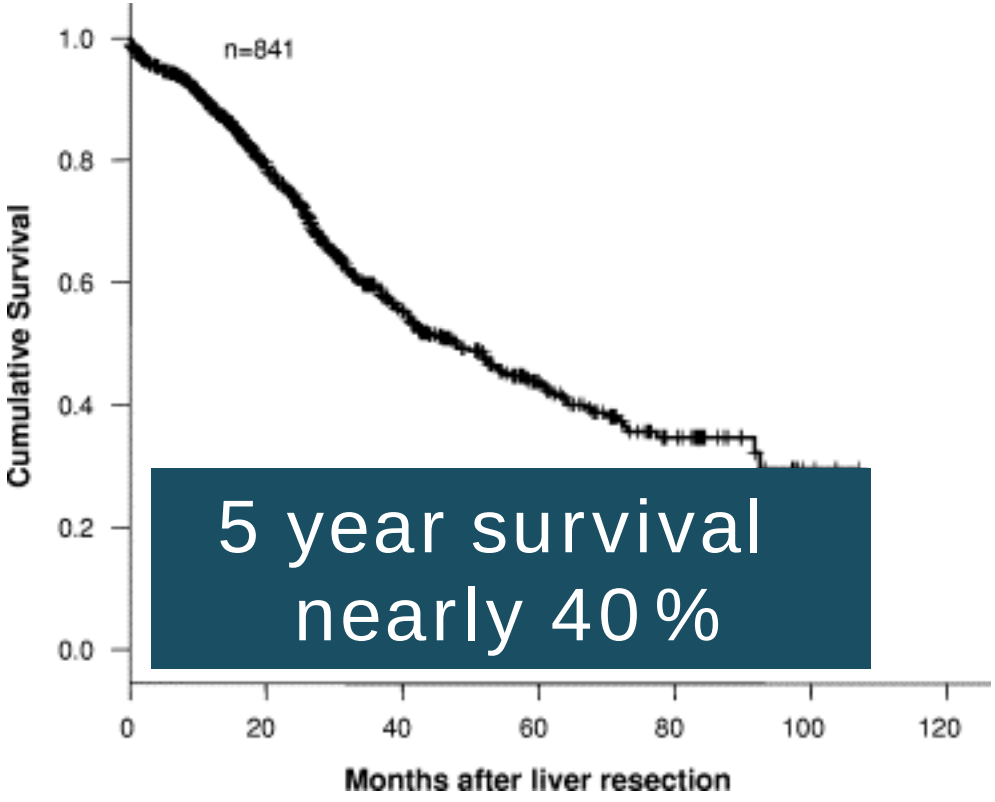
  - IDENTIFY TREATABLE DISEASE

Chemotherapy for Stage IV CRC

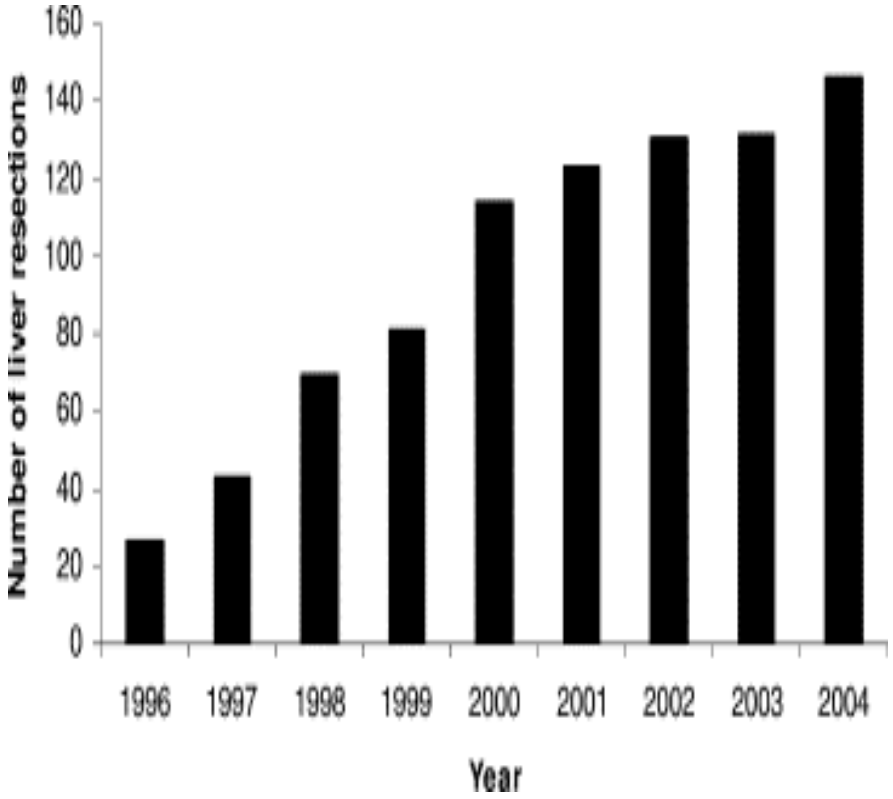
Trends in median survival among patients with metastatic colorectal cancer

