

Surgery for Gastric Carcinoma and Premalignant Lesions



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BC Surgical Oncology Network
Upper GI and Hepatobiliary Cancer Update
Vancouver, BC **October 23, 2010**

Gastric Cancer – Incidence Worldwide

Age standardized incidence per 100,000

2003

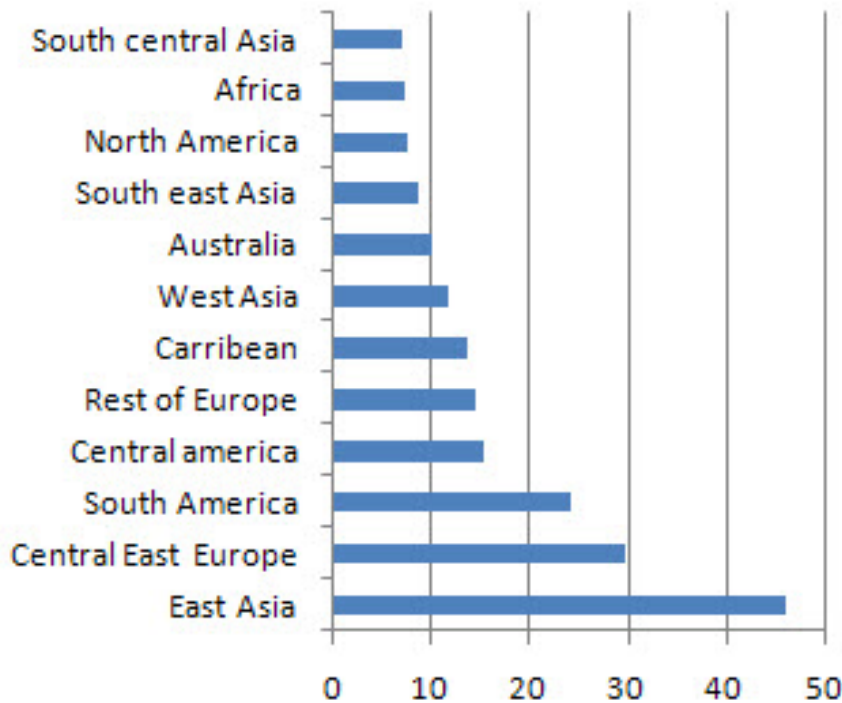


Fig. 5.23 Global incidence of stomach cancer in men; the highest rates occur in Eastern Asia, South America and Eastern Europe.

Data adapted from GLOBOCAN, International Agency for research on Cancer

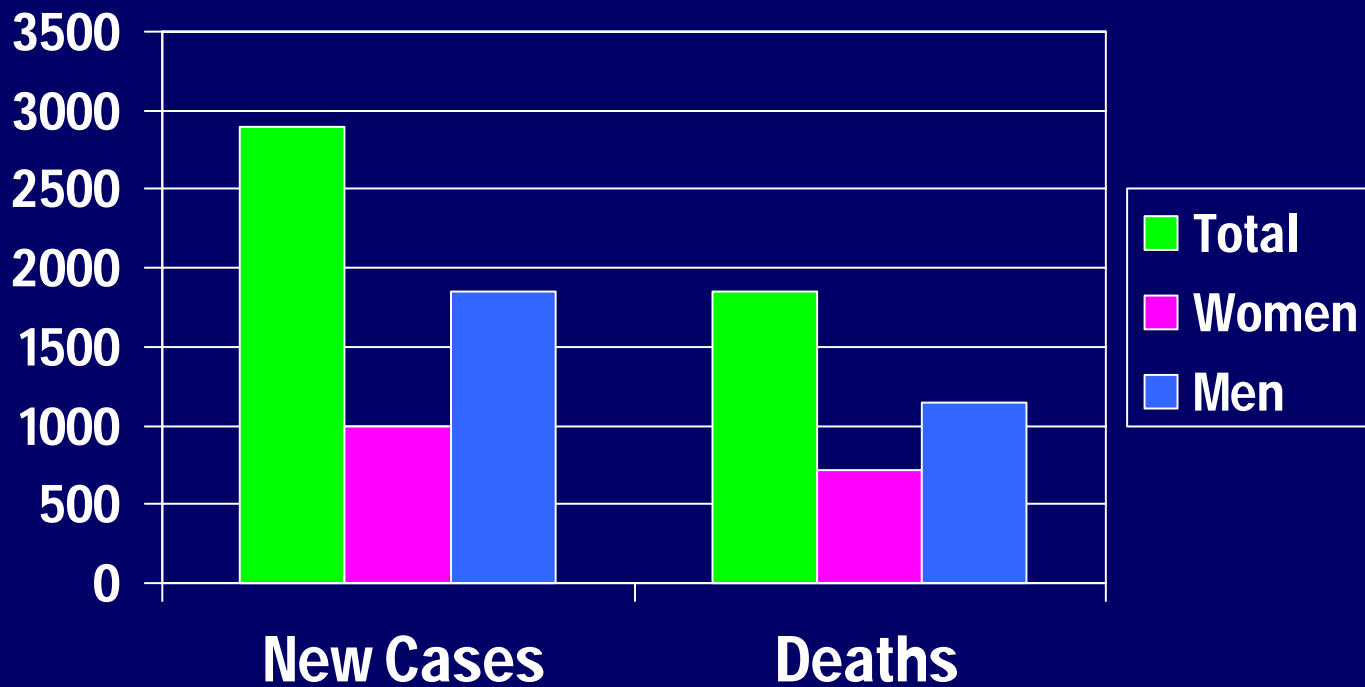
World cancer report

By Bernard W. Stewart, Paul Kleihues, International Agency for Research on Ca

globally: 4th cancer, 2nd cancer-related death

Gastric Cancer in Canada

New Cases and Deaths, 2008



NCIC, 2008

Surgery of Gastric Cancer and Premalignant Lesions

Overview

Evidence

- Investigation & Clinical staging
- Extent of resection/LN dissection
- Surgical issues re: Adjuvant/Neoadjuvant Rx

Issues

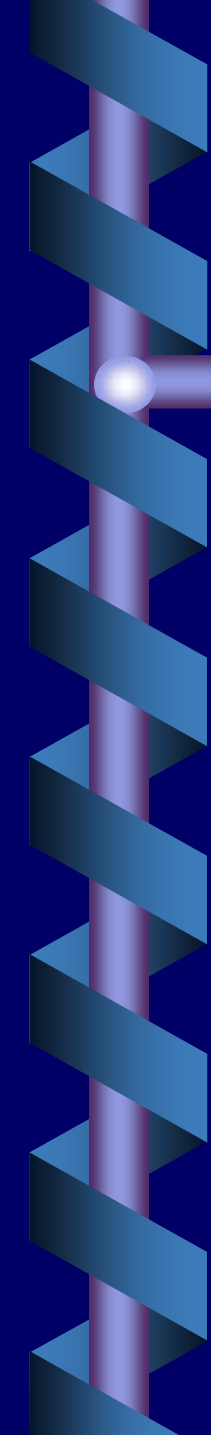
- Premalignant lesions
- Early Gastric Cancer
- Familial DGC
- Quality of resection
 - Laparoscopic gastrectomy
- Advanced GC management

Evaluation & Clinical Staging

Case of Mr. A. H.

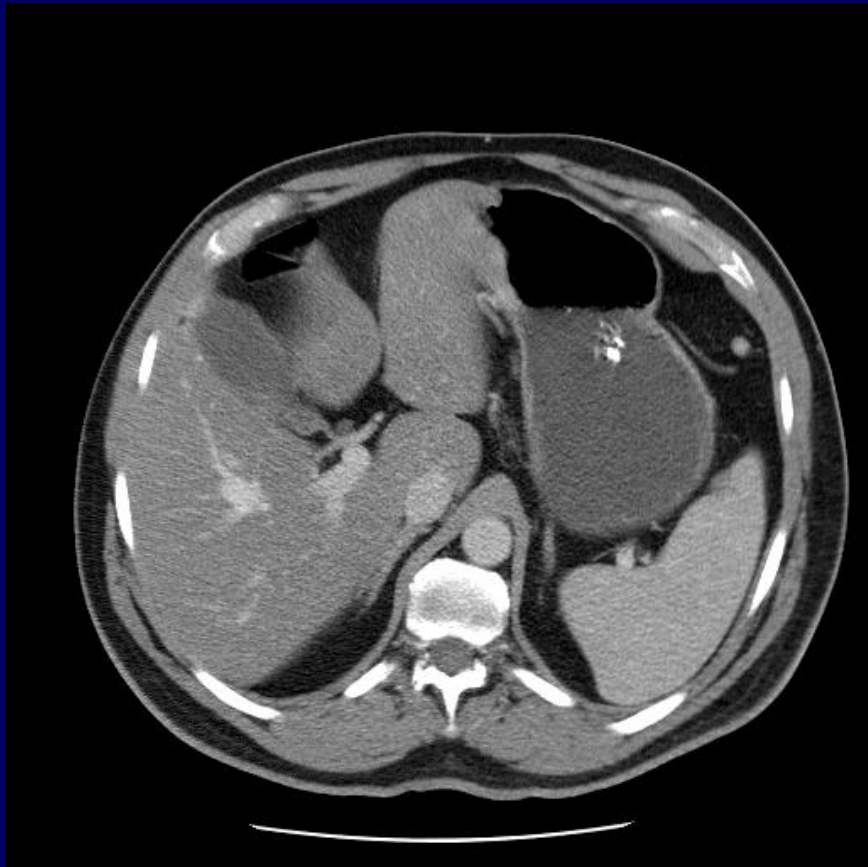
65 year old healthy man
1 year of dyspepsia, anemia
Endoscopy: antral tumour
path: invasive adenoCa,
diffuse type





After UGI scope and Bx, my routine pretreatment workup of gastric cancer would be:

- a. **CT-AP, CXR**
- b. **CT-AP, CXR, laparoscopy**
- c. **CT-AP, CXR, laparoscopy, EUS**
- d. **CT-AP, CXR, laparoscopy, EUS, PET**



Improvements in Staging of Gastric Cancer

Laparoscopy

staging accuracy $\geq 90\%$

resectability accuracy $\approx 90\%$

altered treatment plan in 20- 30%

Sem Oncol 1996; 3: 347

Ann Surg 1997; 3: 262

Ann R Coll Surg Engl 1998; 80: 400

Current Surgery 2005; 62: 35

Improvements in Staging of Gastric Cancer

Endoscopic Ultrasound

T stage: accuracy \approx 80%

N stage: accuracy \approx 75%

Resectability:

