The ROYAL MARSDEN
NHS Foundation Trust

Surgery for Gastric and GE Junction Cancer:

primary
palliative
when and where?

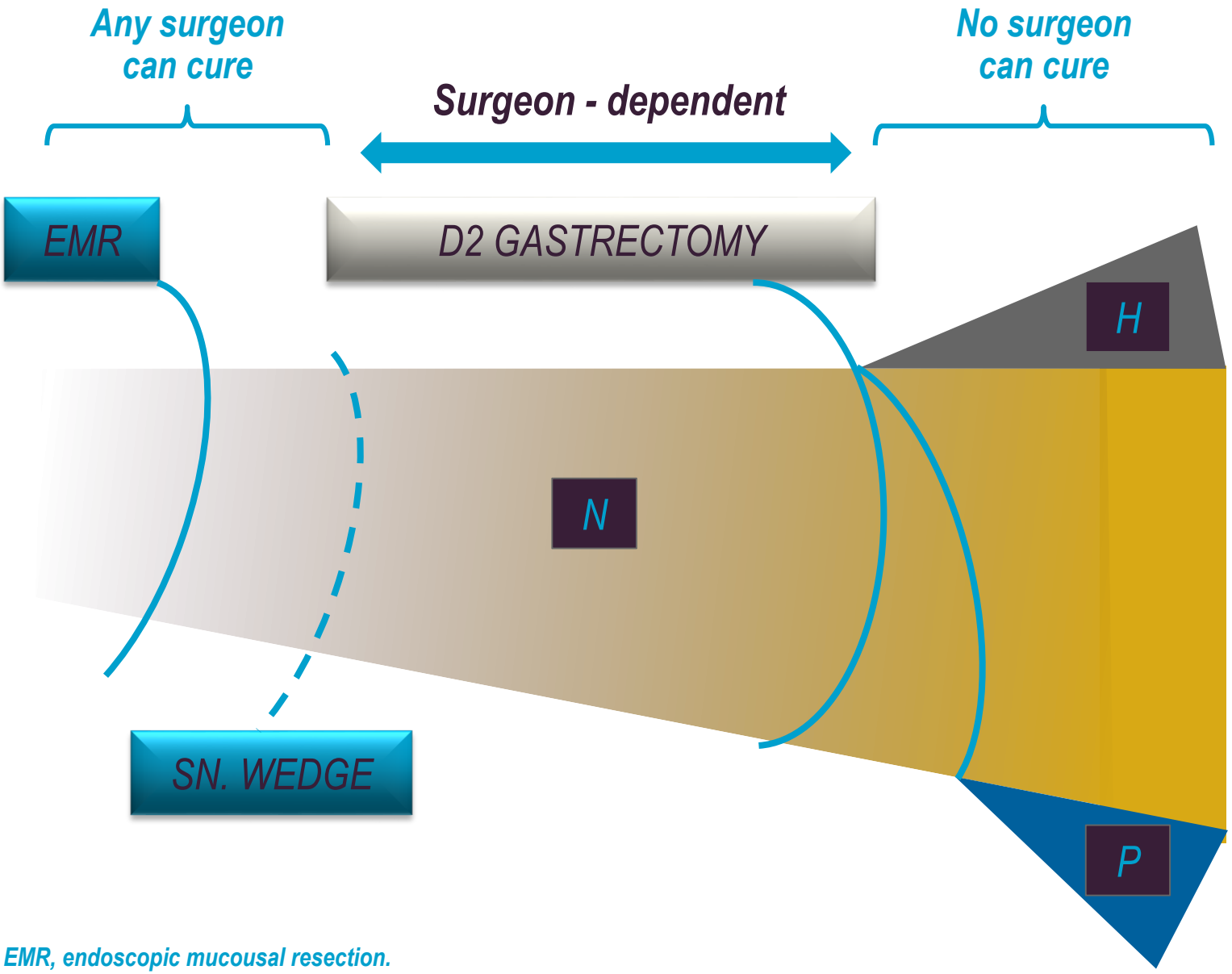
William Allum

NHS

William Allum

Conflict of Interest

None



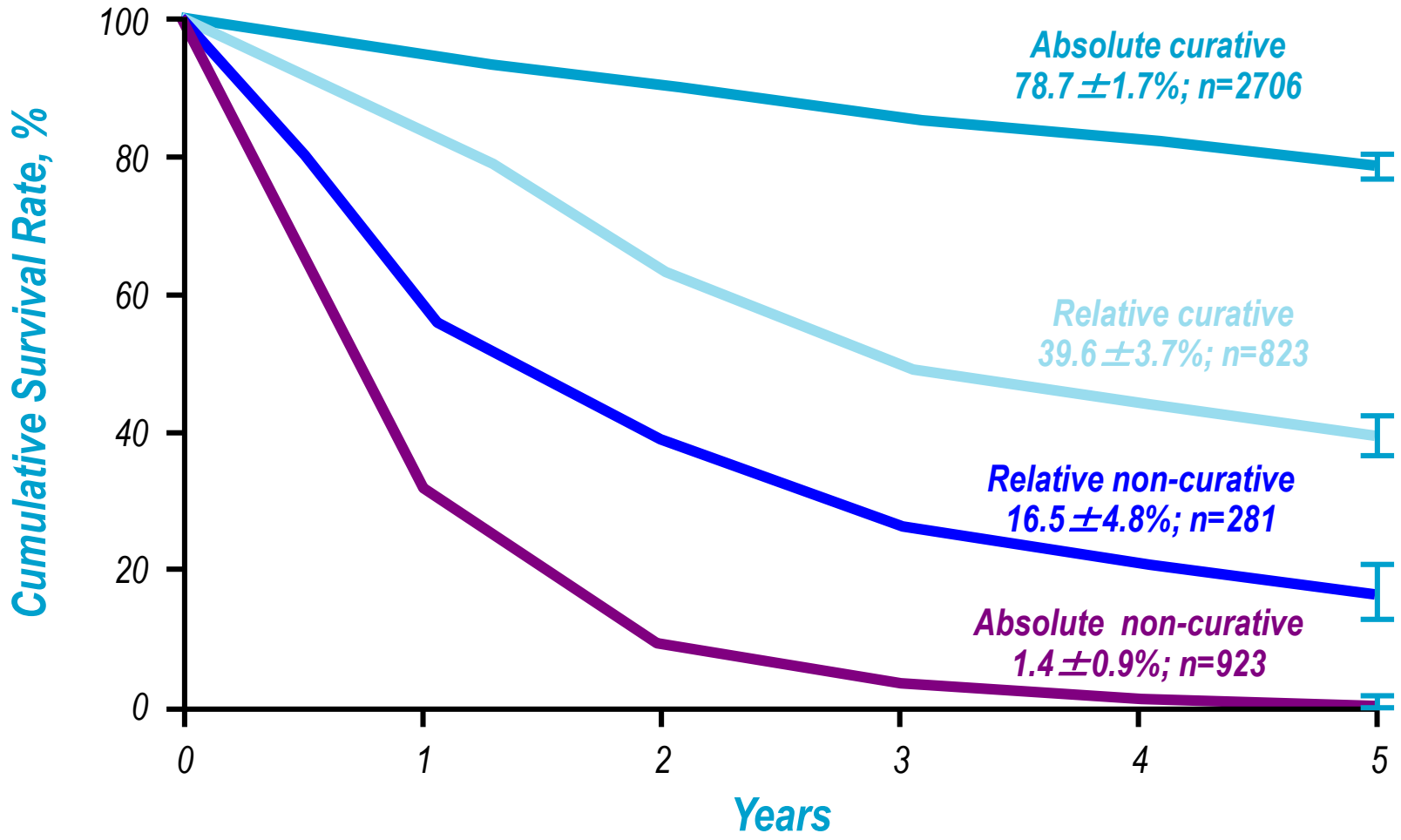
EMR, endoscopic mucousal resection.