Reference	Treatment status	Median survival
Scheithauer *et al.*[181]	Before any active chemotherapy	6 mo
Cochrane Database[182]	Fluoropyrimidine only	10-12 mo
Saltz *et al.*[119] and de Gramont *et al.*[130]	Fluoropyrimidine and one other active cytotoxic chemotherapeutic agent (irinotecan or oxaliplatin)	14-16 mo
Goldberg et al.[134] and Fuchs *et al.*[120] Hurwitz *et al.*[145]	Fluoropyrimidine, irinotecan, and oxaliplatin (in combination or as sequential therapy) or Cytotoxic chemotherapy and targeted therapy	>20 mo

Surgery for Liver Metastases

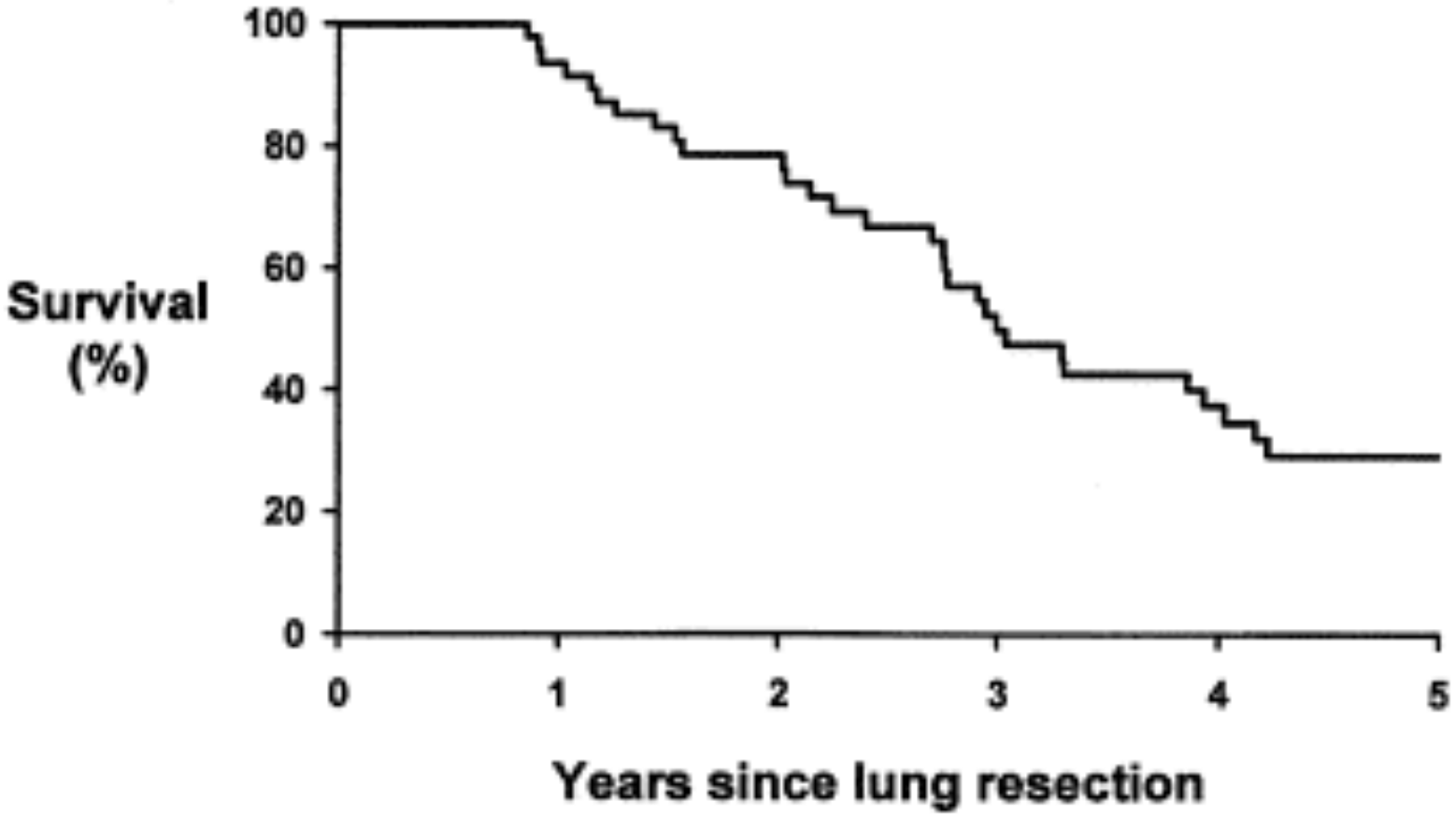


5 year survival nearly 40%



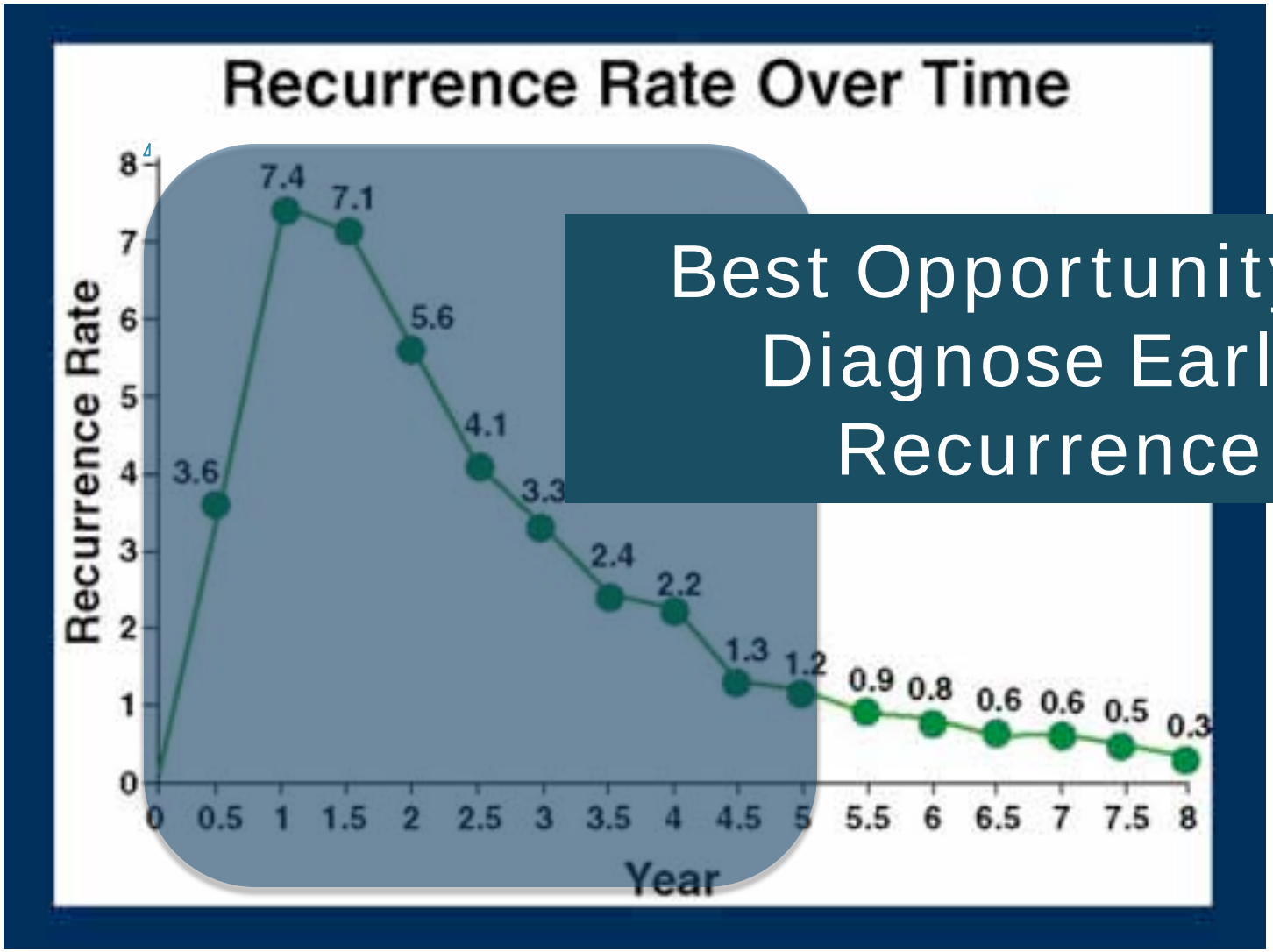
Shah et al, Journal Am Col Surg 2007

Surgery for Pulmonary Metastases



Headreck et al, Ann Thor Surg 2001

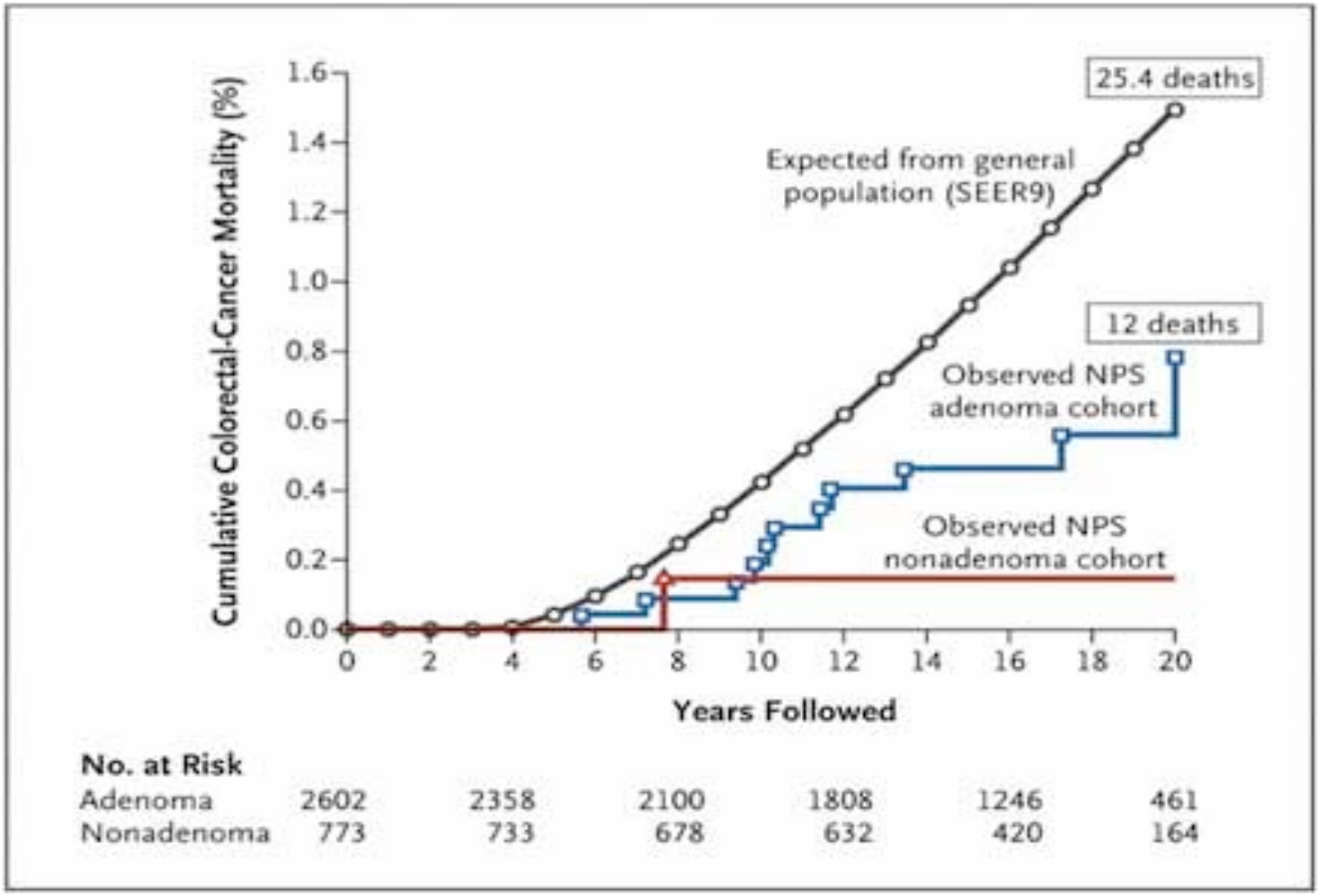
Background


Recurrence Rate Over Time
Recurrence Rate
Year
0
1
2
3
4
5
6
7
8
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8
3.6
7.4
7.1
5.6
4.1
3.3
2.4
2.2
1.3
1.2
0.9
0.8
0.6
0.6
0.5
0.3
Best Opportunity to Diagnose Early Recurrence