sensitivity \approx 90%

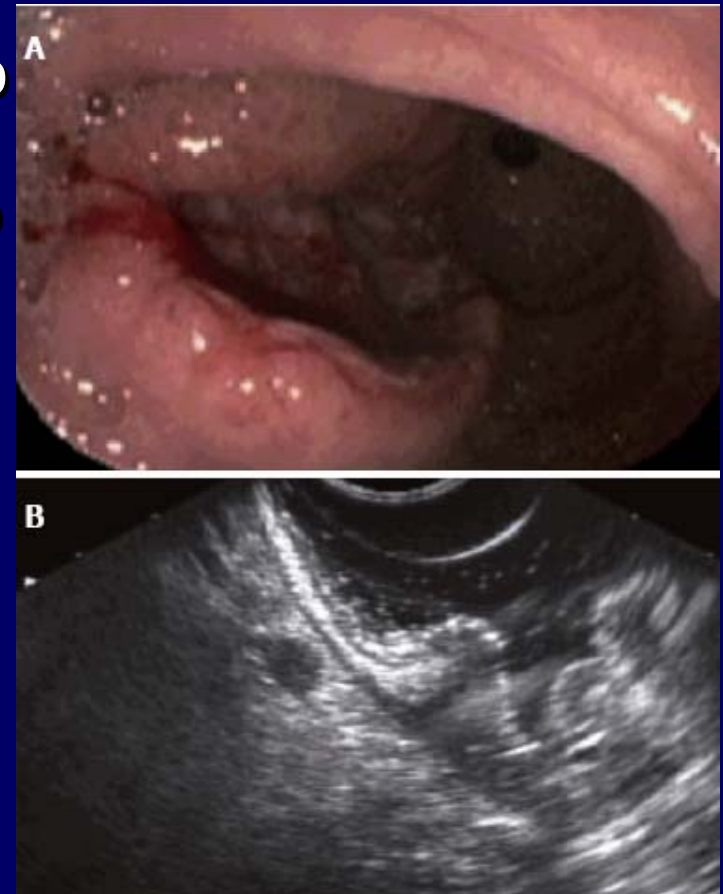
specificity \approx 85%

Surg Endosc 2000; 14: 951

Tumori 2000; 86: 139

Surg Endosc 2006; 20: 559

World J Gastroenterol 2006; 12: 43



Improvements in Staging of Gastric Cancer

Tsendsuren T *et al.* EUS in TNM staging of gastric cancer

45

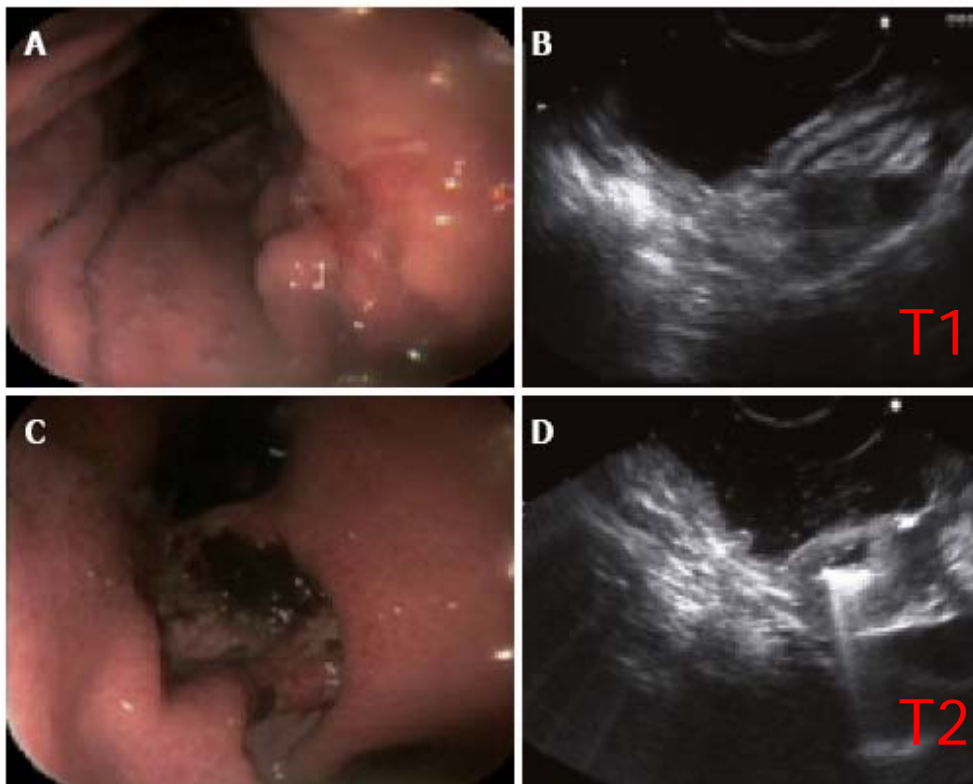
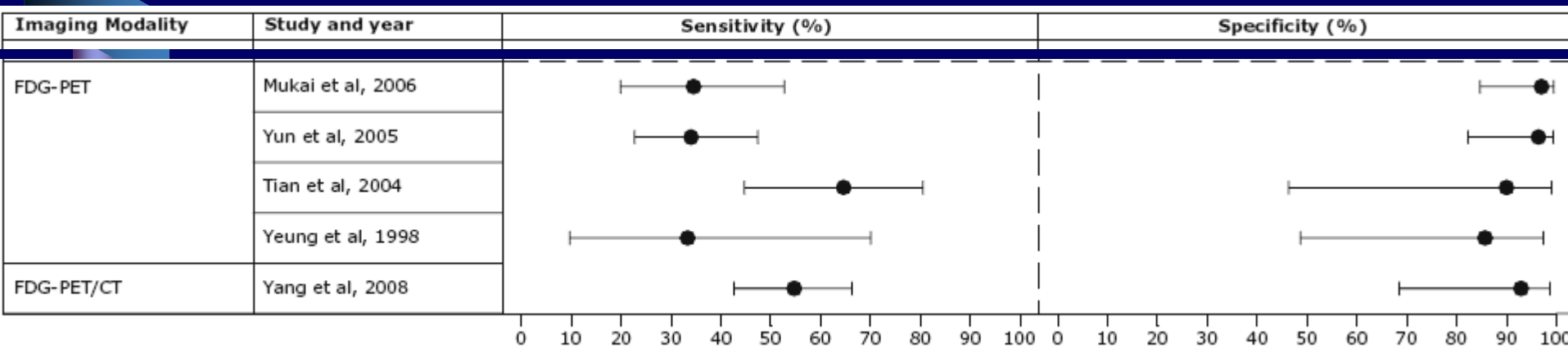


Figure 1 Early and advanced gastric cancer cases. **A:** Endoscopic view of superficial depressed type of early gastric cancer; **B:** EUS image shows cancer invasion of 1st and 2nd (mucosal) layers of gastric wall, while 3rd (submucosal) layer is clear (T1 category). Histopathological findings of the surgically resected specimen corresponded with the EUS findings; **C:** Endoscopic view of advanced Borrmann II type of gastric cancer; **D:** EUS images show disruption of 1-4 layers of the gastric wall with hypochoic cancer tissue, but 5th (serosal) layer is not involved (T2 category).

5 layers of the wall

Staging of Gastric Cancer

FDG-PET and LN Status: Systematic Review



Staging of Gastric Cancer

FDG-PET

Approx 30% of GC are NOT PET avid

**In those which are, prognosis depends on
PET response to preop chemotherapy**

**Prognosis of PET non avid GC is same as
non-responders**

Ott et al., Gastric Cancer 2008; 11:1-9

Treatment Planning

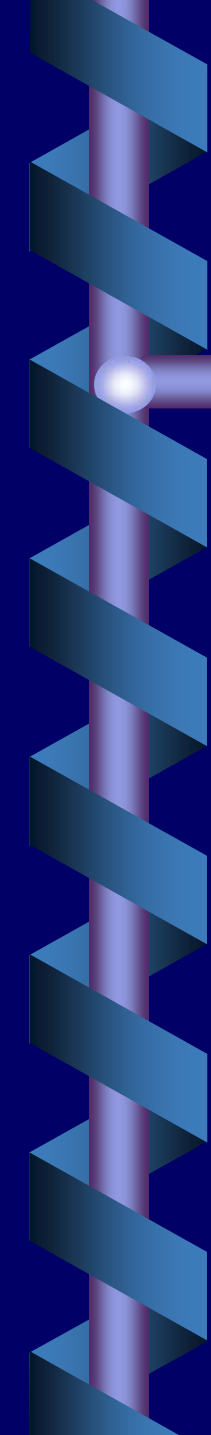
Case of Mr. A. H.

**EUS: T3 N+ (5 enlarged
perigastric nodes)**

Laparoscopy clear

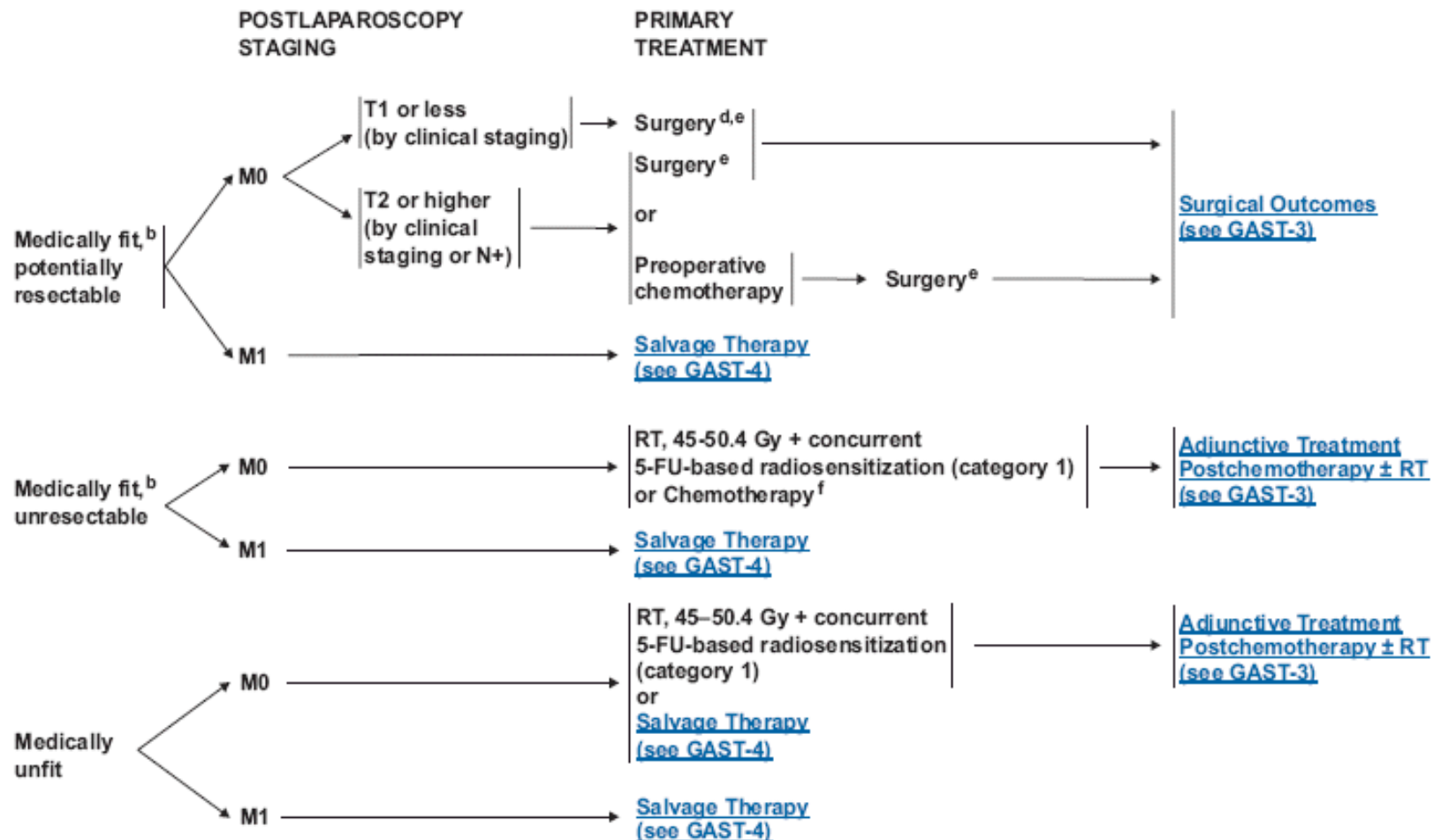
Good performance status





For clinical stage T3N+M0 antral cancer in a fit patient, my next step would be:

- a. **resect**
- b. **3 cycles chemo**
- c. **PET scan**
- d. **chemo + RT**



^bMedically able to tolerate major abdominal surgery.

^dSurgery as primary therapy is appropriate for T1 cancer or actively bleeding cancer, or when postoperative adjuvant therapy is preferred.

^eSee Principles of Surgery (GAST-A).

^fSee Principles of Systemic Therapy (GAST-B).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