R0 Resection

A surgical procedure in which there is no evidence of macroscopic residual tumour in the tumour bed, lymph nodes and/or distant sites with microscopic negative resection margins

Hermanek P, Wittekind C. Pathol Res Pract. 1994;190(2):115-123.

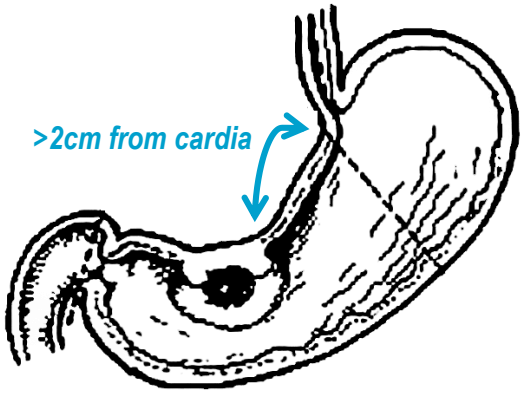
Japanese Rules
End Results of Surgical Resection



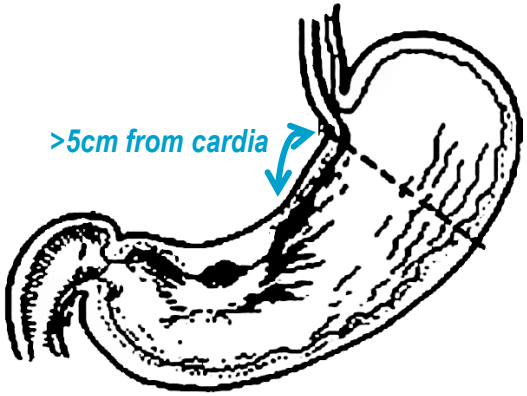
Maruyama 1981. Jpn J Surg 11: 127-45

Indication and Division Lines for Distal Subtotal and Total Gastrectomy

Distal subtotal gastrectomy

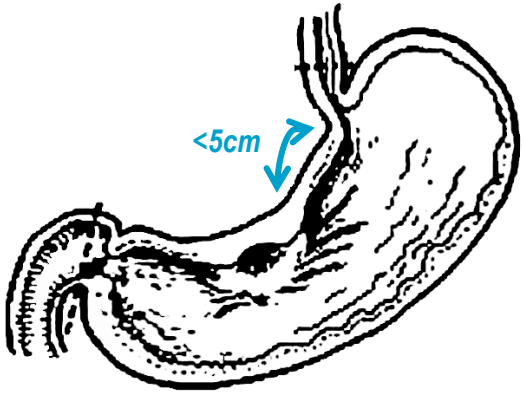


Early cancer or well-circumscribed advanced cancer

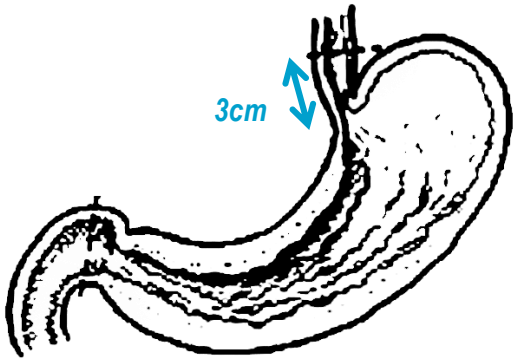


Infiltrative advanced cancer

Total gastrectomy

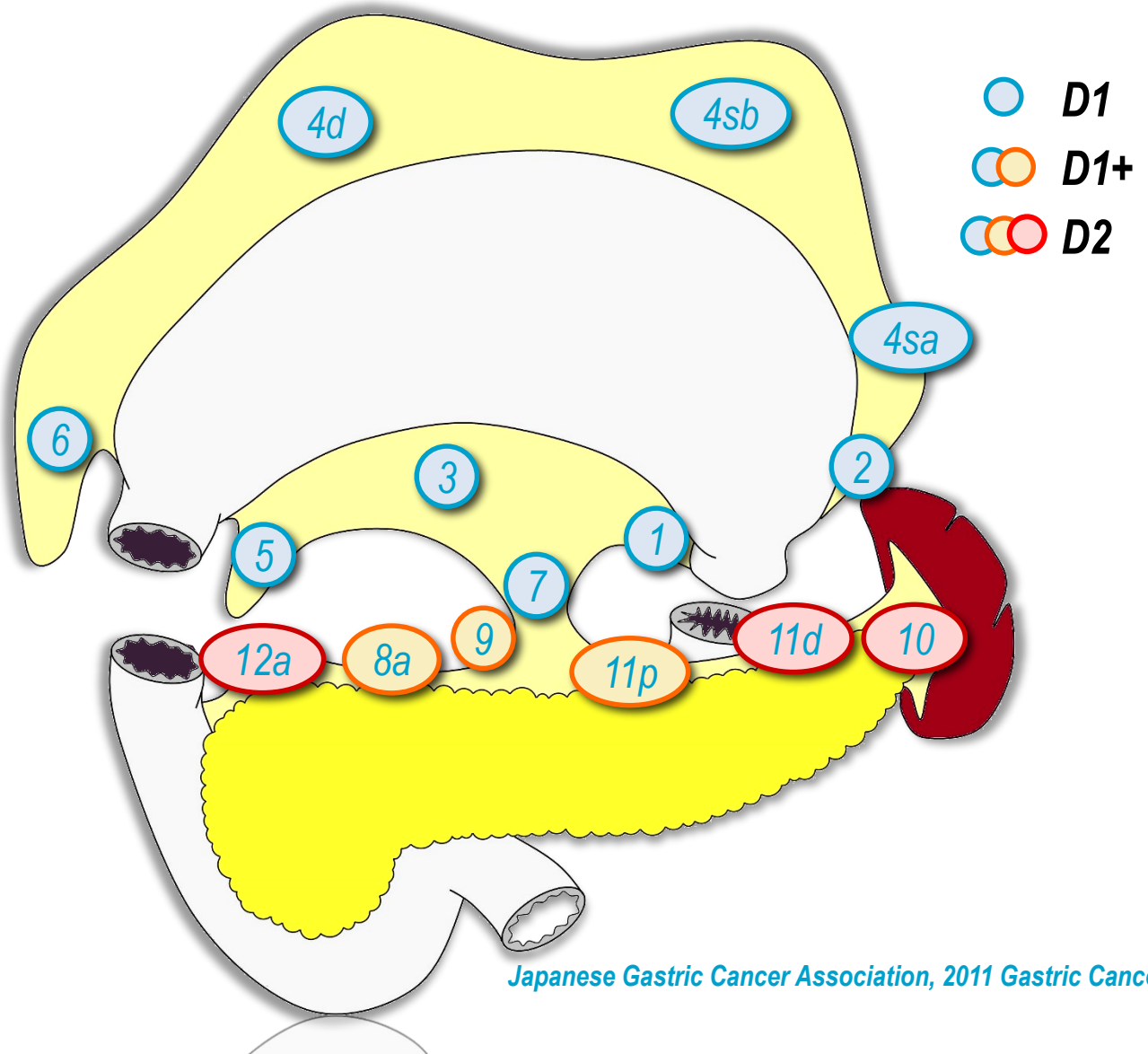


When the proximal distance from the cardia is less than the required length, total gastrectomy is indicated