Strategies for CRC Follow Up

- Colonoscopy
- CEA
- CT / US
- Chest Xray
- Clinical Examination

Colonoscopy – All Patients After CRC

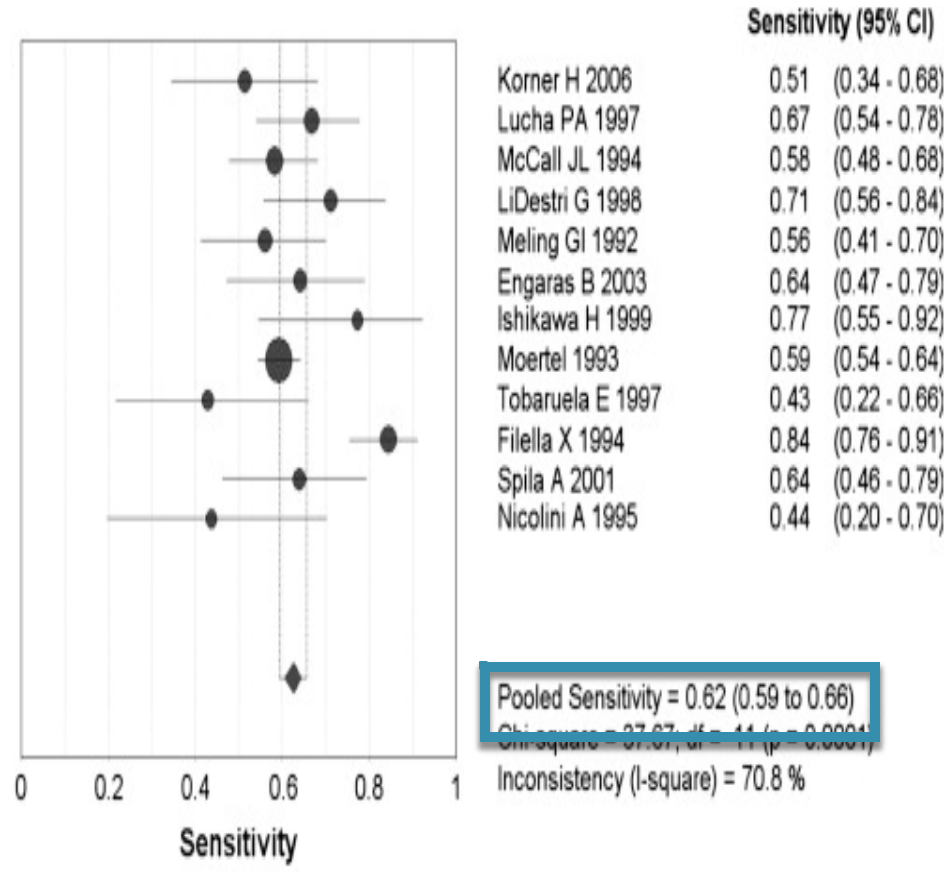


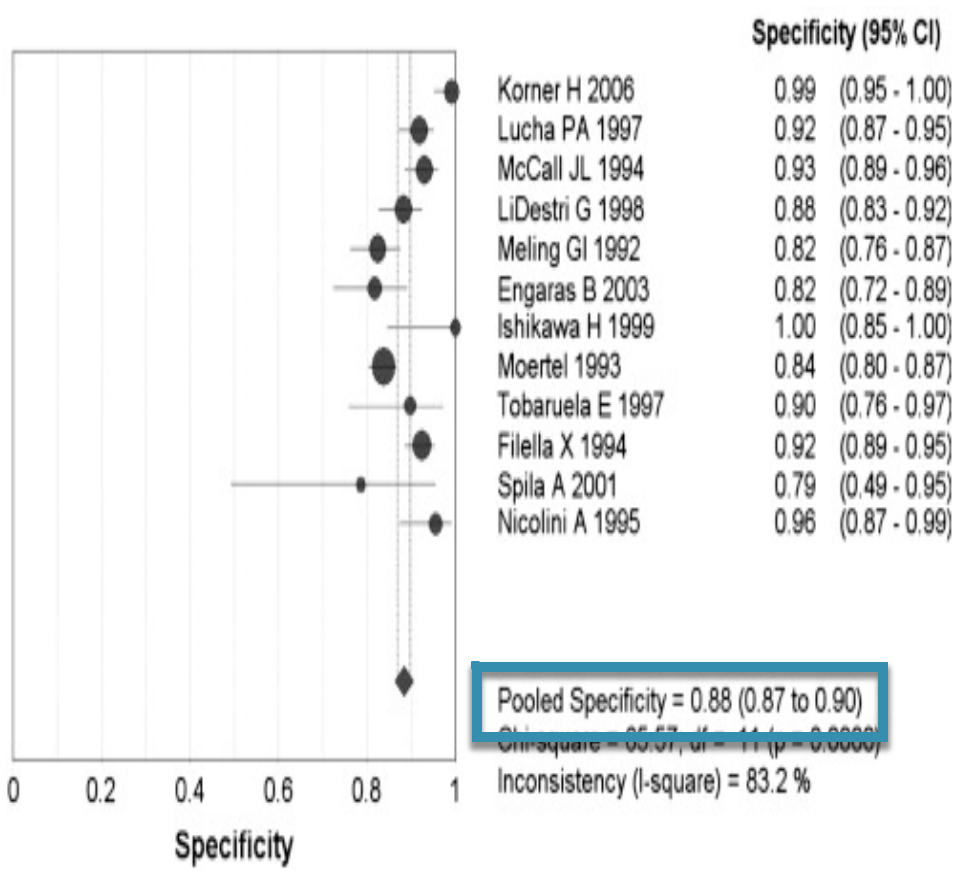
Zauber et al, NEJM 2012

Carcinoembryonic Antigen (CEA)

- A glycoprotein involved in cell adhesion
- Typically produced in utero, stops after birth
- Phil Gold and Samuel Freedman discovered in CRC specimens in 1965