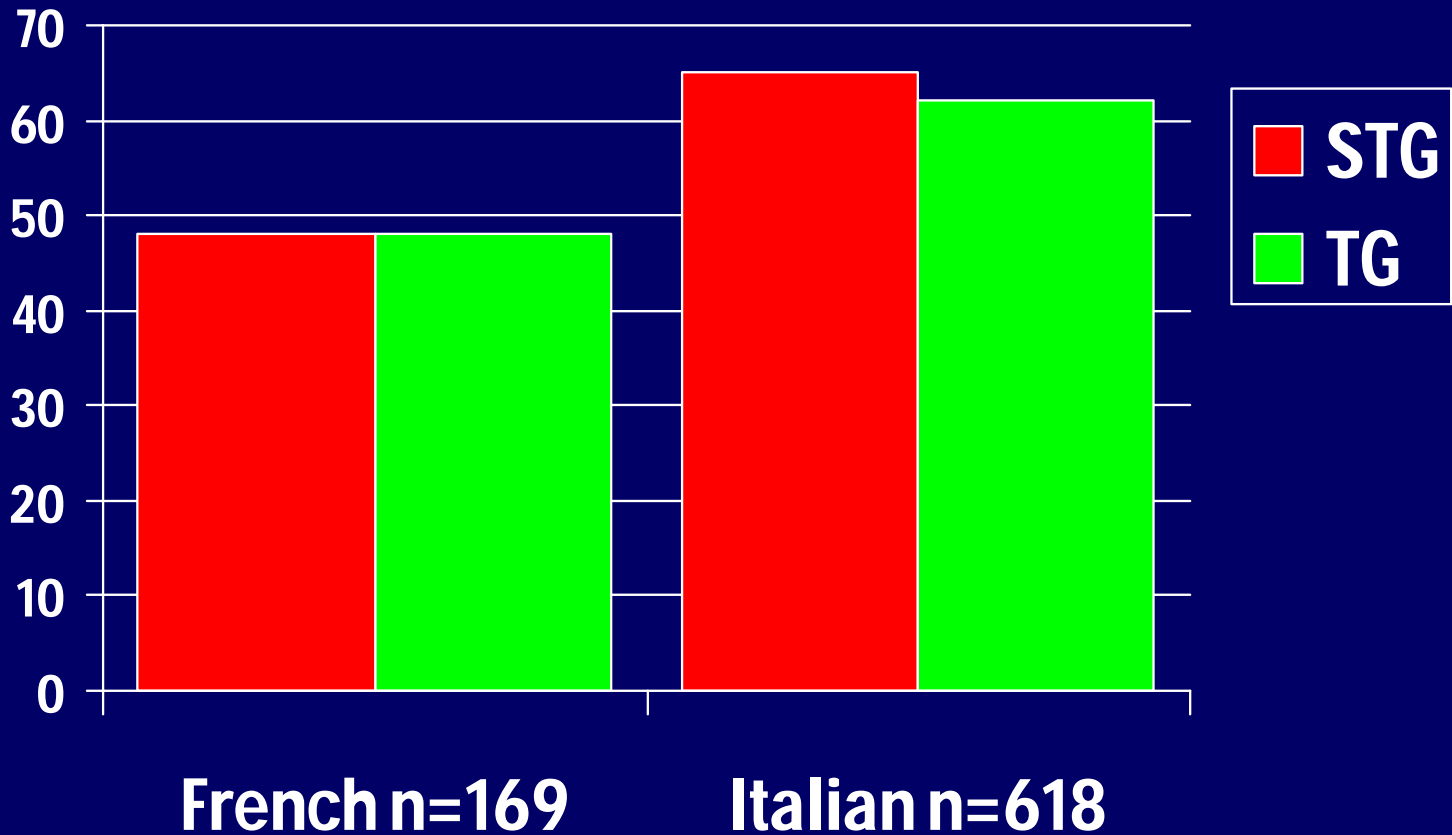


Extent of Resection/Dissection

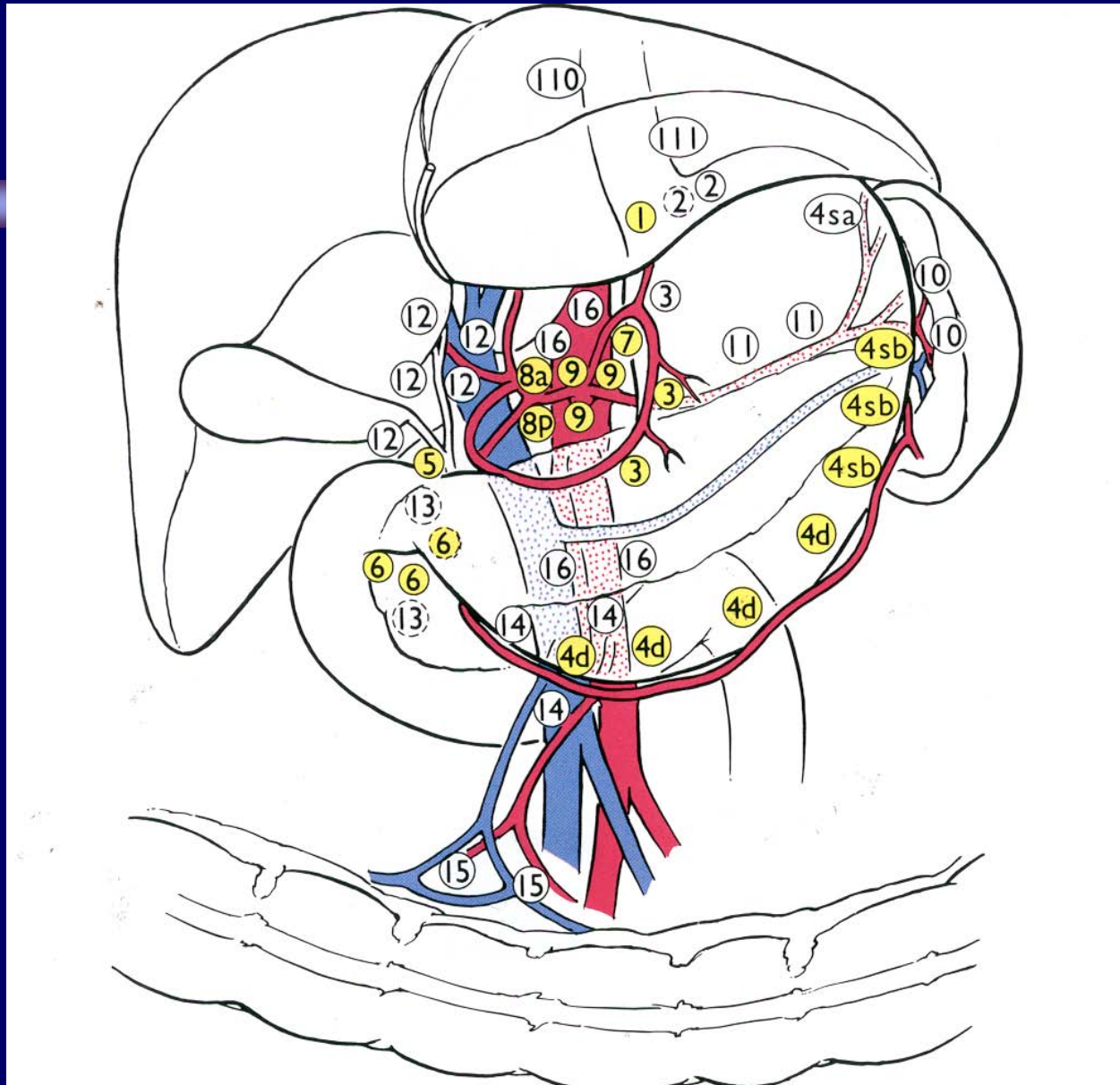
- I. Extent of Gastrectomy
- II. Extent of Lymphadenectomy
- III. Margins

French and Italian RCT Antral Ca TG vs STG: Longterm Survival

overall survival at 5 years

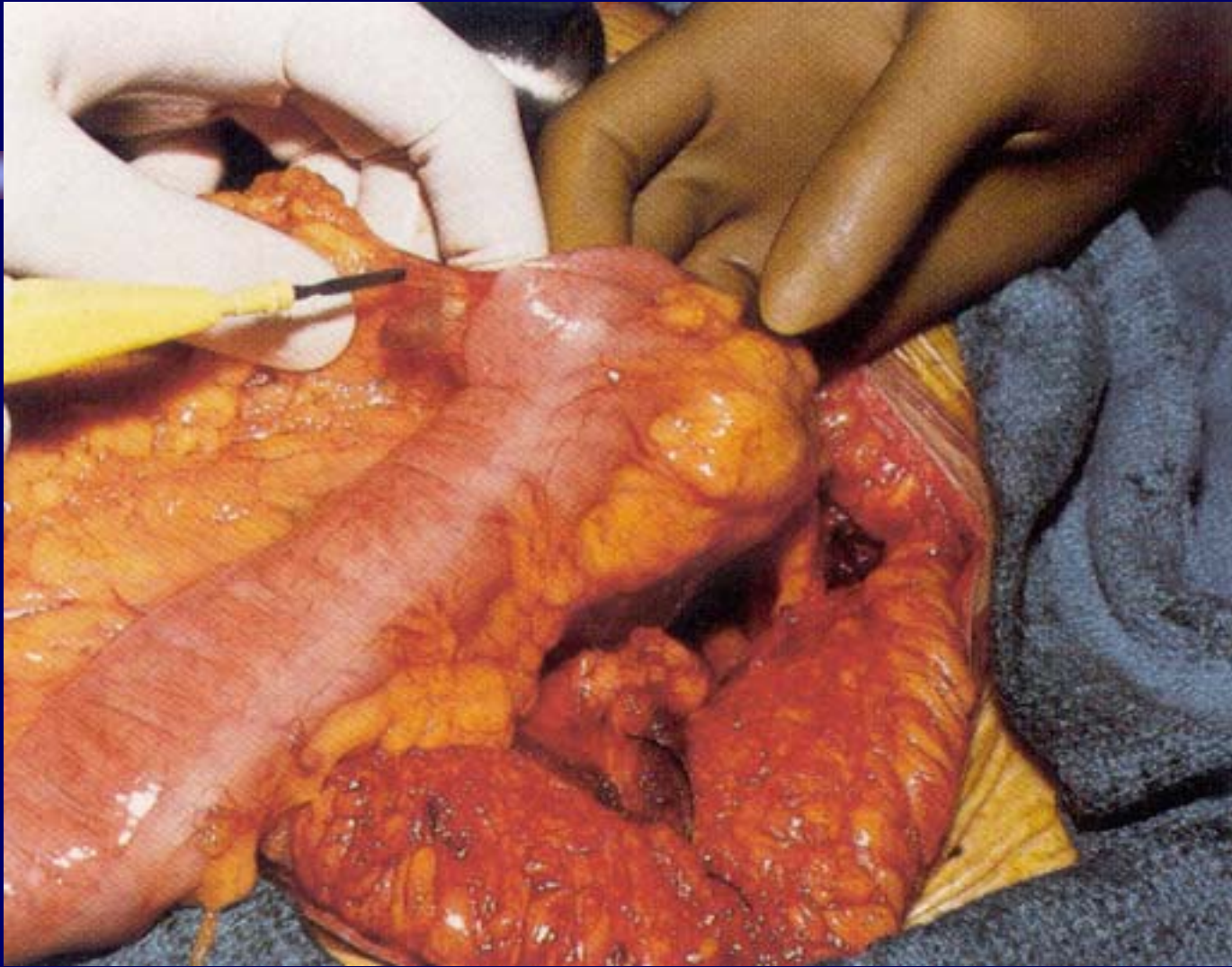


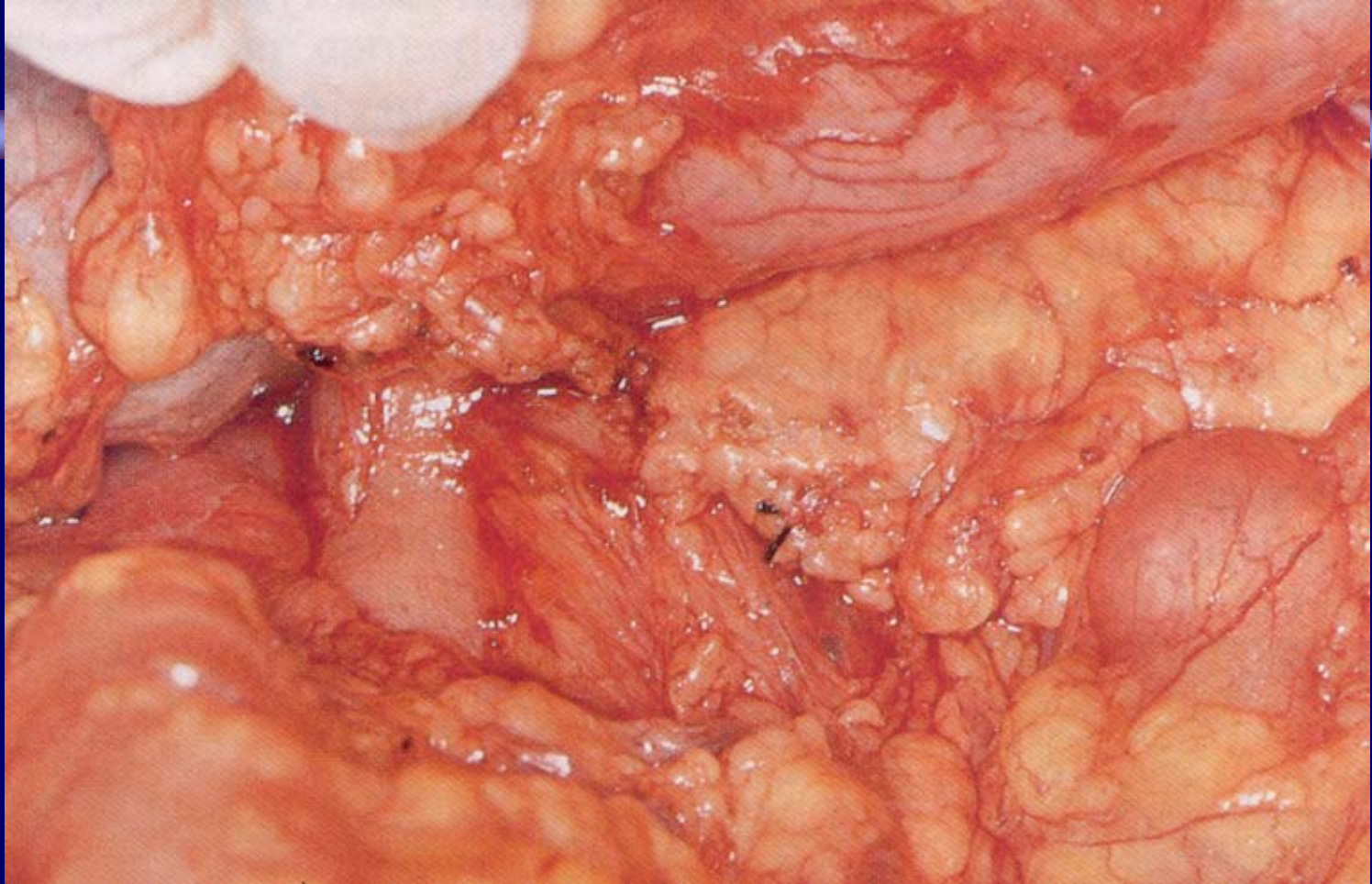
The Great Debate: D1 vs. D2



D1 Dissection

- **Level 1 nodes (perigastric, stations 1 - 6)**
 - right & left cardiac (1 & 2)
 - lesser & greater curve (3 & 4)
 - supra- and infra- pyloric [5 & 6]
- **omentum**