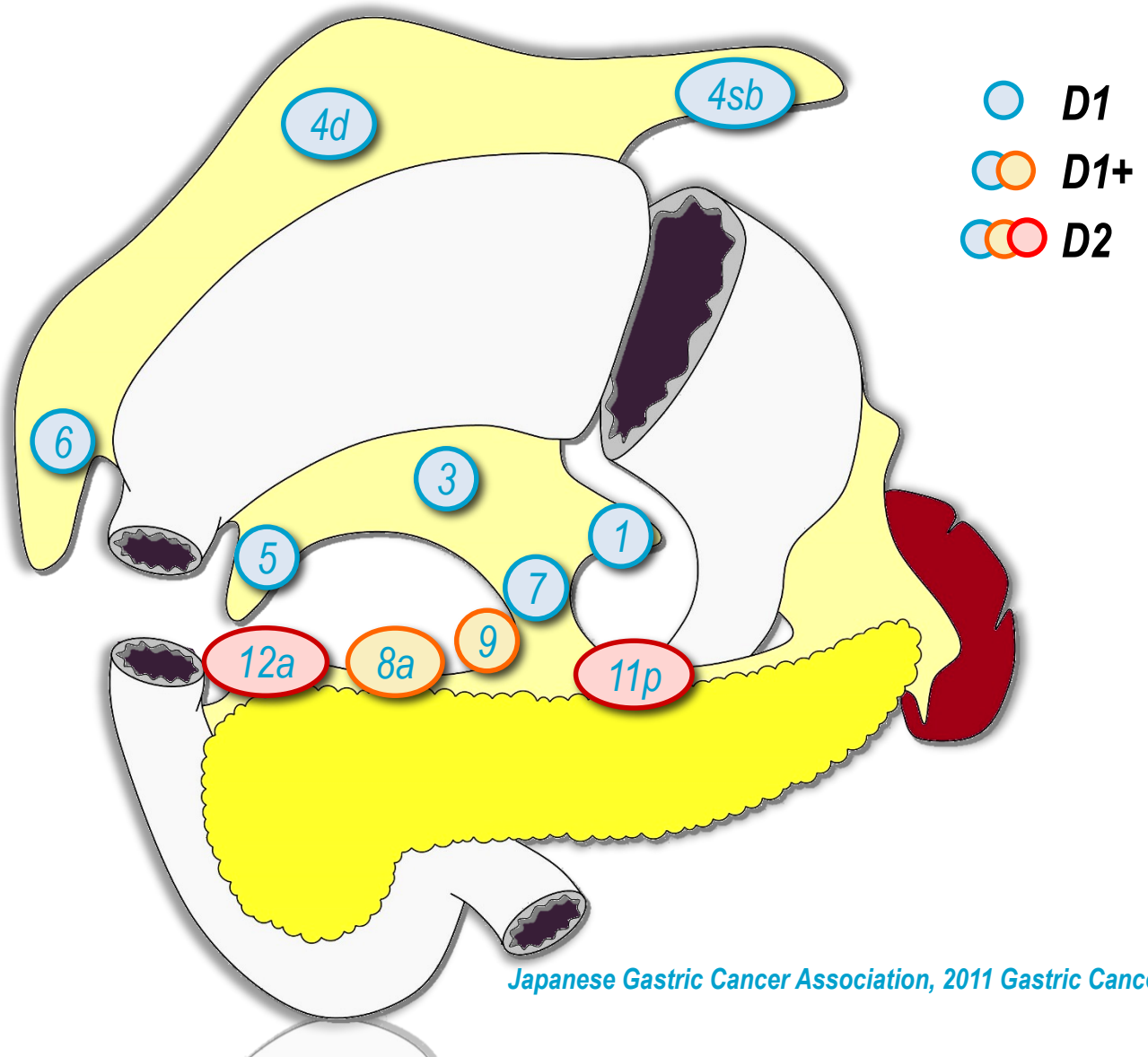
Total gastrectomy is always indicated in diffuse carcinoma (Borrmann type 4) regardless of its size

Total Gastrectomy and Lymph Node Dissection



Japanese Gastric Cancer Association, 2011 Gastric Cancer 14: 113-23.

Distal Gastrectomy and Lymph Node Dissection



Japanese Gastric Cancer Association, 2011 Gastric Cancer 14: 113-23.

Western Trials

- UK MRC D1 vs D2 (1996, 1999)
  - 5 year survival D1 35% D2 33%
  - Operative mortality D1 6.5% D2 13%

- Dutch Gastric Cancer trial (2010)
  - operative mortality D1 4% D2 10%
  - 15 year survival D1 21% D2 29% (NS)
  - gastric cancer deaths D1 48 D2 37 (p 0.01)

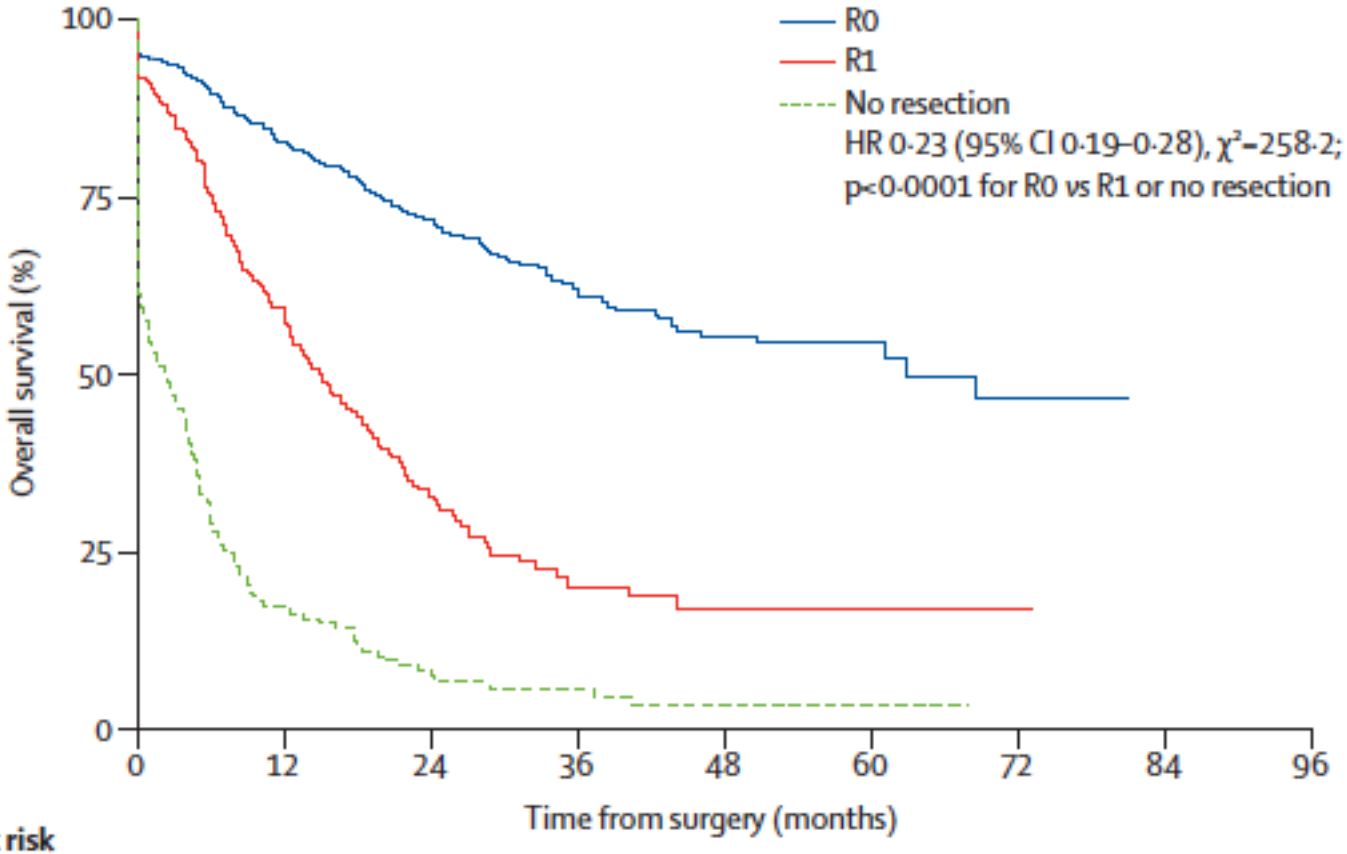
- Italian trial (2014)
  - operative mortality D1 3.0% D2 2.2%
  - 5 year survival D1 66.5% D2 64.2%
  - pT2-4 / N0 D1 38% D2 59%