CEA Accuracy in CRC Recurrence





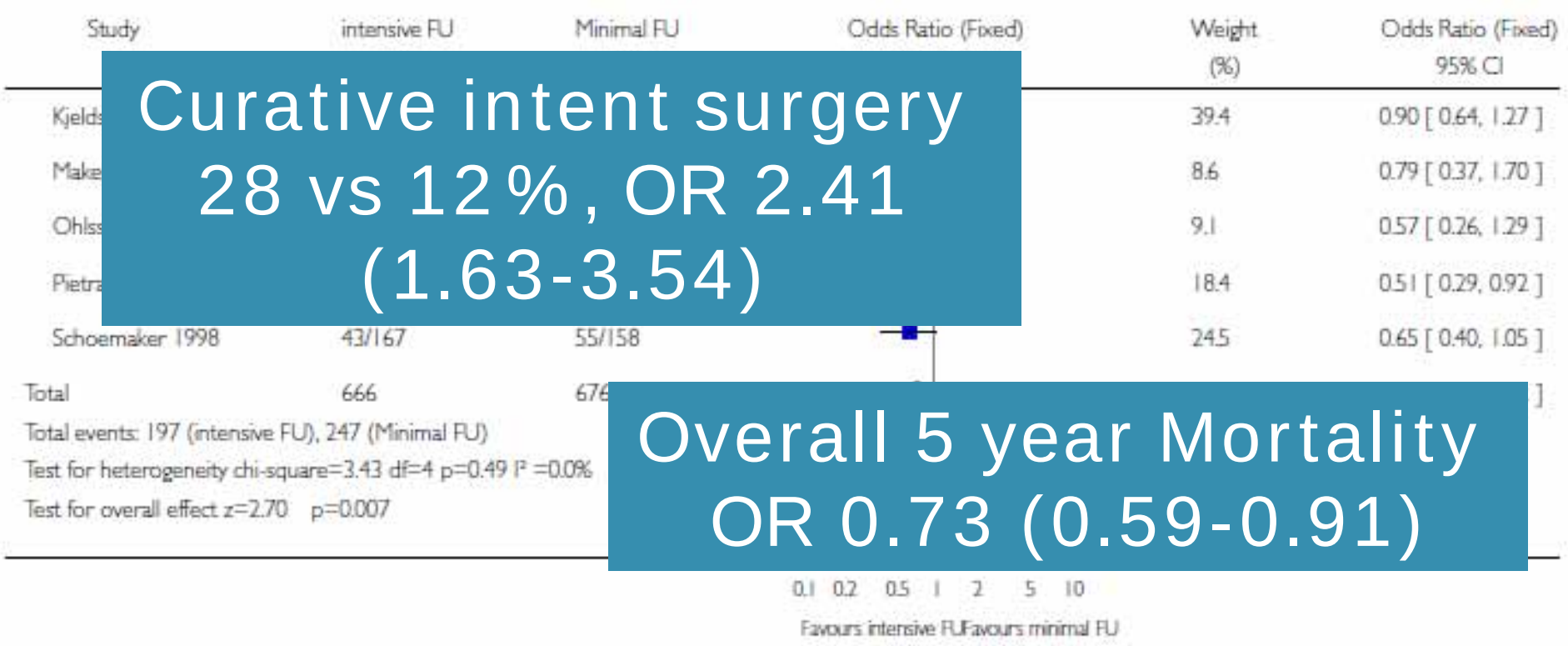
Tan et al, Surg Onc 2009

Intensive Follow Up

- Jeffery, Cochrane, 2007
  - 8 RCTs comparing “intensive follow up” with “minimal follow up”
    - Poorly defined
  - 2141 patients with Stage I-III CRC

Colorectal Cancer Follow Up