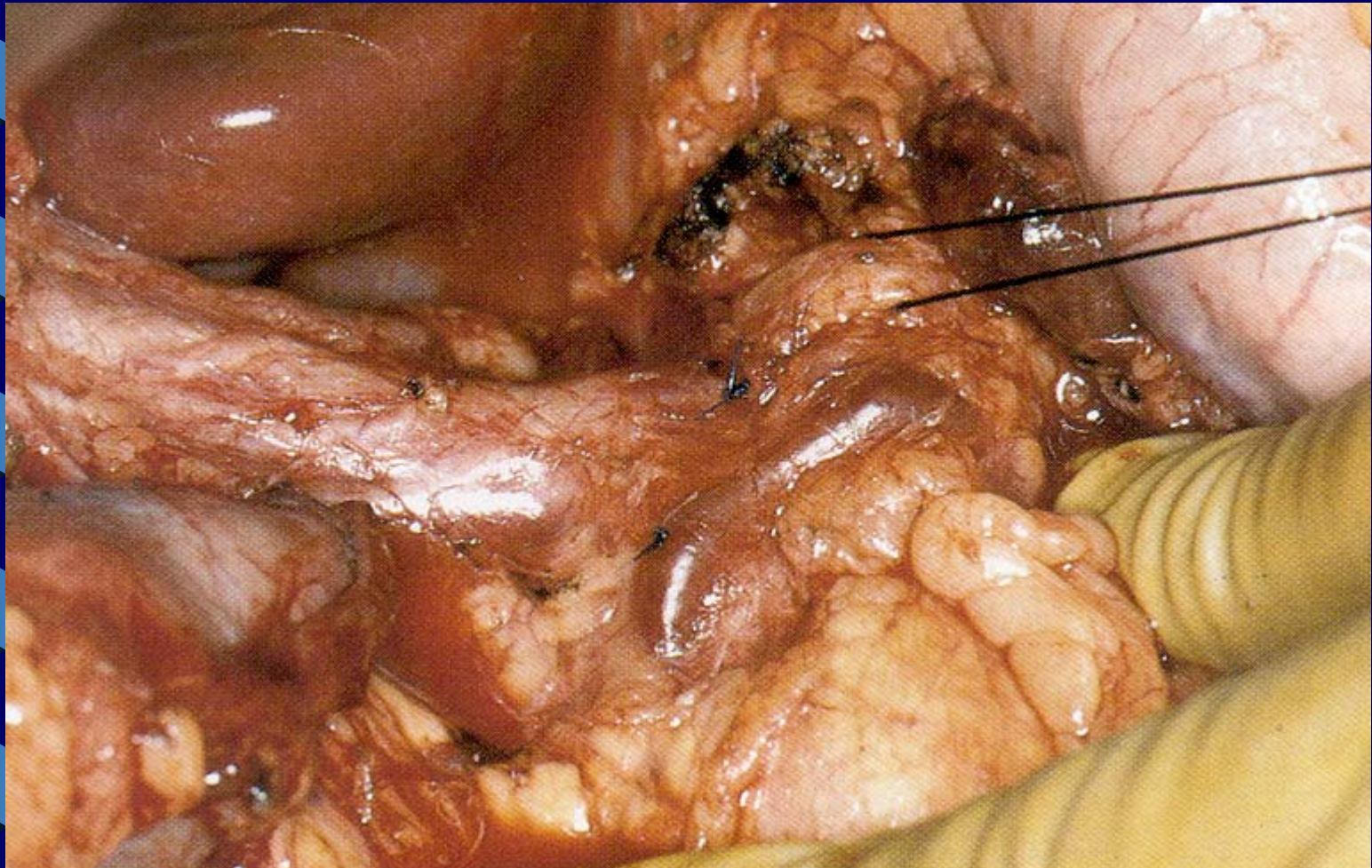




D2 Dissection

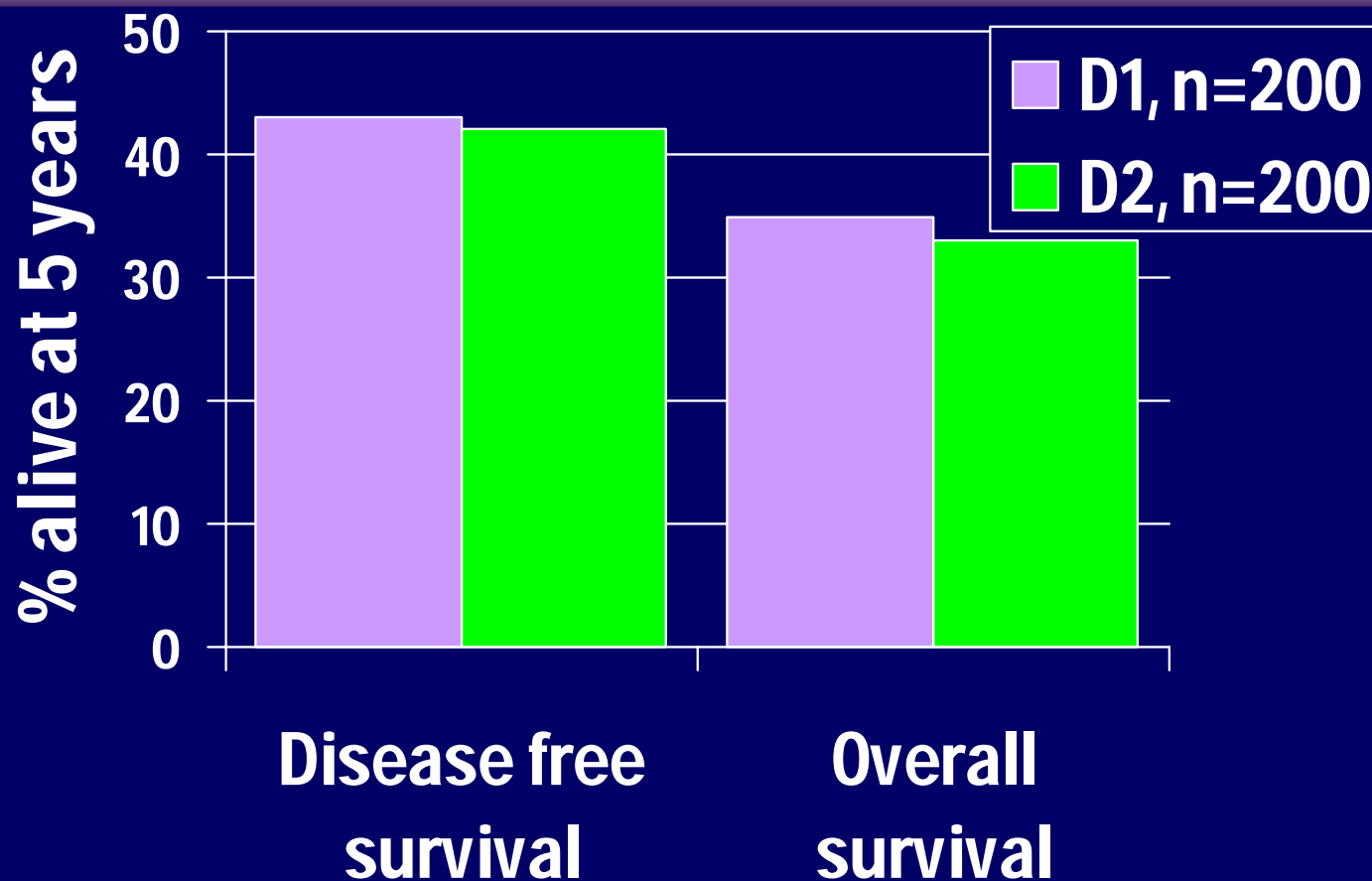
- **Level 1 nodes (perigastric, stations 1 - 6)**
- **Level 2 nodes (intermediate, stations 7 - 9)**
 - **left gastric (7), common hepatic (8), celiac (9)**
- **stations 10 (splenic hilum) and 11 (splenic artery) nodes**
- **omental bursa, anterior leaf of mesocolon**

D2 Dissection for Gastric Cancer



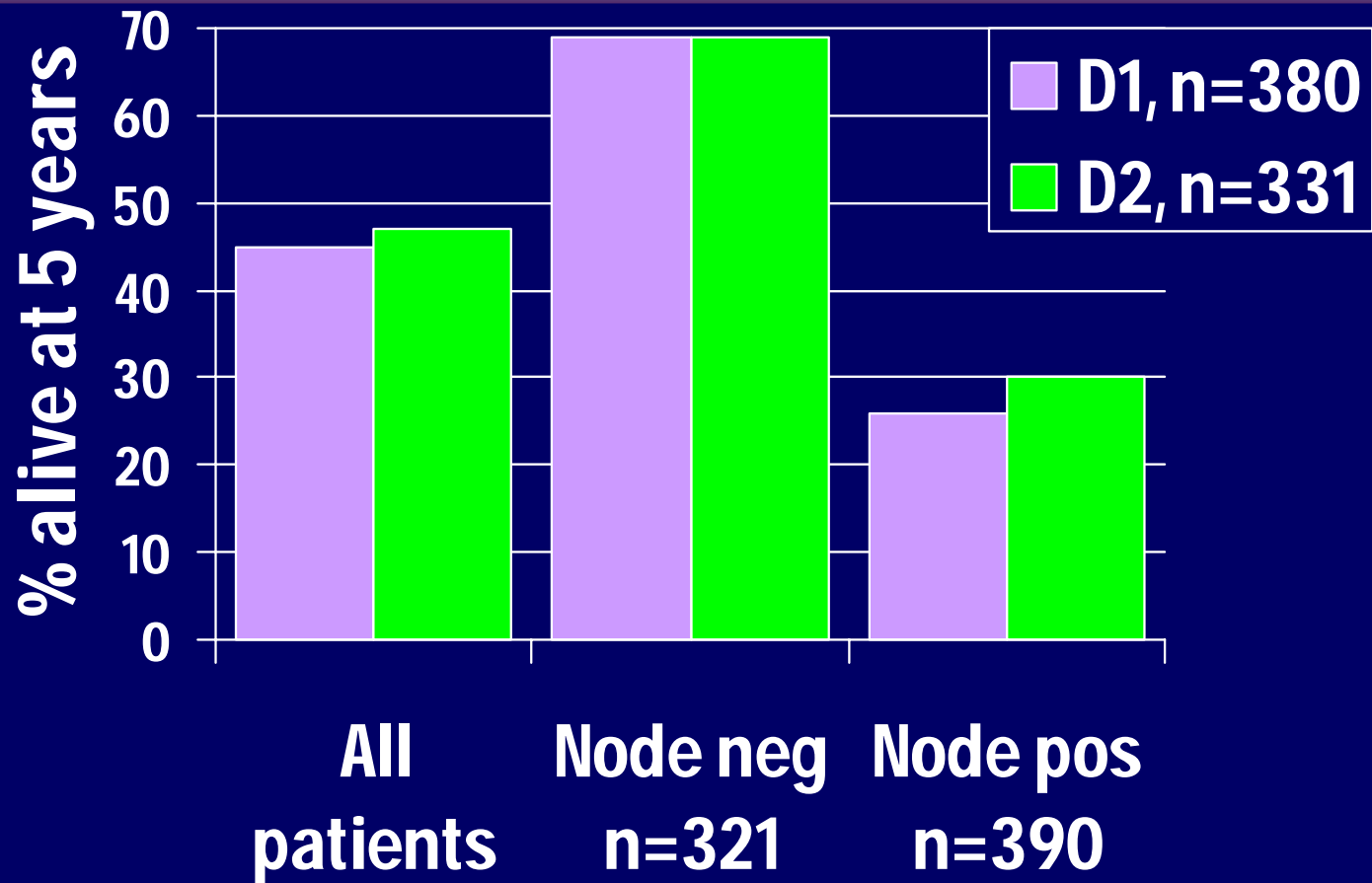
MRC RCT: D1 vs D2 Dissection

Longterm Survival



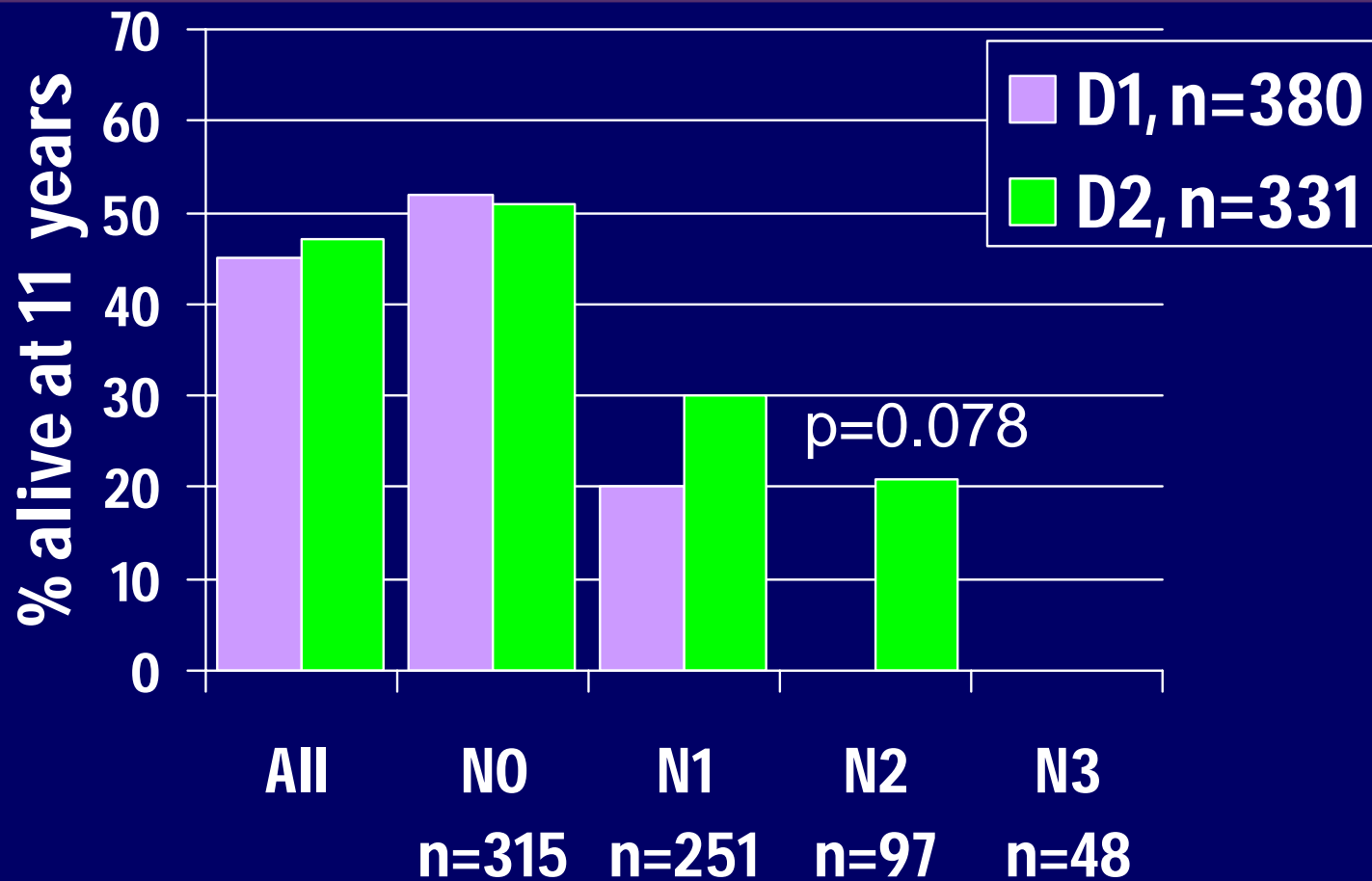
Dutch RCT: D1 vs D2 Dissection

Longterm Survival



Dutch RCT: D1 vs D2 Dissection

Very Longterm Survival

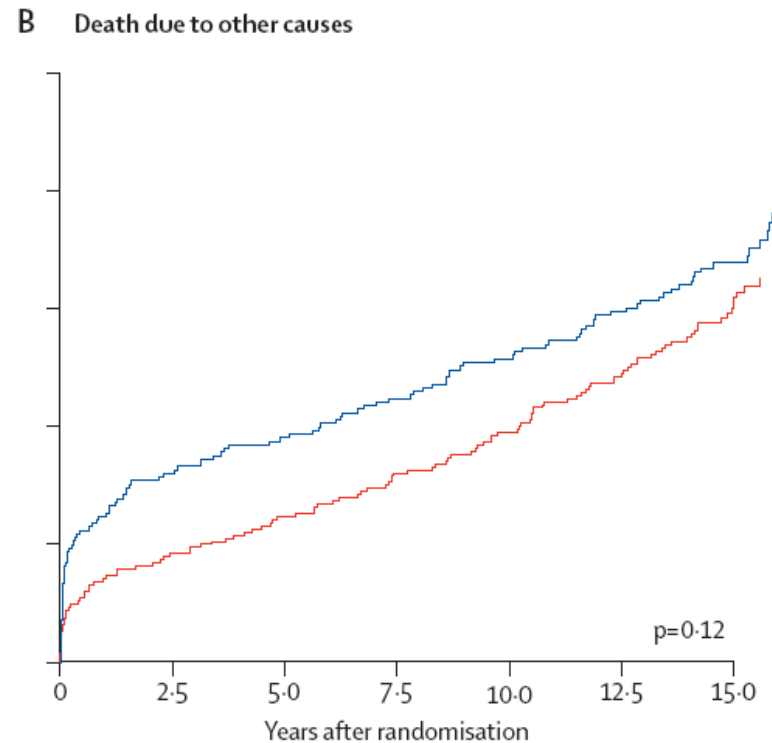
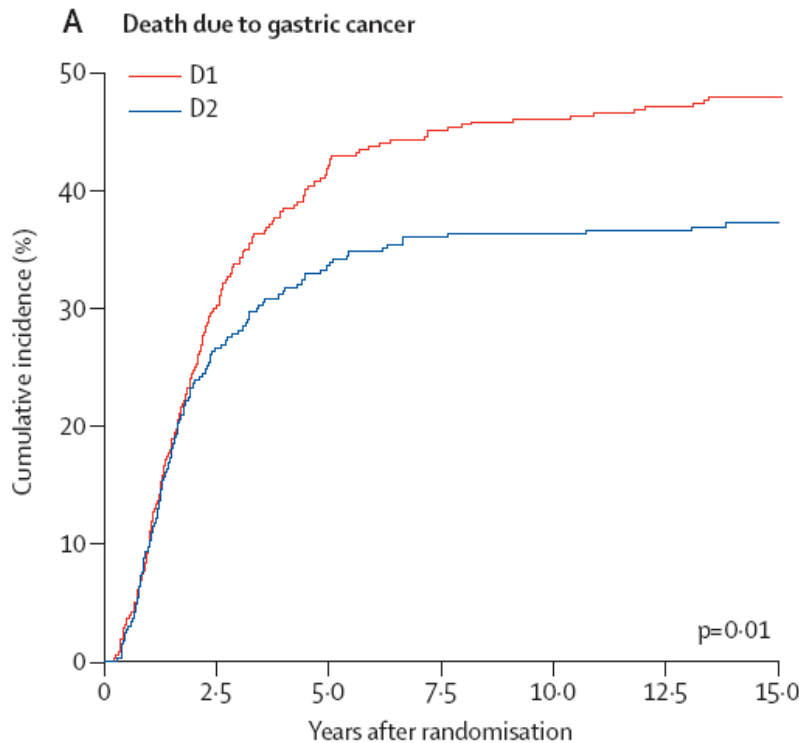