European Guidelines
Surgery

Guideline	Gastric Resection	Lymphadenectomy
SIGN	R0 (proximal, distal circumferential margins)	D2 ≥ 25 lymph nodes
	R0 (proximal, distal circumferential margins)	D2 > 25 lymph nodes
German S3	5cm intestinal 8cm diffuse	> 16 nodes for TNM
		No pancreatectomy/splenectomy
UK	R0	D2 for stage II & III – if fit
		> 15 nodes for TNM
St Gallen	cT1 diffuse – resect	D2 – without pancreatectomy or splenectomy
	R0	

SIGN, Scottish Intercollegiate Guidelines Network; TNM, tumour node metastases..
Allum W et al Gut 2011; 60:1449-72; Lutz MP, et al. Eur J Cancer. 2012;48(16):2941-2953; Moehler M, et al. Z Gastroenterol. 2011;49(4):461-531; Scottish Intercollegiate Guidelines Network. Management of oesophageal and gastric cancer: a national clinical guideline. http://www.sign.ac.uk/pdf/sign87.pdf. Published June 2006. Accessed September 9, 2013.

Post-operative survival by Resection Status MRC UK ST03 trial



Number at risk (number censored)									
R0	626 (33)	487 (114)	312 (162)	119 (43)	64 (37)	26 (19)	4 (4)	0 (0)	0 (0)
R1	208 (9)	116 (22)	47 (17)	15 (8)	5 (2)	3 (3)	1 (0)	0 (0)	0 (0)
No resection	168 (2)	28 (4)	10 (2)	5 (3)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)

European Chapter of IGCA

D2 Audit

Main findings

Early GC

The extent of lymphadenectomy is highly variable among European surgeons

In cN+ cases a complete D2 dissection is performed only by 53% of surgeons

- *There is an impact of diffuse histology with a higher number of D2 performed in cN0 cases*
- *The presence of comorbidity reduces the indication to D2 in cN+ cases*

Main findings

Advanced GC

Most surgeons perform a D2,
but still some variations persist

- *Histology also have an impact :*

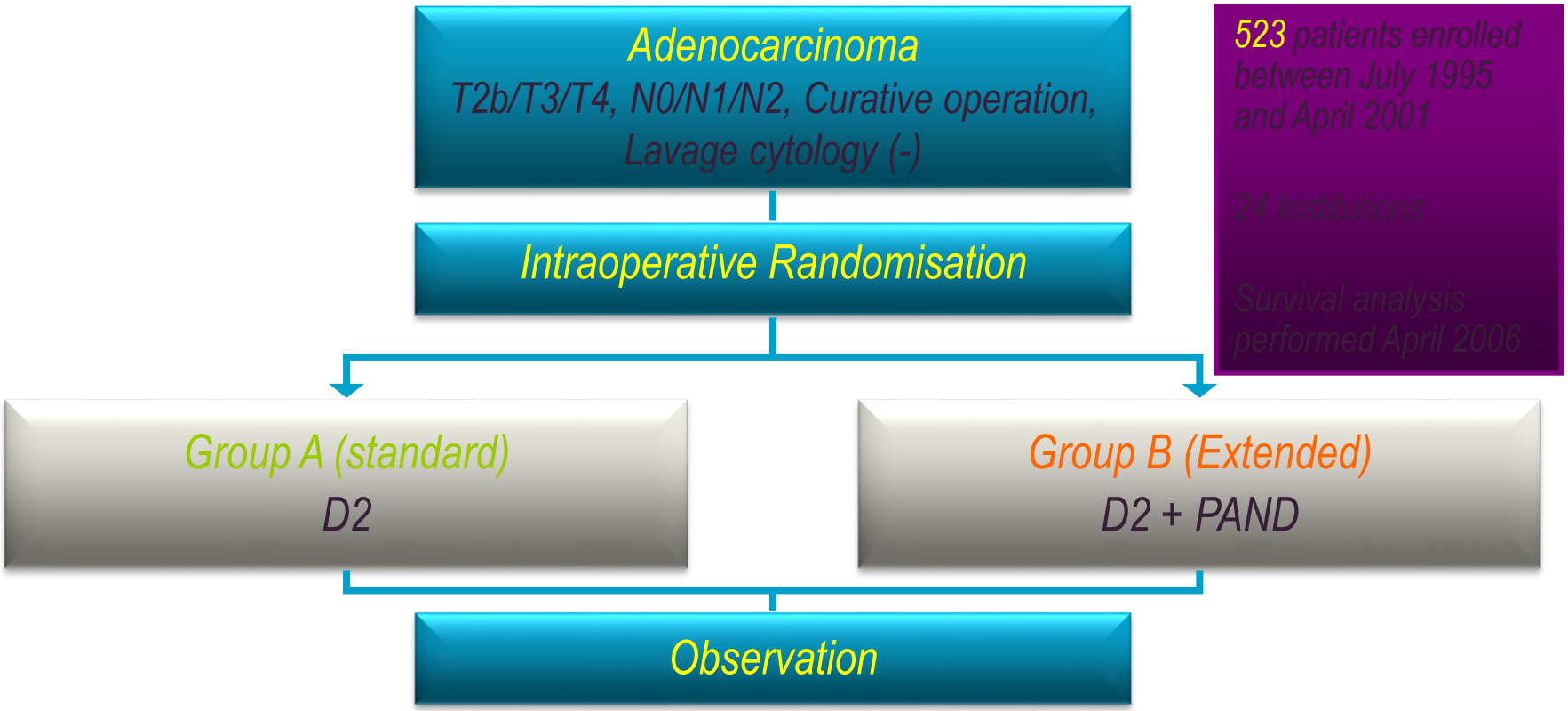
  the number of surgeons performing a D2 and the number of total gastrectomies for tumours located in the lower third is higher in tumours with diffuse histology compared with the intestinal histology

JCOG 9501

D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer

Sasako M, et al. N Eng J Med. 2008;359(5):453-462.