Intensive Follow-up vs. Minimalist follow-up

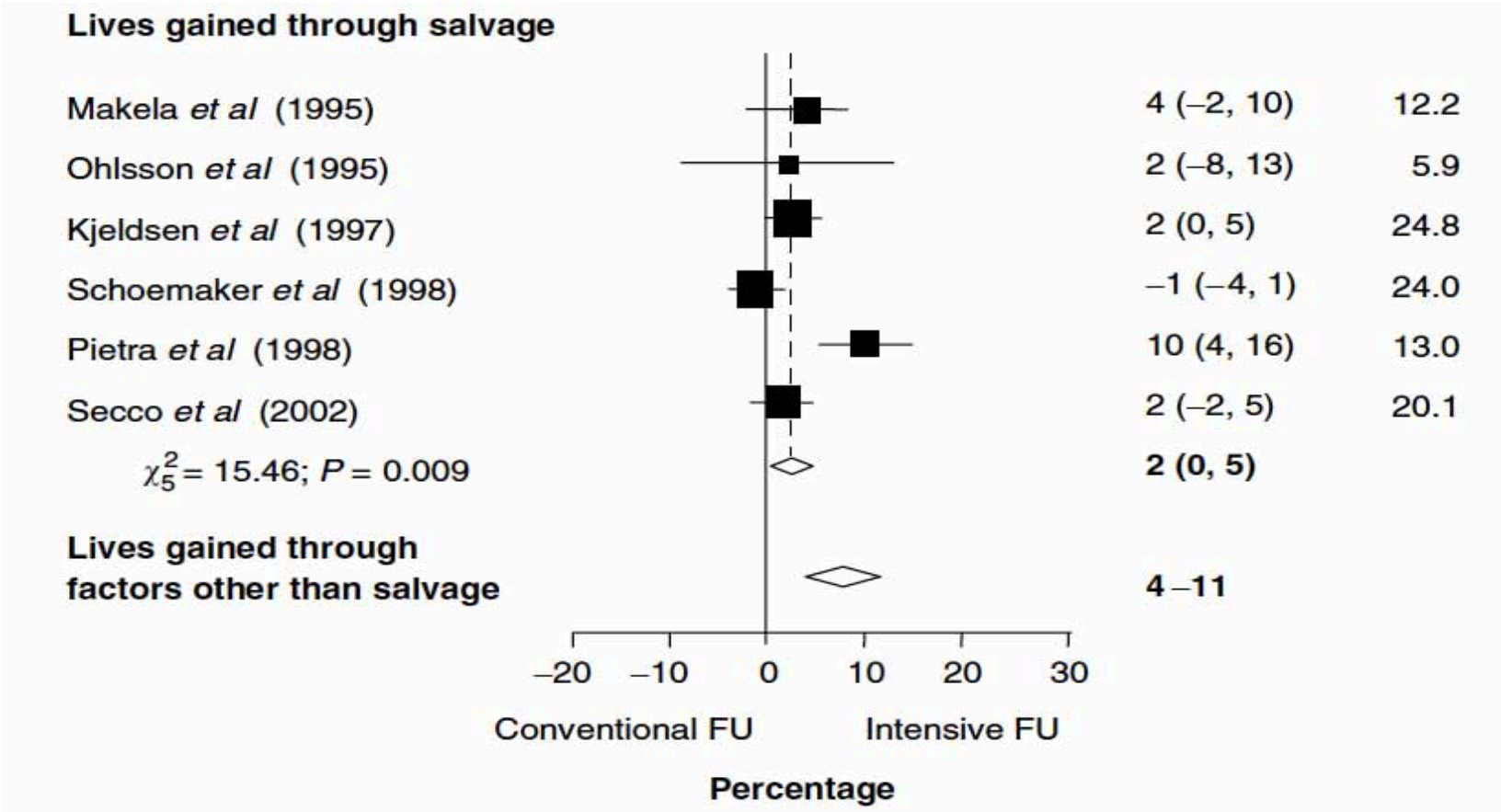


Curative intent surgery
28 vs 12%, OR 2.41
(1.63-3.54)

Overall 5 year Mortality
OR 0.73 (0.59-0.91)

Jeffey et al. Follow-up strategies for patients treated for non-metastatic colorectal cancer (Review). Cochrane Collaboration 2004.