median f/u time = 11 years

J Clin Oncol 2004; 22:2069

Dutch RCT: D1 vs D2 Dissection

Very Very Longterm Survival



Number at risk

D1	380	231	174	149	132	108	47
D2	331	191	158	138	125	110	70

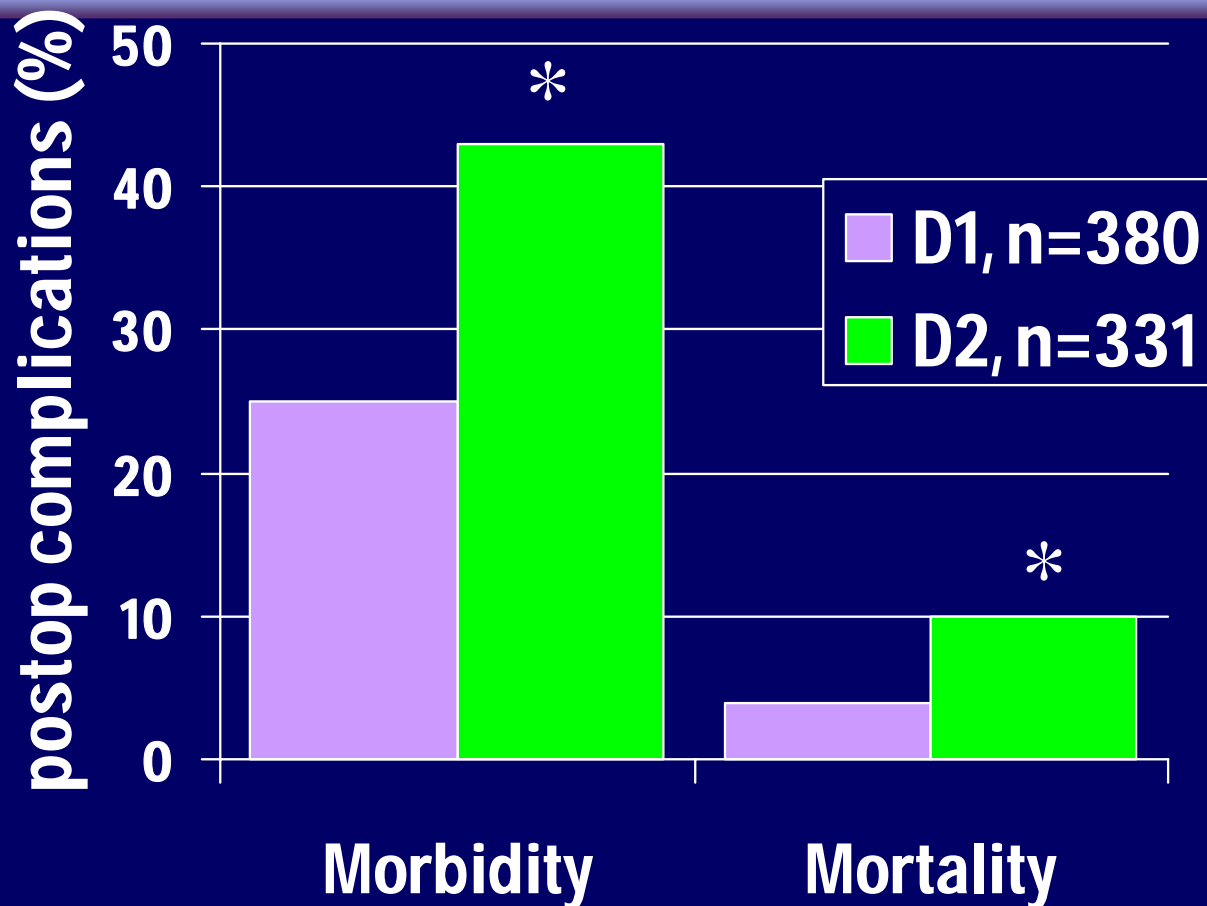
380	231	174	149	132	108	47
331	191	158	138	125	110	70

median f/u time = 15 years

Lancet Oncol 2010; 11: 439

Dutch RCT: D1 vs D2 Dissection

Postoperative M & M Rates

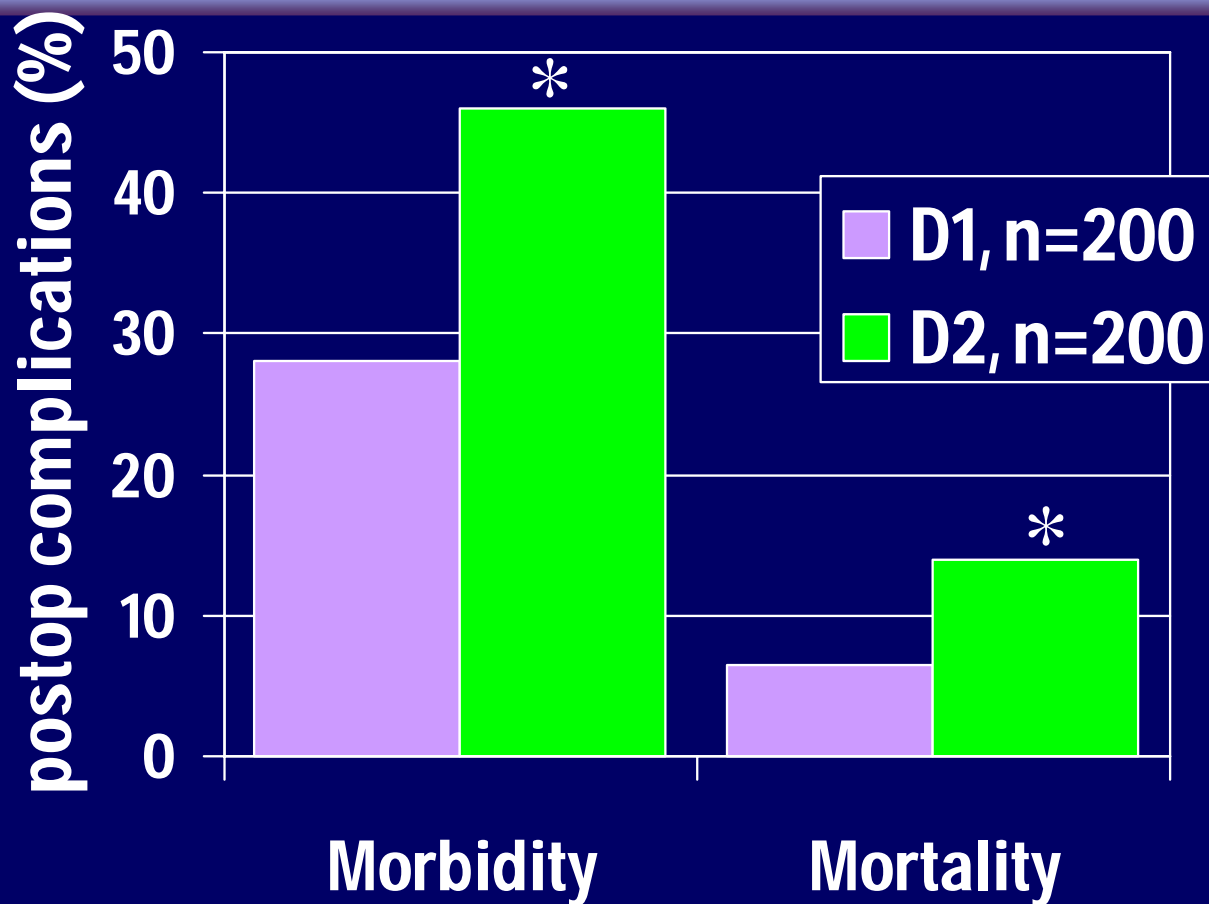


* $p < 0.004$

NEJM 1999; 340:908

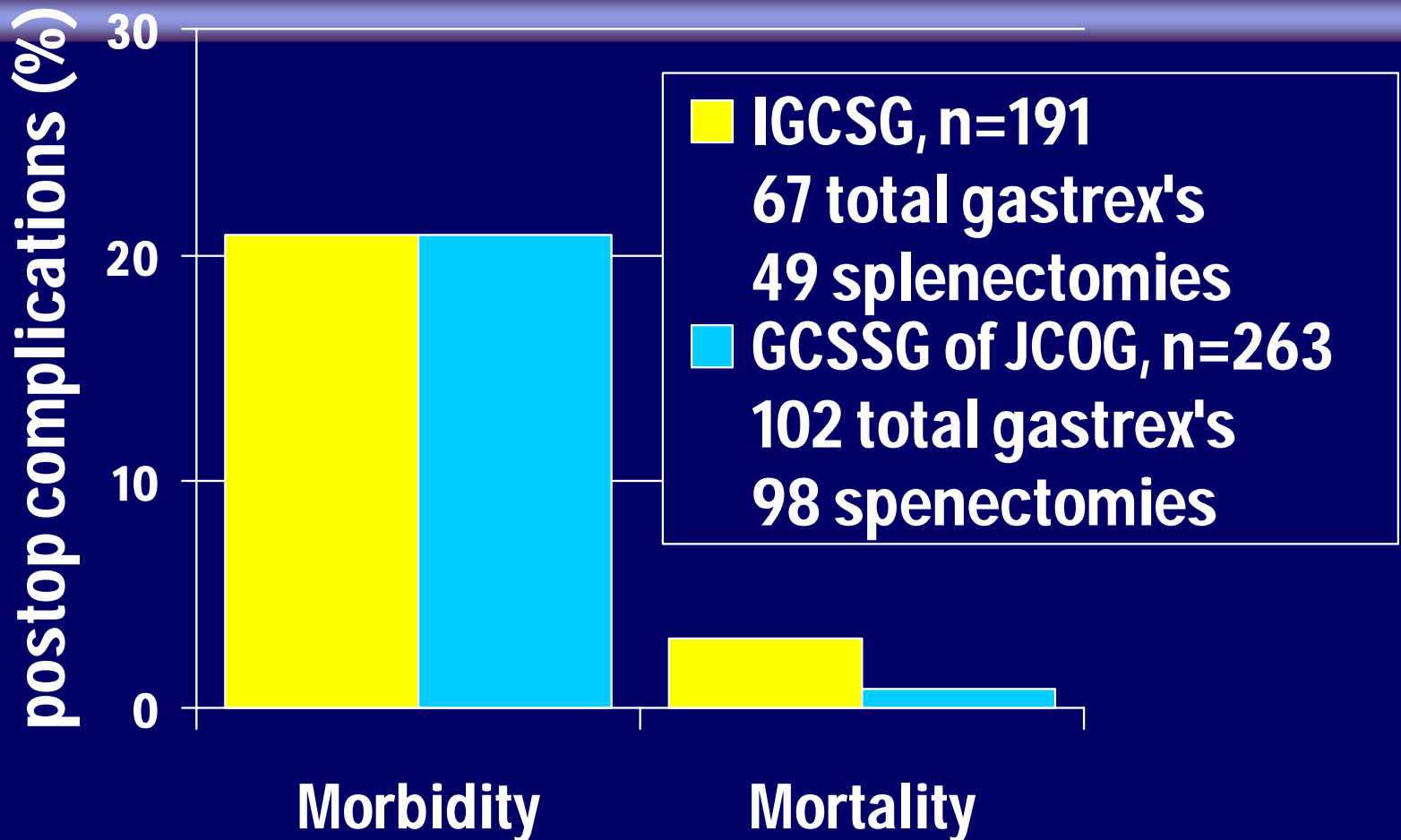
MRC RCT: D1 vs D2 Dissection

Postoperative M & M Rates



* $p < 0.04$

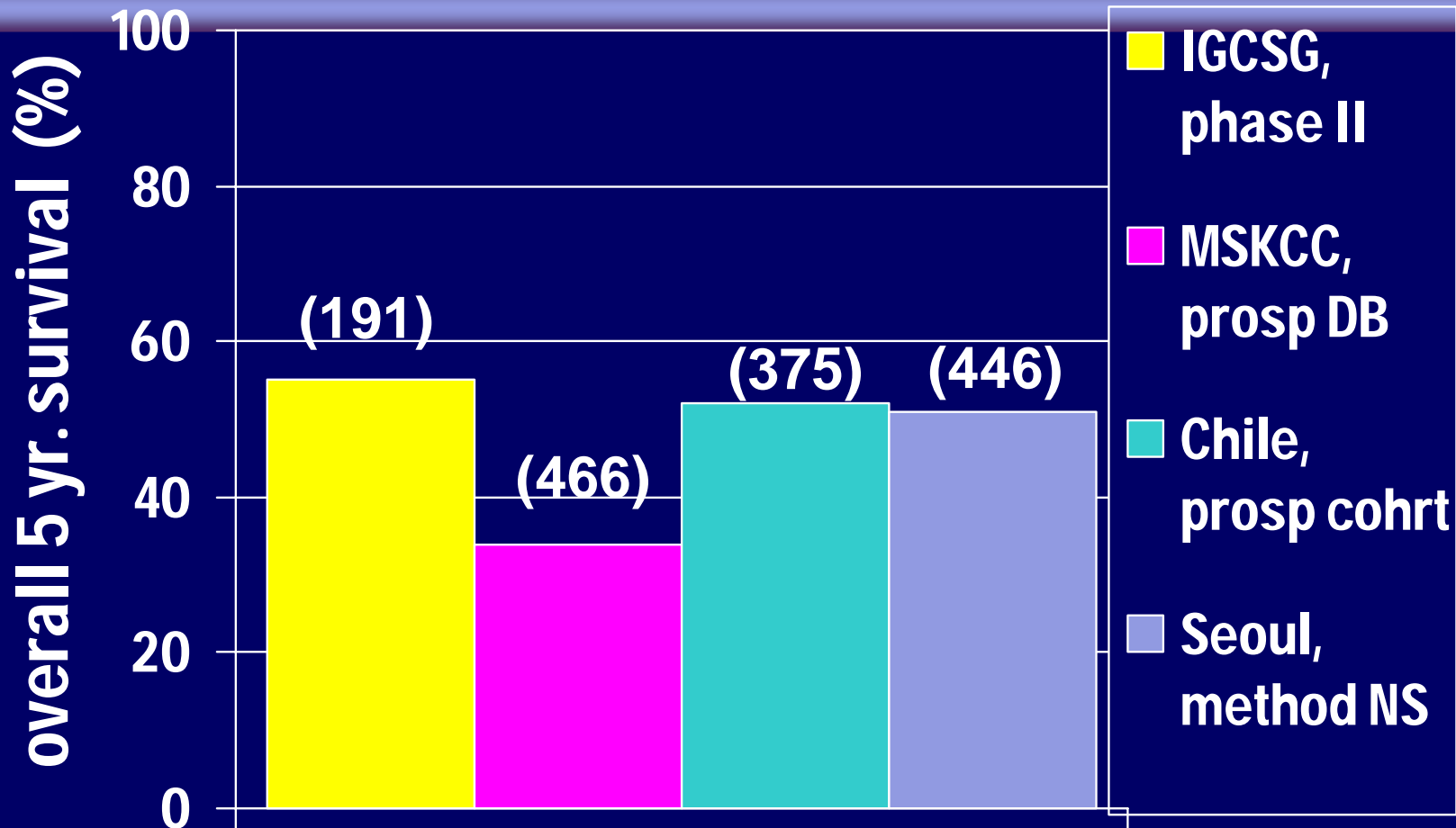
"Standard" D2 Dissection: Japanese RCT & Italian multicentre phase II trial