JCOG 9501
Scheme



523 patients enrolled between July 1995 and April 2001

24 Institutions

Survival analysis performed April 2006

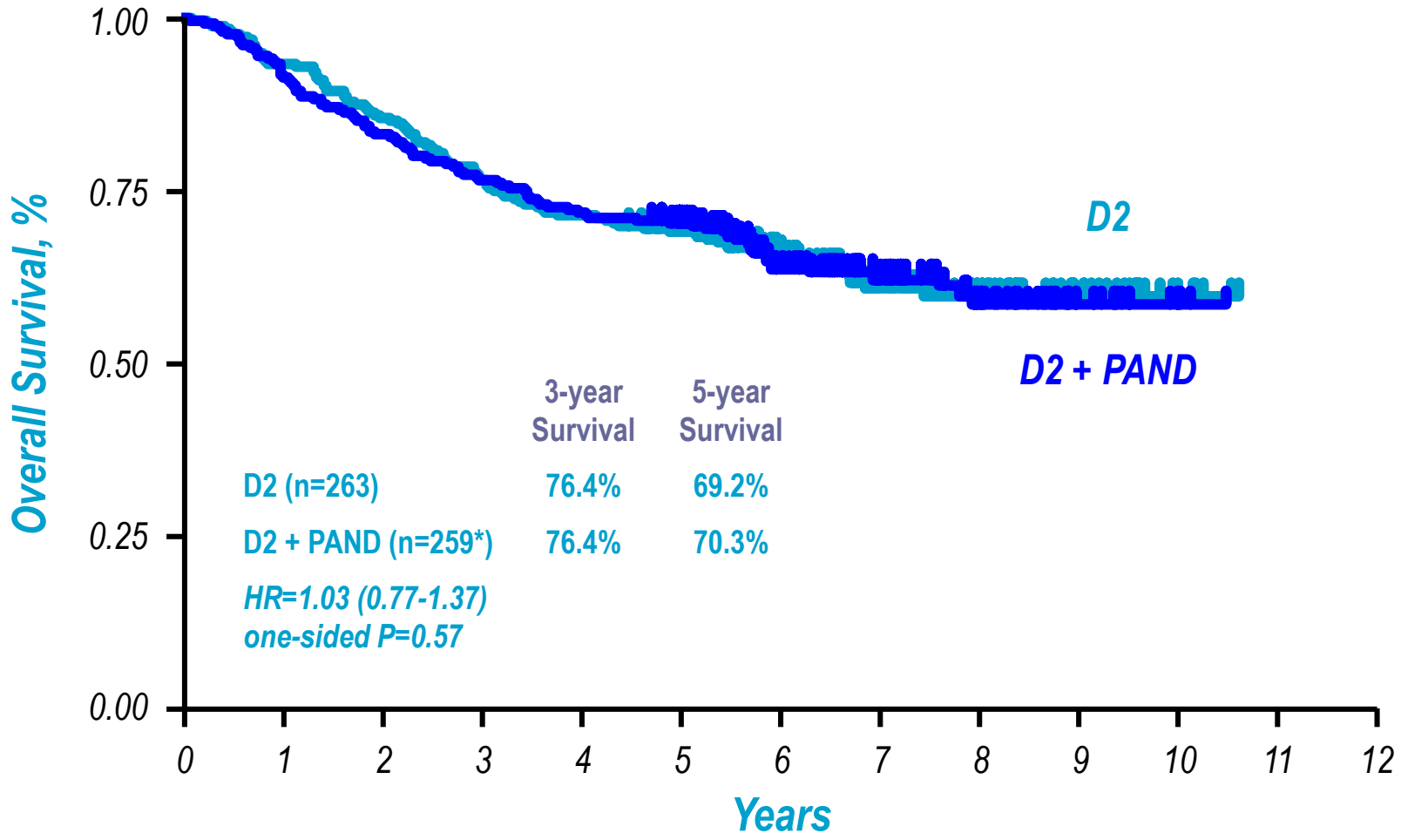
Endpoints

1. Overall survival
2. Recurrence-free survival, morbidity/mortality

PAND, para-aortic nodal dissection.

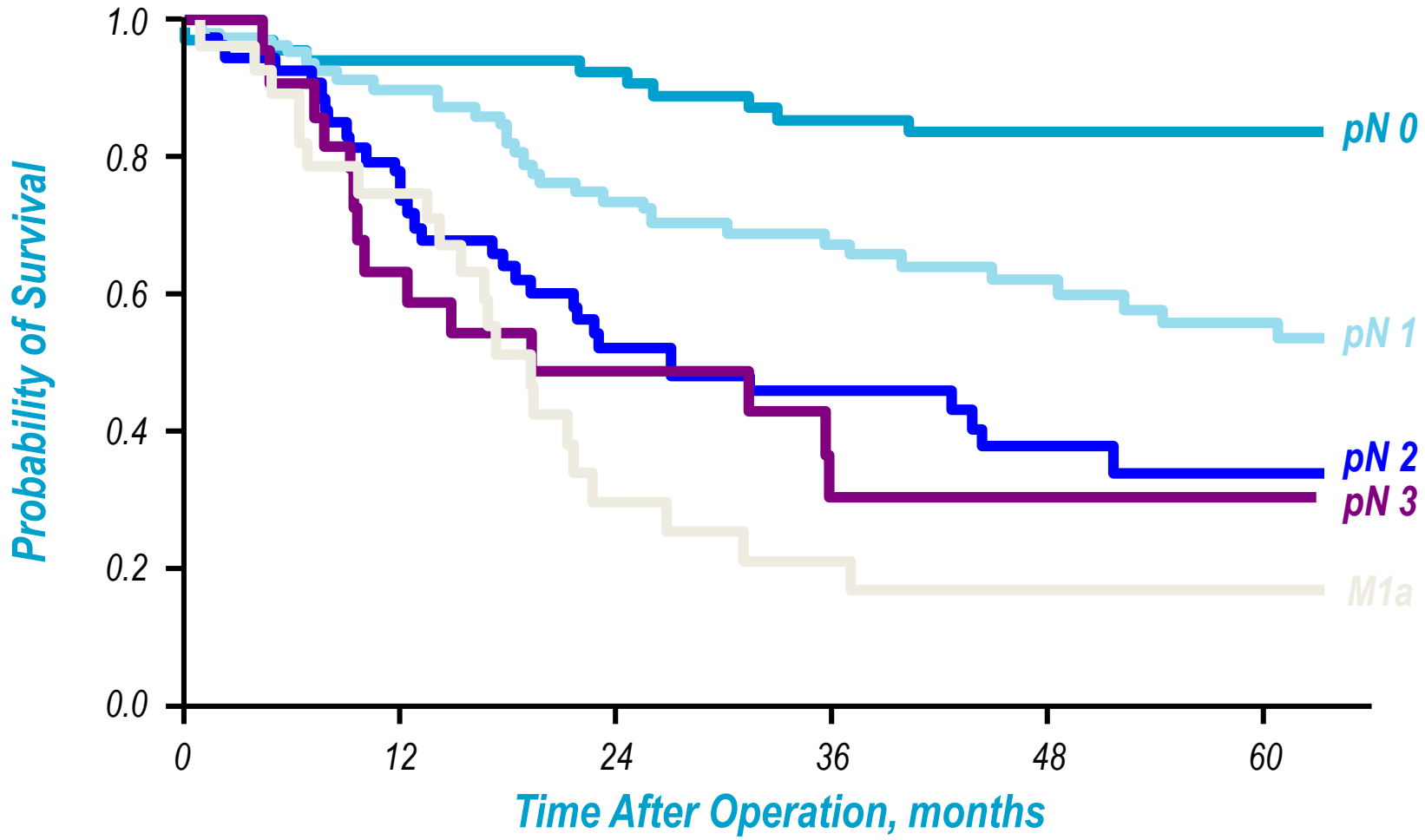
Sasako M, et al. N Eng J Med. 2008;359(5):453-462.