Mechanism of Improved Survival



Renahan, Br J Cancer 2005

The Evidence

- The randomized trials were fraught with inconsistencies
- Three meta-analyses were done[1,2,3]
  - 33 % reduction in risk of death from all causes
  - absolute difference = 7%
- Wide variation of follow-up programs
- No conclusions on exact surveillance protocols

1. Jeffery GM, et al. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2002; (1):CD002200.
2. Renehan AG, et al. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. BMJ 2002 Apr 6;324(7341):813.
3. Figueredo A, et al. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. BMC Cancer 2003 Oct 6;3(1):26.

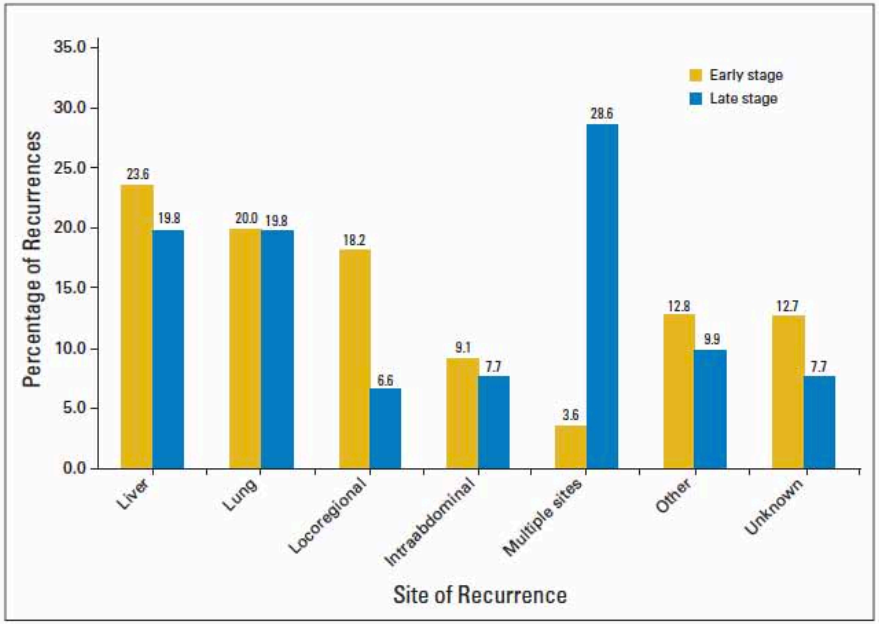
What about Stage I Cancer?

- Risk of recurrence depends on surgical approach

Study	Local Recurrence (%)			5 year Survival (%)		
	TAE	Rad	p	TAE	Rad	p
Melgren 2000	18	0	0.03	72	80	0.5
Nascimbeni 2004	7	3	0.26	72	90	0.008
Endreseth 2005	12	6	0.01	70	80	0.04
Bentrem 2005	15	3	0.001	89	93	0.26

Early Stage Colon Cancer

- Tsikitis et al, J Clin Onc 2009
  - 872 pts with colon CA,
    - 537 "early" (I &IIa)
    - 254 late (IIB and III)
  - Recurrence
    - 55 early, 20 curative surgery
    - 91 late, 32 curative surgery
  - Cumulative recurrence at 2 and 5 years
    - Early 6.0% (95% CI, 4.0% to 8.0%) and 9.5% (95% CI, 7.0% to 12.0%)
    - Late 23.7% (95% CI, 18.7% to 29.3%) and 35.7% (95% CI, 29.9% to 42.1%)



Early Stage Colon Cancer

Tsikitis et al, J Clin Onc 2009

- However, 1/3 of recurrences discovered by endoscopy
  - Ultimately, only 2.2% early stage pts had curative resection for lesion discovered on CT or CEA (NNT ~50)

Table 1. Surveillance Recommendations

Parameter	COST Protocol	ASCO (2005)[3]	NCCN (2008)[7]
History and physical exam	Every 3 months for 1 year then every 6 months to 5 years	Every 3 to 6 months for 3 years; then every 6 months to 5 years	Every 3 to 6 months for 2 years then every 6 months to 5 years
CEA	Every 3 months for 1 year then every 6 months to 5 years	Every 3 months for 3 years*	Every 3 to 6 months for 2 years then every 6 months to 5 years†
Chest screening	CXR every 6 months for 2 years then every 1 year to 5 years	CT chest every 1 year for 3 years‡	CT chest every 1 year for 3 years§
Colonoscopy	Annual exam if positive for neoplasm; exam every 3 years if negative	At 3 years and if results are normal, then every 5 years	At 1 year, 3 years, and 5 years if negative‖
CT abdomen	At discretion of physician for symptoms, signs, or increased h CEA	CT every 1 year for 3 years‡	CT abdomen/pelvis every 1 year for 3 years§