Br J Cancer 2004; 90: 1727

J Clin Oncol 2004; 22: 2767

Survival after "Standard" D2 Dissection



Br J Cancer 2004; 90: 1727
Gastrointest Surg 1999; 3: 24

Dig Surg 1999; 16: 385
Int J Radiat Oncol Biol Phys 2005; 63: 1279

Extent of Lymphadenectomy: Cochrane Review – D2

- more dangerous when
 - spleen/panc resected
 - surgeon inexperienced
- studies limited by
 - learning curves, poor compliance
 - contamination
- no PROVEN survival benefit
- MAY benefit
 - T3+
 - Stage II & IIIa

Taiwanese: D1 vs D3 Dissection

- 1993-1999
- 335 patients registered
- 221 eligible & randomized
- 64 did “not fit” histologically
- 156 treated “per protocol”
- Median f/u for 110 survivors = 94.5 mos.
- Per protocol 5 yr. OS = 51% in D3 (n=76) and 45% in D1 (n=80)
- “D3 or not D3...that is not the question”

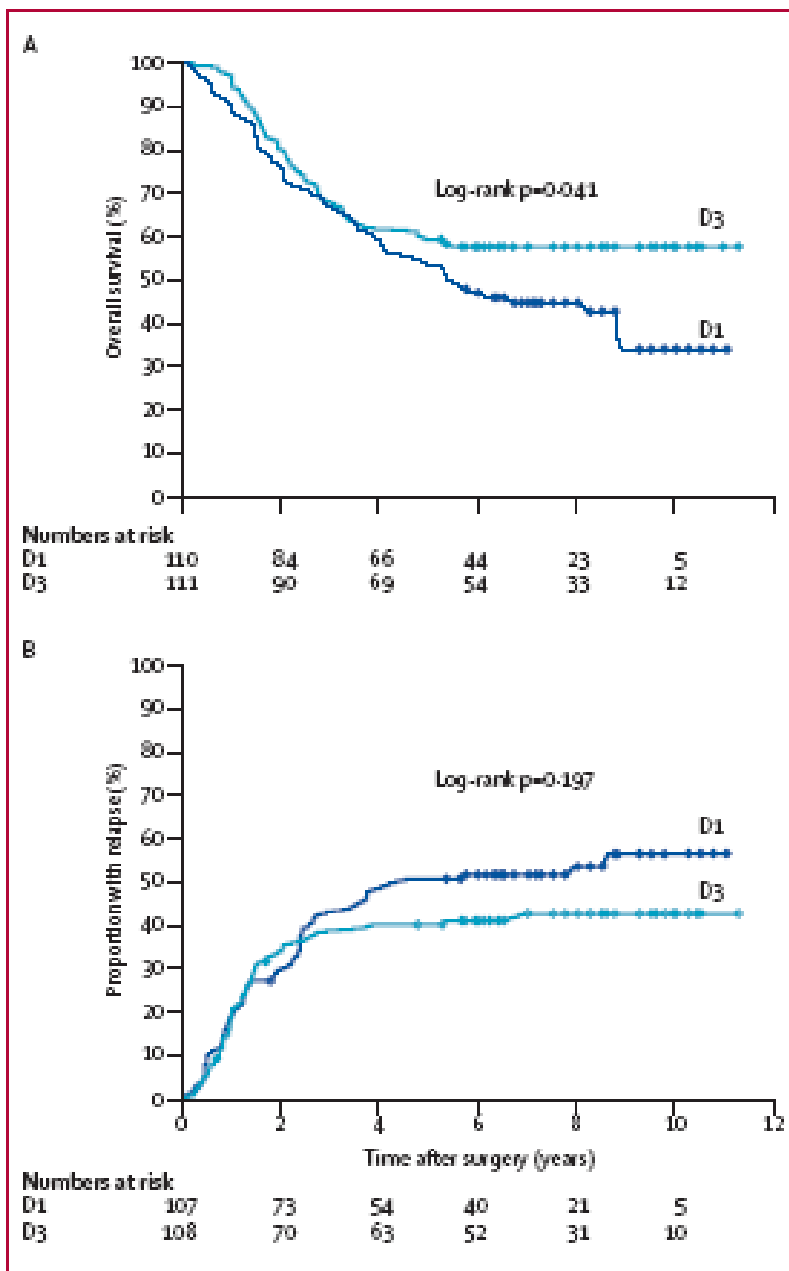


Figure 2: (A) Overall survival in intention-to-treat population (n=221). (B) Proportion of patients who relapsed during follow-up for patients with R0 resection (n=215)

Japanese: D2 vs D2+PANDissection

- Japan Clinical Oncology Group
- 1995-2001
- 24 hospitals
- D2 n=263
- D2 + PAND n=260
- no difference in recurrence-free or overall survival

Sasako et al., NEJM 2008, 359:453-62

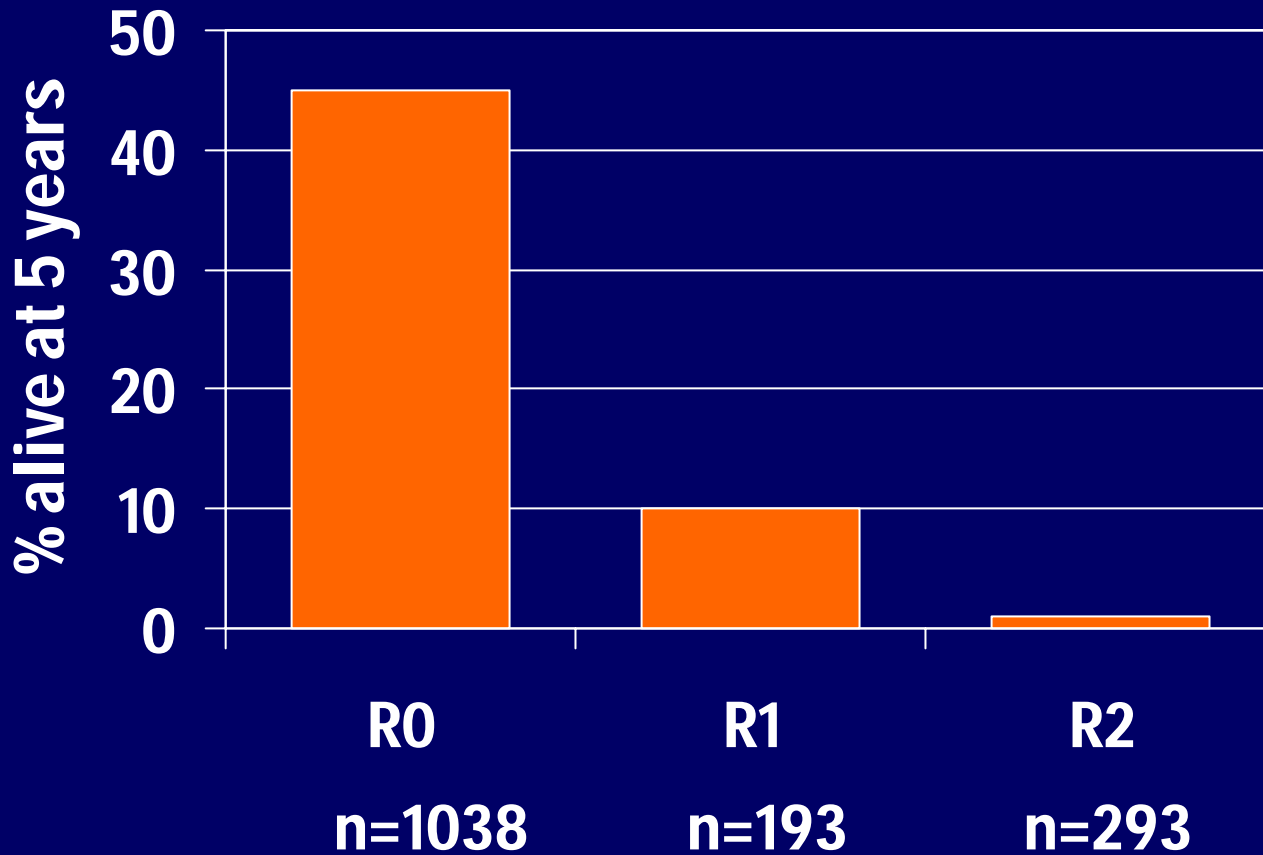


Extent of Lymphadenectomy: **Current Recommendations**

- obtain adequate # of nodes for accurate staging
- D2: -not harmful in expert hands
-more nodes = better staging
-direct survival benefit unclear
- D1+/D1.5 should be the minimum standard

Margin status – should you check?