JCOG 9501
Overall Survival



HR, hazard ratio.
**One case was ineligible because of changed histologic diagnosis.*
Sasako M, et al. N Engl J Med. 2008;359(5):453-462.

Extended Lymphadenectomy



Roviello F, et al. Eur J Surg Oncol. 2010;36(5):439-446.

Extended Lymphadenectomy

T3/4 cancers

Mixed or diffuse histology

Upper third of the stomach

De Manzoni G, et al. Ann Surg Oncol. 2011;18(8):2273-2280.

Subtypes of Gastric Cancer.

Type	Features
Diffuse, signet ring cancer	CDH-1 mutation Lepidic growth Peritoneal metastasis
Intestinal type, distal gastric cancer	Correa hypothesis – chronic inflammation H. pylori associated
Proximal, non-diffuse cardia / junctional cancer	Obesity / GORD related H. pylori protective Poorest prognosis HER2 strong expression

Minimally Invasive Surgery

Shorter inpatient stay

Less blood loss

Quicker return to GI function

? Anastomotic leak rates

Intraluminal bleeding

Minimally Invasive Surgery
Total Gastrectomy

Variables	Extent of LND		*P* value
	D1 + ß (n=103)	D2 (n=19)	
Operating time, mean, min ± SD	277 ± 86	350 ± 76	0.001
EBL, mean, mL ± SD	231 ± 190	350 ± 250	0.019
Harvested lymph nodes, mean, n ± SD	42 ± 16	44 ± 16	0.484
Morbidity, n %	19 (18.4)	10 (52.6)	0.003
Mortality, n %	0	2 (10.5)	<0.001
Hospital stay, mean, d ± SD	10.8 ± 9.1	17.1 ± 20.8	0.032

EBL, estimated blood loss; LND, lymph node dissection; SD, standard deviation.
Jeong O, et al. J Am Coll Surg. 2013;216(2):184-191.

Minimally Invasive Surgery

Early gastric cancer

Distal Gastrectomy

KLASS Trial

Comparison of laparoscopic vs open gastrectomy for gastric cancer: a prospective randomized trial

JCOG 0912

Phase III study of laparoscopy-assisted vs open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: a multicenter study

KLASS, Korea Laparoscopic Gastrointestinal Surgery Study Group.
Kim HH, et al. Ann Surg. 2010;251(3):417-420; Nakamura K, et al. Jpn J Clin Oncol. 2013;43(3):324-327.

Minimally Invasive Surgery

KLASS and JCOG 0912 Trial

Safe – morbidity 14.8%, mortality 0%

Technically skilled surgeons

Long term outcomes awaited

.

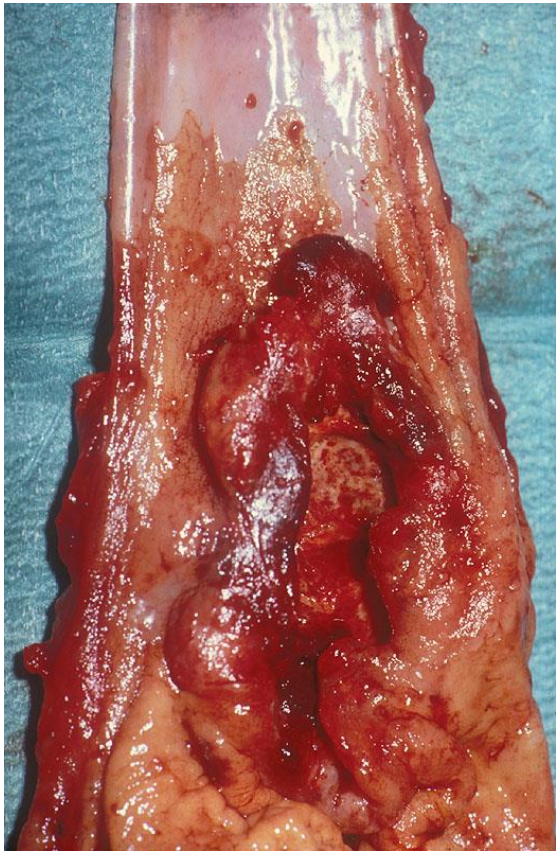
Minimally Invasive Surgery

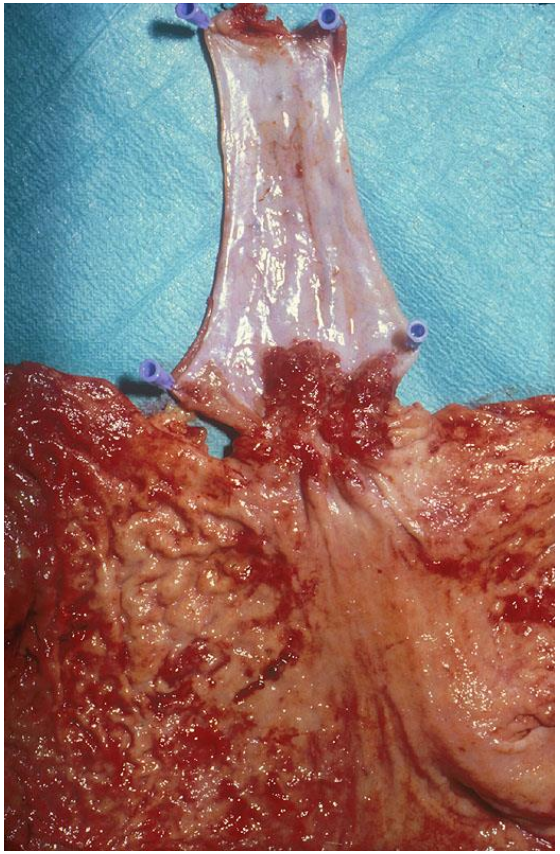
Advanced Disease

LAG vs Open – feasible D2 dissection

	Intraoperative Complications	Postoperative Complications
LADG	1.1%	7.5%
LATG	1.9%	20.1%

OESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA





TNM-8 Oesphagogastric Junction

Oesophagus and Gastric Carcinomas

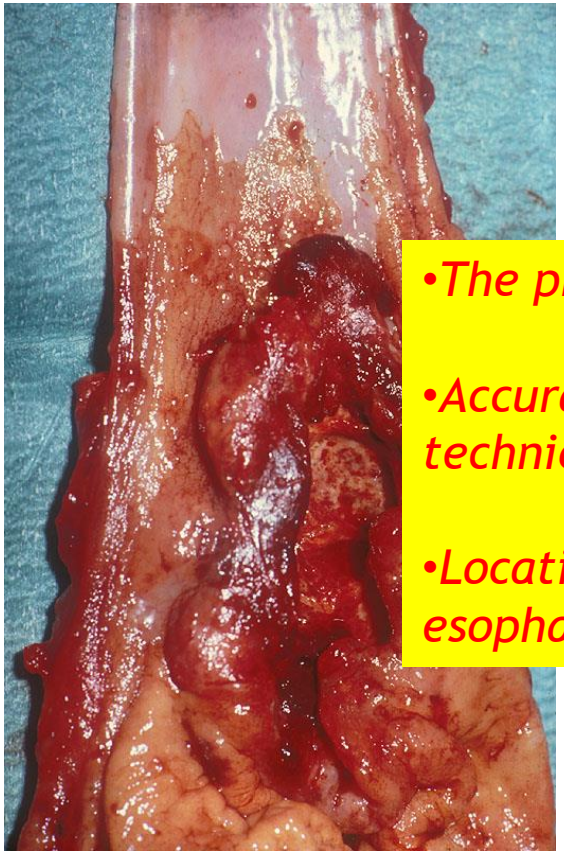
- **A tumour the epicenter of which is within 2 cm of the oesophagogastric junction and also extends into the oesophagus is classified and staged using the oesophageal scheme.**

  Cancers involving the oesophagogastric junction (OGJ) whose epicenter is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal

- Cancers whose epicenter is more than 2 cm distal from the OGJ will be staged using the Stomach Cancer TNM and Stage even if the OGJ is involved.

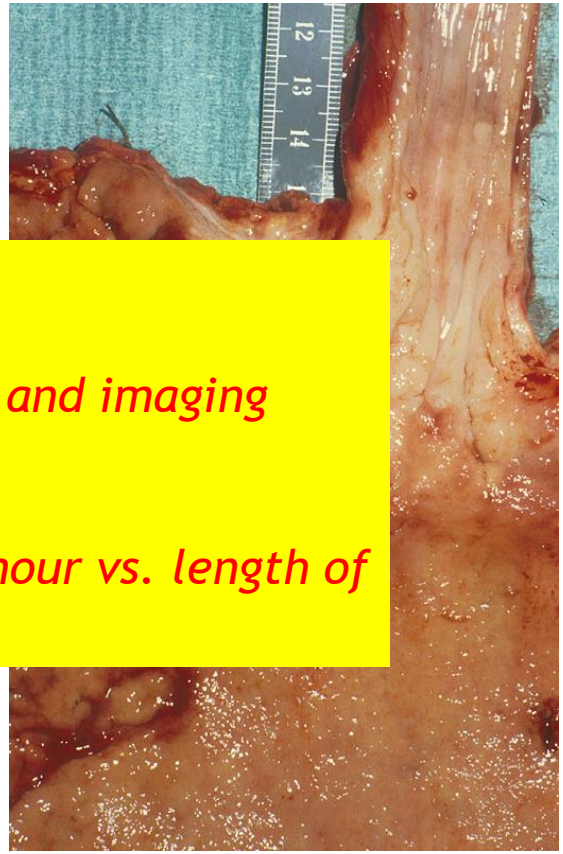
OESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA

Type I



Type II

Type III



- *The problem of large tumours*
- *Accuracy of preoperative endoscopy and imaging techniques*
- *Location of the epicenter of the tumour vs. length of esophageal or gastric involvement*

Operation Selection

Surgical Approach

Margins

Lymphadenectomy

EORTC Consensus
St Gallen 2012

- Type I – Oesophago-gastrectomy
- Type II – Oesophago-gastrectomy or
  - Extended Total Gastrectomy
- Type I & II – Mediastinal Lymphadenectomy
  – 2 field
- Type III - Extended Total Gastrectomy

Dutch Trial
Trans Hiatal Oesophagectomy vs Trans Thoracic Oesophagectomy

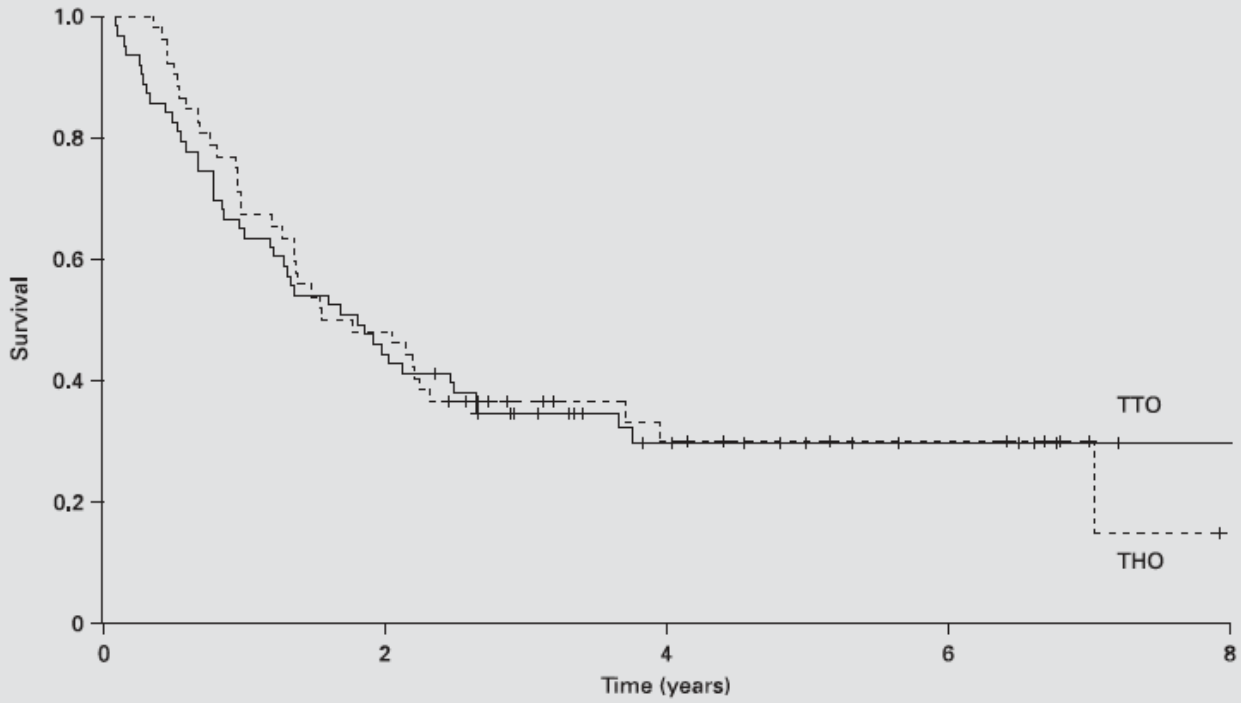
220 patients with mid and lower oesophageal ACA

THO
- Lower morbidity

TTO
- More nodes
- More respiratory complications

Hulscher et lN Engl J Med 2002;347:1662-9.