CRC Follow Up - Guidelines

Guideline	History and Physical Examination	CEA	CT	Colonoscopy
ASCO	Every 3–6 mo for 3 y, then every 6 mo for 2 y, then at discretion of physician	Every 3 mo for 3 y in patients with stage II or III disease who are candidates for chemotherapy	CT of chest/abd/pelvis annually for 3 y in candidates for surgery with curative intent	At 3 y postresection, then every 5 y or as clinically indicated
ASCRS	Every 3 mo for 2 y	Every 3 mo for 2 y	NR	Periodic
ESMO	Every 3–6 mo for 3 y, then every 6–12 mo for 2 y	Every 3–6 mo for 3 y, then every 6–12 mo for 2 y	CT of chest/abd/pelvis every 6 mo for 3 y in patients at high risk for recurrence	At 1 y postresection, then every 3 y
NCCN	Every 3–6 mo for 2 y, then every 6 mo for 3 y	Every 3–6 mo for 2 y, then every 6 mo for 3 y	CT of abdomen/pelvis annually for 3 y	At 1 y postresection, then as clinically indicated

ASCO = American Society of Clinical Oncology; ASCRS = American Society of Colon and Rectal Surgeons; ESMO = European Society for Medical Oncology; NCCN = National Comprehensive Cancer Network; Abd = abdomen; NR = not recommended.

Current Standards In Canada

	Hx & Px	Colonoscopy	CEA	Liver Imaging	CXR
BC	q3m x 3yrs then q6m x 2yrs	Within 12m post-op then q3-6yrs	q3m x 3yrs then q6m x 2yrs	q6m x 3 yrs then annually x 2 yrs (CT)	Q6-12m x 5 yrs
Alberta	q3m x 3yrs then q6m x 2yrs	Within 12m post-op then q3-5yrs	q3m x 3yrs	CT abdo/pelvis 1-2 yrs post-op	Not routine
Sask	q6m x 3yrs	Within 12m post-op then q3-5yrs	q3m x 2yrs	Not routine	Not routine
Manitoba	q3m x 3yrs then q6m x 2yrs	Wi op			
Ontario	q6m x 3yrs then annually x 3yrs	Wi op			l x
Nova Scotia	q3m x 2yrs then q6m x 3yrs	Wi op			

4/10 Provinces and Territories – No Guideline

BCCA Recommendations

Follow Up	Year 1, 2, 3	Year 4, 5
Physician Visits* *Complete History & Physical including Rectal Exam*	**Every 3 months**	**Every 6 months**
Bloodwork* *Carcinoembryonic antigen (CEA)**	**Every 3 months**	**Every 6 months**
Liver Imaging* *CT Abdomen/Ultrasound*	**Every 6 months**	**Annually**
Chest X-Ray*	**Annually**	**Annually**
Colonoscopy*	**End of Year 1** **Then every 3 – 5 years (if no polyps)**	
Monitoring* *Long-term Toxicities of Chemotherapy*	**No specific monitoring required**	

How are we doing?

- Giordano, Tech Coloproct 2006
  - Survey of 582 CR Surgeons in North America
    - Colonoscopy/Clinical Exam performed well
    - <30% Liver Imaging

Test	Surgeons, n (%)	
Clinical history and physical examination	582	(100)
Carcinoembryonic antigen	570	(98)
Complete blood count	533	(92)
Liver function tests (LFT)	300	(52)
Fecal Occult Blood Test (FOBT)	156	(27)
Proctosigmoidoscopy	173	(30)
Full colonoscopy	582	(100)
Annually	81	
First 2 years	156	
First and fourth years	283	
Once in 5 years	62	
Liver ultrasound	15	(3)
Liver CT	143	(25)
Chest radiography	358	(60)
Bone scan	0	(0)
Position emission tomography	0	(0)

How are we doing?

- Parsons, JACS, 2012
  - Influence of >12LN evaluation in Stage III colon cancer follow up care
  - SEER Data – 1992-2007
    - N = 17,906 pts >66years Stage III Colon CA

Surveillance colonoscopy					
Colonoscopy within 3 y of surgical treatment, all patients	3,956	47.2	4,729	49.6	0.002
Colonoscopy within 3 y of surgical treatment, 3-y survivors	3,074 of 4,406	69.8	3,852 of 5,610	68.7	0.20
CT scan					
CT scan of the chest or abdomen within 3 y of surgical treatment, all patients	5,420	64.7	6,661	69.4	<0.001
CT scan of the chest or abdomen within 3 y of surgical treatment, 3-y survivors	3,064 of 4,406	69.5	4,058 of 5,610	72.3	0.002
CEA test					
Any CEA test within 3 years of surgical treatment, all patients	5,757	68.8	7,101	74.5	<0.001
Any CEA test within 3 y of surgical treatment, 3-y survivors	3,751 of 4,406	85.1	4,945 of 5,610	88.2	<0.001

Conclusions

- Follow up for patients with Stage II/III CRC reduces mortality
- Follow up for CRC should include
  - Clinical Examination
  - Colonoscopy
  - CEA
  - Liver Imaging
  - Chest Imaging
- Strategies to ensure adherence to follow up are needed

Questions?