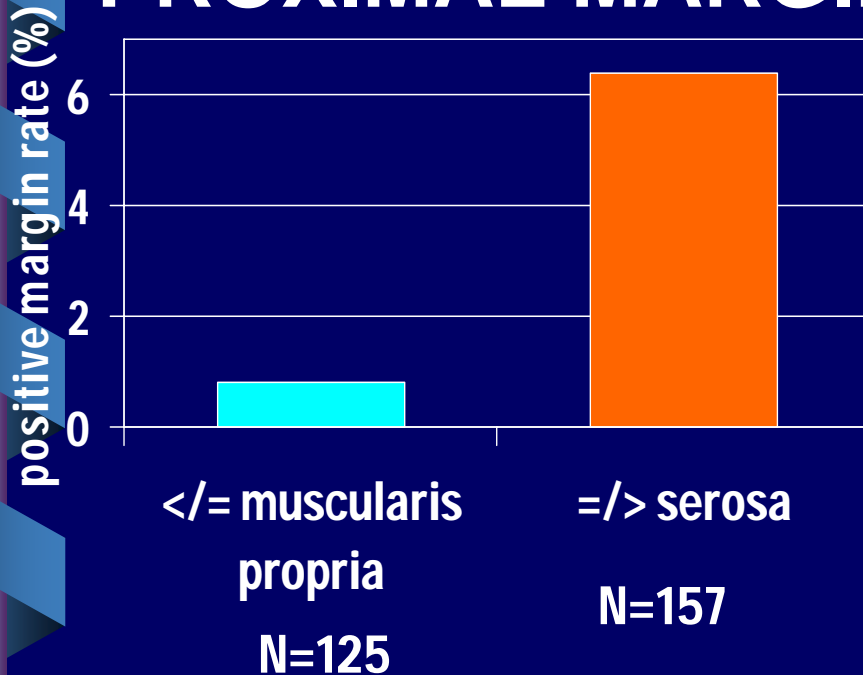
R Status Determines Prognosis



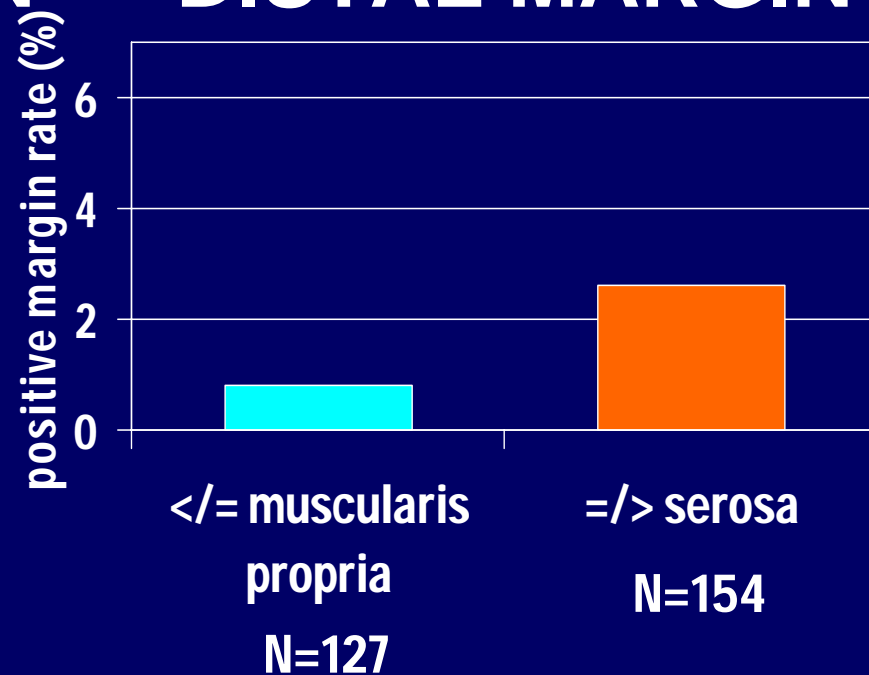
M. Karpeh, MSKCC, SSO 2002

Incidence of Positive Margins \propto Tumor Depth

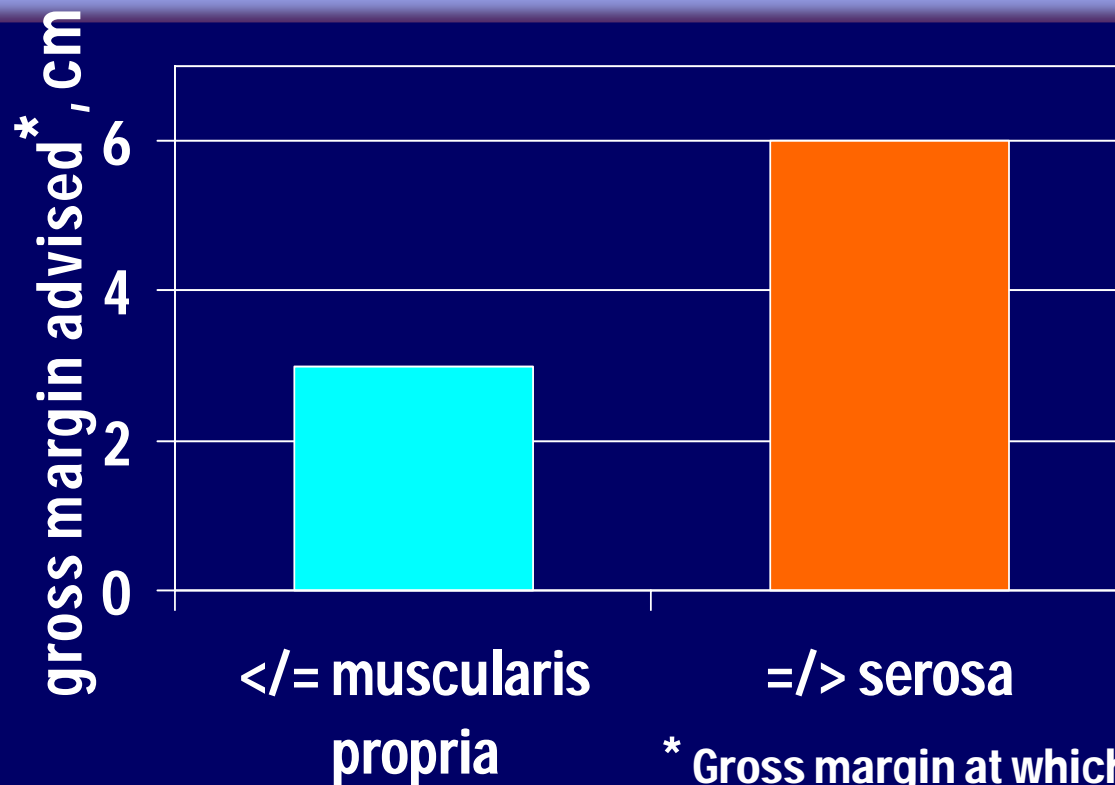
PROXIMAL MARGIN



DISTAL MARGIN



"Safe" Gross Margin \propto Tumor Depth



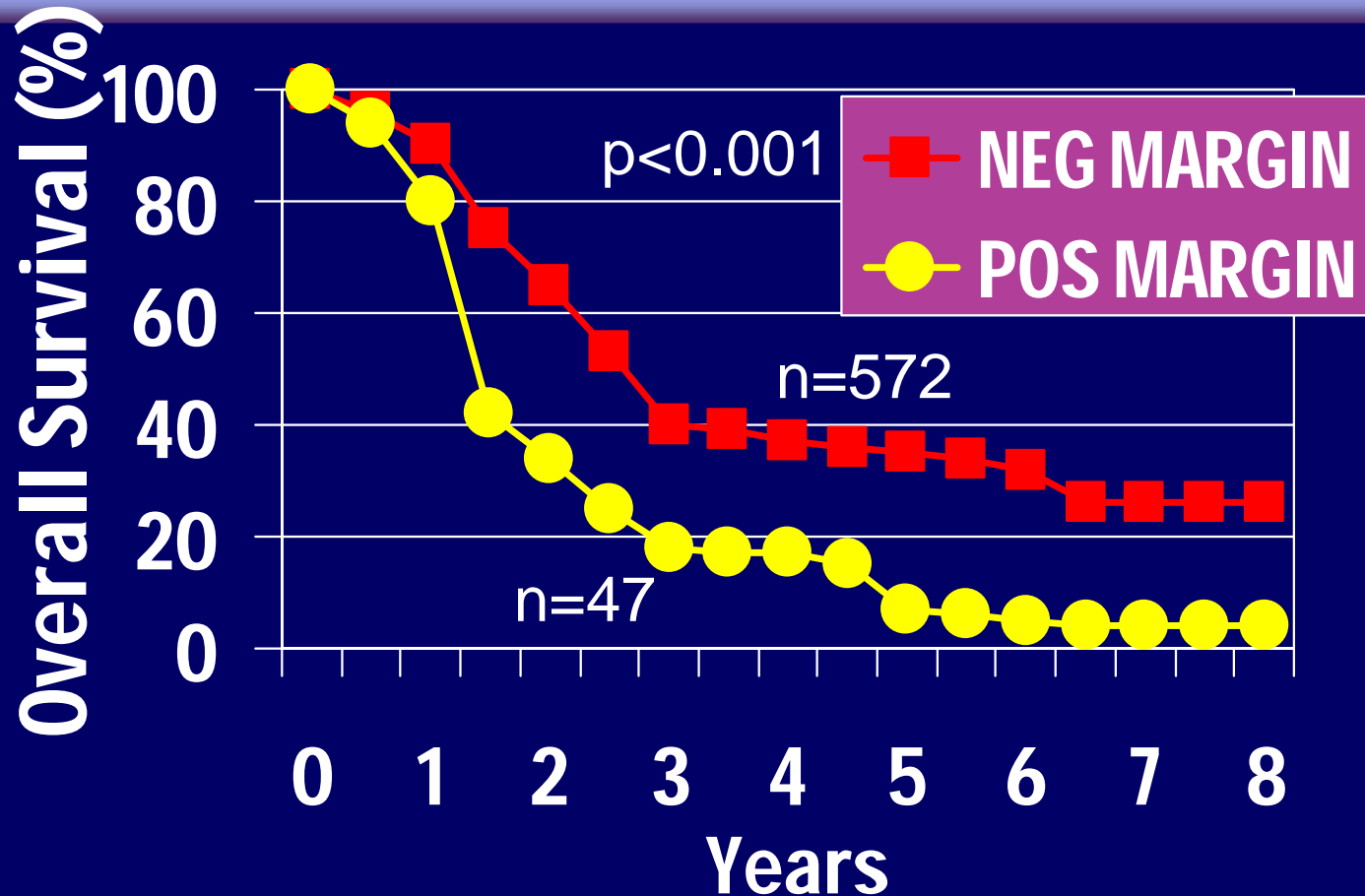
* Gross margin at which none of cases had positive final margins

Fresh specimen examined by pathologist and gross margin measured.

Bozzetti et al, Ann Surg 1982, 196: 685

Margin status – should you check?

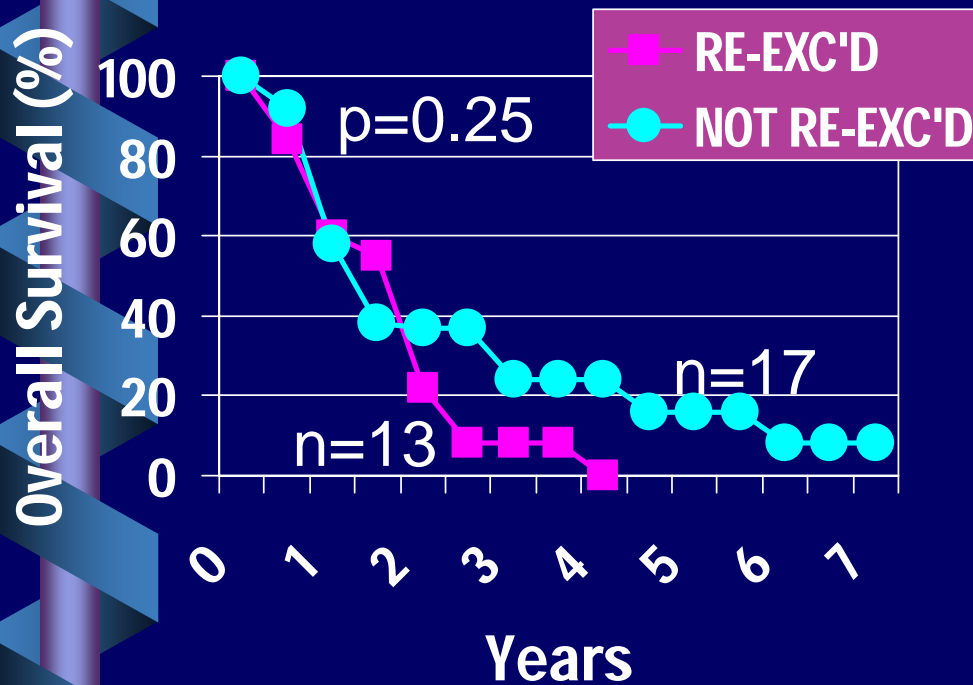
Positive Margins and Survival



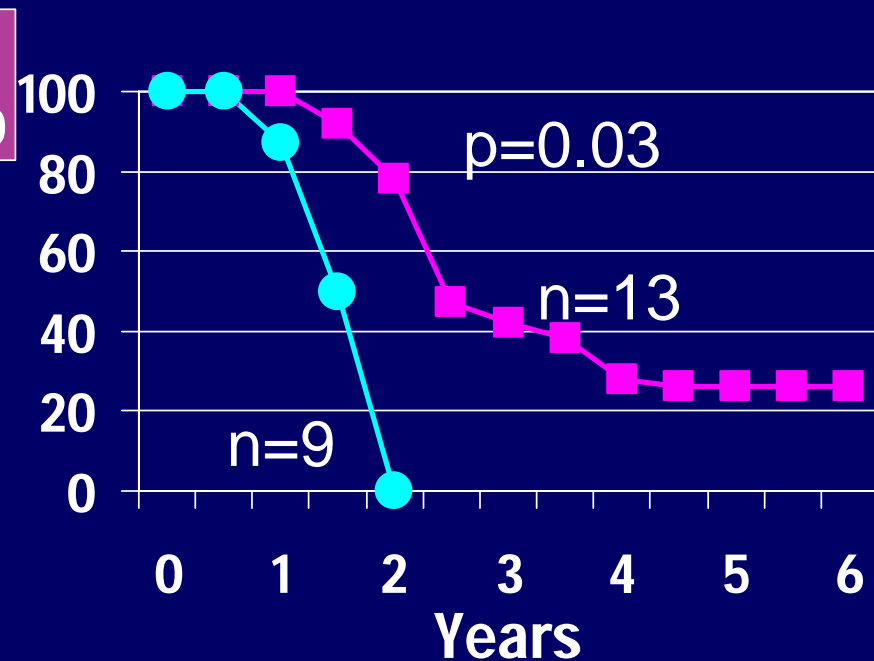
Stage II & III, 1985-1997 Kim et al, J Gastrointest Surg 1999; 3:24

Frozen Section Analysis and Re-Excision of Positive Margins

> 5 pos nodes



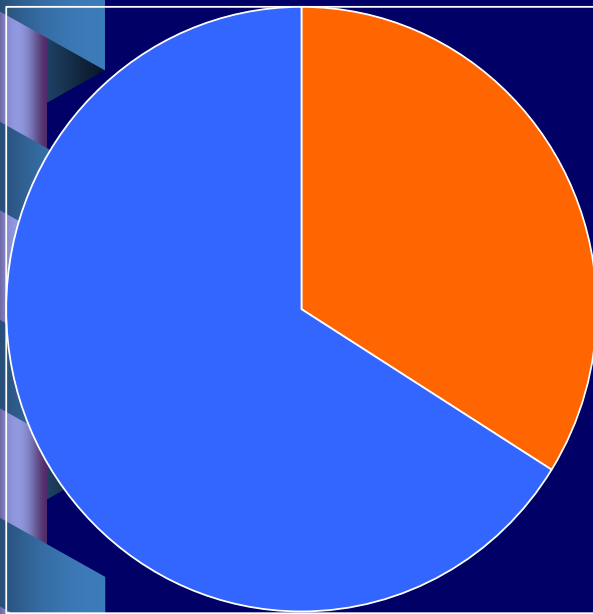
≤ 5 pos nodes



80% had T3N+ disease

Margin management reported by Ontario general surgeons

GROSS MARGIN DESIRED



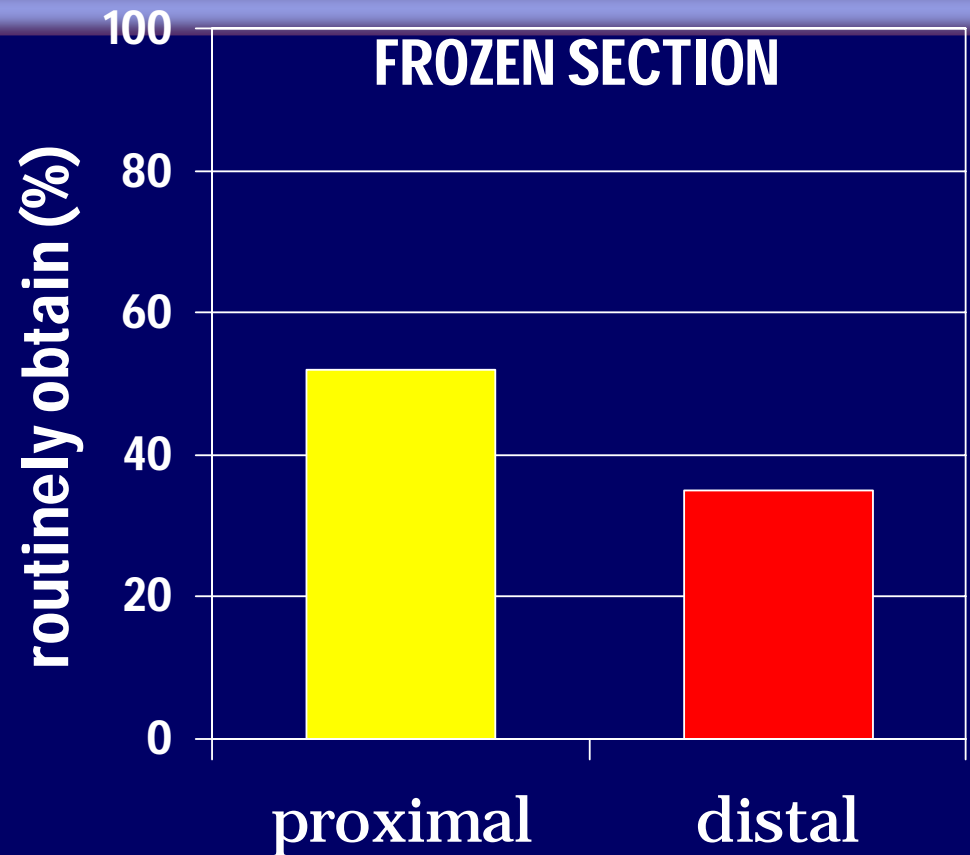
$\leq 4\text{ cm}$

$\geq 5\text{ cm}$

n=206

Helyer, Coburn, O'Brien, Swallow, ASCO 2006

Helyer et al, Gastric Cancer 2007: 10 (4): 205-14





Case Mr. S.H. Pathology Report

- **diffuse type adenocarcinoma**
- **tumour penetrates serosa**
- **proximal and distal margins negative**
- **3 of 20 nodes positive**

What stage and NOW WHAT?

TNM Staging of Gastric Cancer: T Stage

AJCC 2002, 6th edition

AJCC 2010, 7th edition

- T1** Lamina propria, submucosa
- T2** Muscularis propria, subserosa
- T3** Penetrates serosa
- T4** Adjacent structures

- T1 Lamina propria, submucosa
 - T1a Lamina propria
 - T1b Submucosa
- T2 Muscularis propria
- T3 Subserosa (*was T2b*)
- T4a Perforates serosa (*was T3*)
- T4b Adjacent structures

TNM Staging of Gastric Cancer: N Stage

AJCC 2002, 6th edition

N0 no regional nodes involved

N1 1 to 6 nodes

N2 7 to 15 nodes

N3 > 15 nodes

AJCC 2010, 7th edition

N1 1 to 2 nodes

N2 3 to 6 nodes (*was N1*)

N3a 7 - 15 nodes (*was N2*)

N3b 16 or more (*was N3*)

TNM Staging of Gastric Cancer

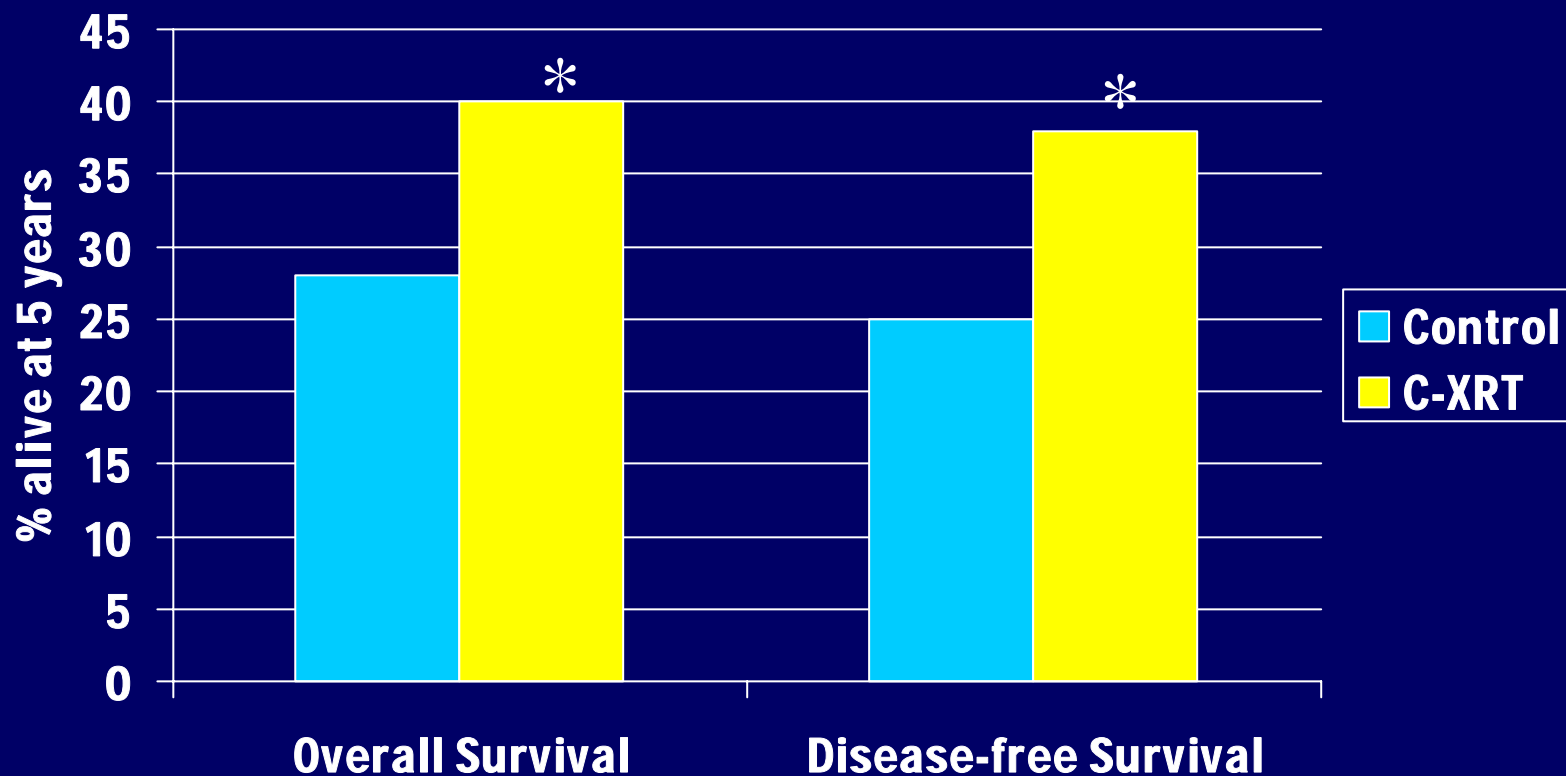
AJCC 2002, 6th edition

Stage 1	A	T1; N0
	B	T1; N1 T2; N0
Stage 2		T1; N2 T2; N1 T3; N0
Stage 3	A	T2; N2 T3; N1 T4; N0
	B	T3; N2
Stage 4		T4; N1, N2, N3 T1, T2, T3; N3 M1

AJCC 2010, 7th edition

Stage IA	T1	N0
Stage IB	T2	N0
	T1	N1
Stage IIA	T3	N0
	T2	N1
	T1	N2
Stage IIB	T4a	N0
	T3	N1
	T2	N2
	T1	N3
Stage IIIA	T4a	N1
	T3	N2
	T2	N3
Stages IIIB, IIIC, IV...		

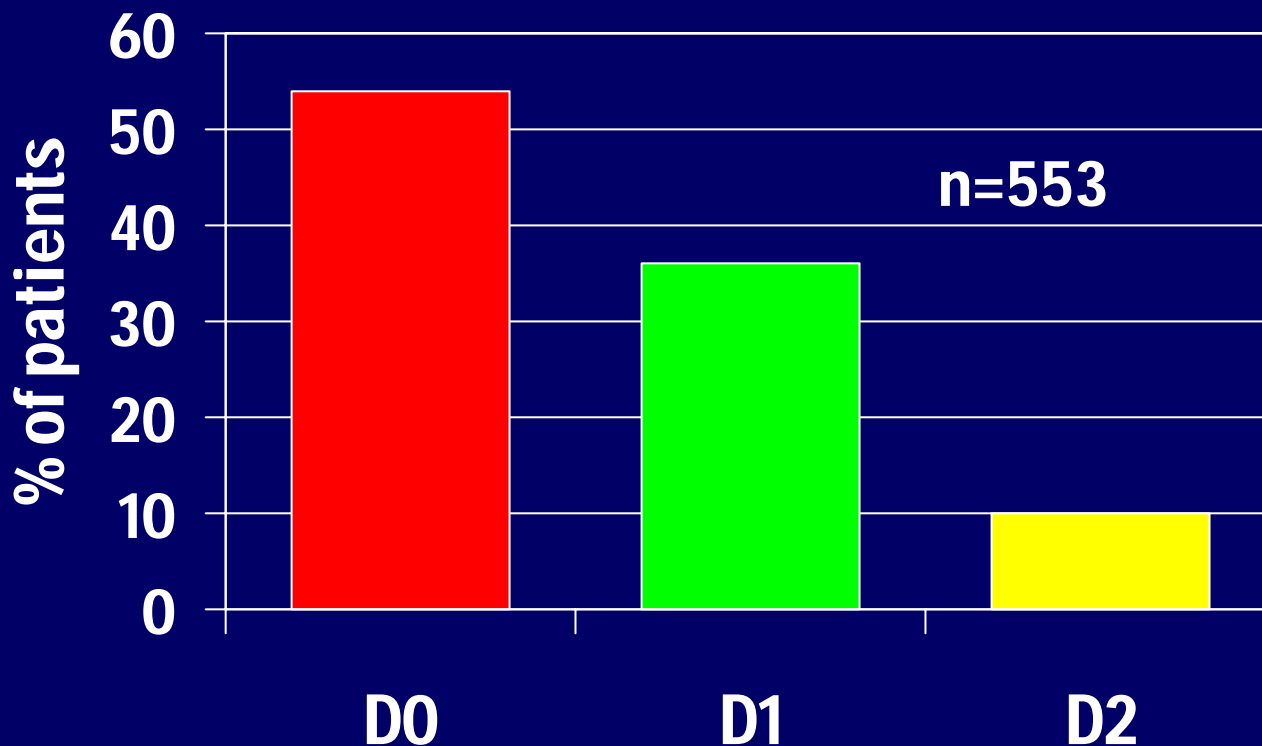
Intergroup-0116 RCT of Postoperative Adjuvant Chemoradiation



* $p < 0.001$

NEJM 2001 345:725

Extent of LND in Intergroup 0116



D2 recommended in protocol
LND assessed from surgical checklist



Intergroup-0116 RCT of Postoperative Adjuvant Chemoradiation: M & M

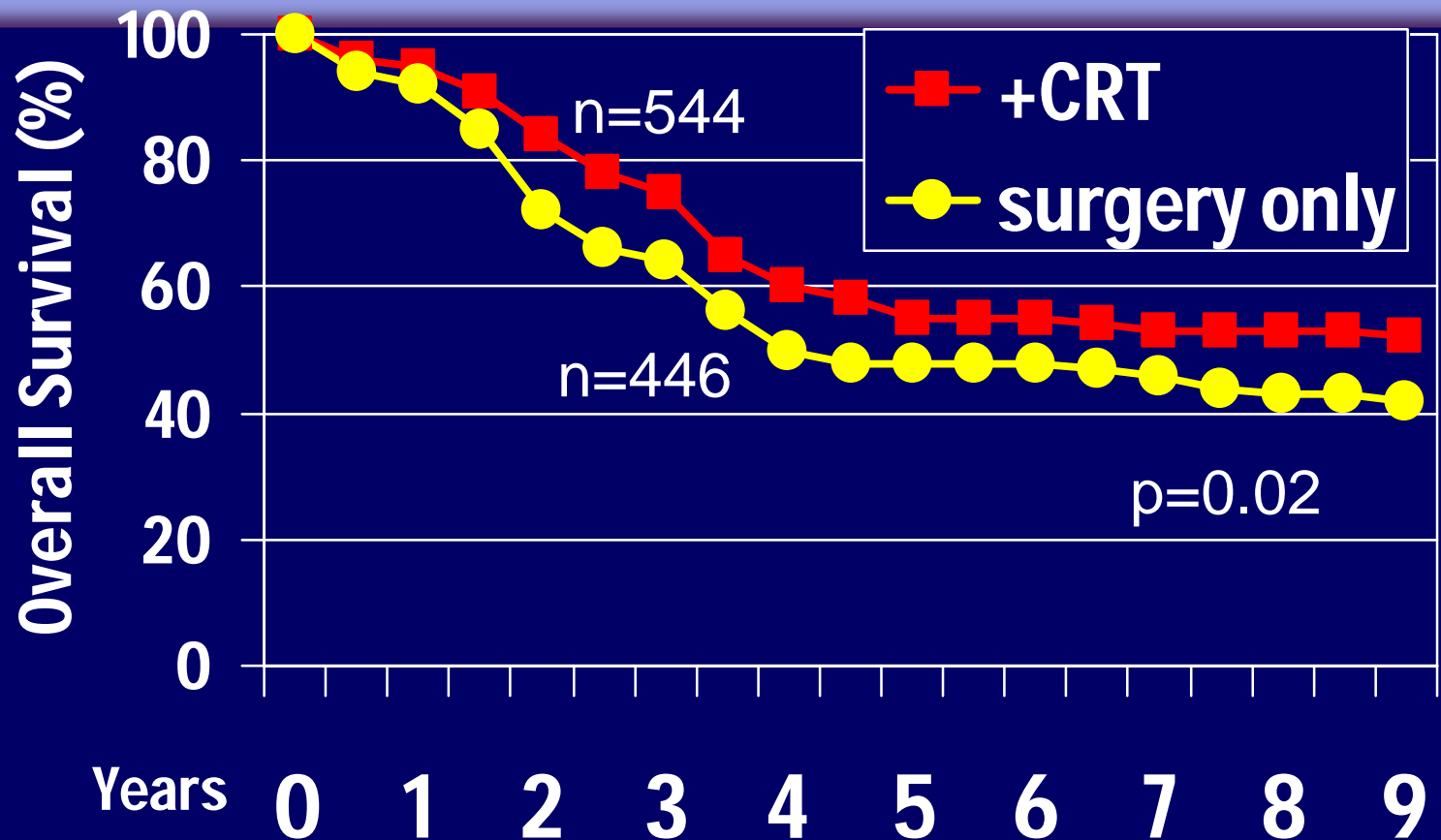
32% needed change in XRT plan

30% couldn't complete Rx

34% Grade IV toxicity

1% mortality in C-XRT arm

ONE HOT QUESTION OF TODAY: What is the role of postoperative adjuvant chemoradiation with D2 dissection?



NB: observational study!

MRC Trial Neoadjuvant Chemotherapy for Gastric (74%), GE (12%), lower E (14%) Cancer

	Periop Chemo	Surgery only	p
n	250	253	
explored [%]	92	96	
R0 resection (%)	79	70	0.03
op mortality (%)	6	6	
morbidity (%)	46	45	
post op stay (d, med)	13	13	
OS (% , 5 yr)	36	23	0.009

It's MAGIC!

**Median f/u
= 48 mos.**