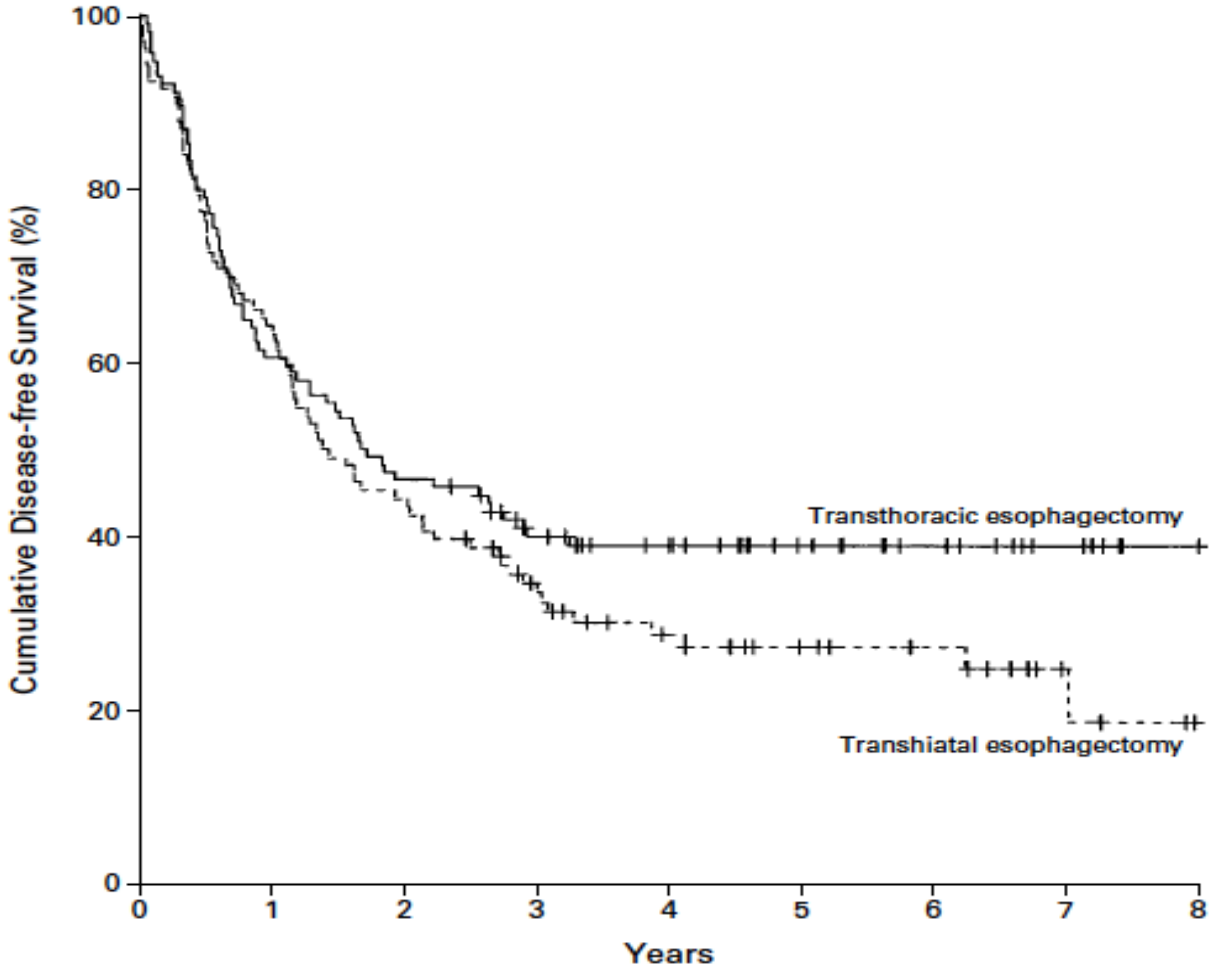
Dutch Trial
THO vs TTO



Numbers at risk:

THO	52	25	9	6
TTO	63	28	11	6

Dutch Trial
THO vs TTO



No. at Risk								
Transhiatal esophagectomy	106	68	47	32	20	15	11	4
Transthoracic esophagectomy	114	69	53	39	31	20	13	7

Minimally Invasive Oesophagectomy

101 open;
65 MIO;
9 Conversion

pT1a & pT1b. N0

	Intraoperative	Morbidity	Medium Term
MIO	Less blood loss	Gastroparesis	Less pain
OPEN	Shorter time	Respiratory	More fatigued

Nafteux et al 2011 Eur J Cardio Surgery 40: 1455

Minimally Invasive Oesophagectomy

MIRO trial

Open right thoraco-abdominal oesophago-gastrectomy (OE) vs

Hybrid – laparoscopic mobilisation / open thoracotomy (HMIE)

	Major Complications	Respiratory Complications	Survival 3 yr
OE (n=104)	67 (64.4%)	31 (30.1%)	54.8%
HMIE (n=103)	37 (35.9%)	18 (17.7%)	67.0%

Mariette et al ESMO 2017

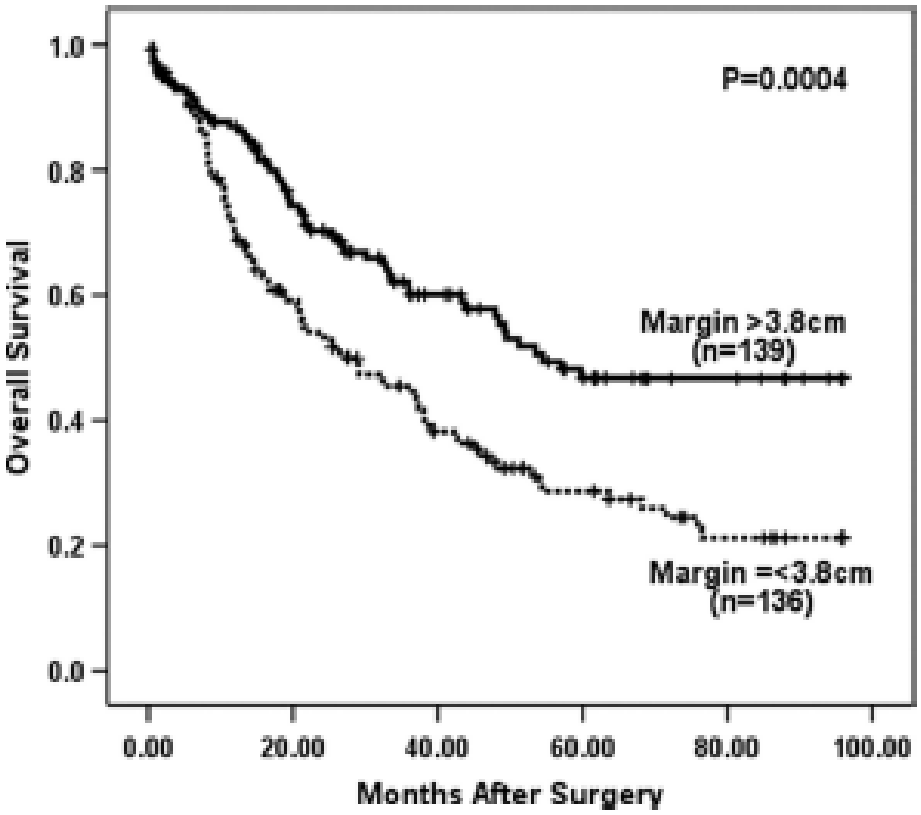
Operation Selection

Surgical Approach

Margins

Lymphadenectomy

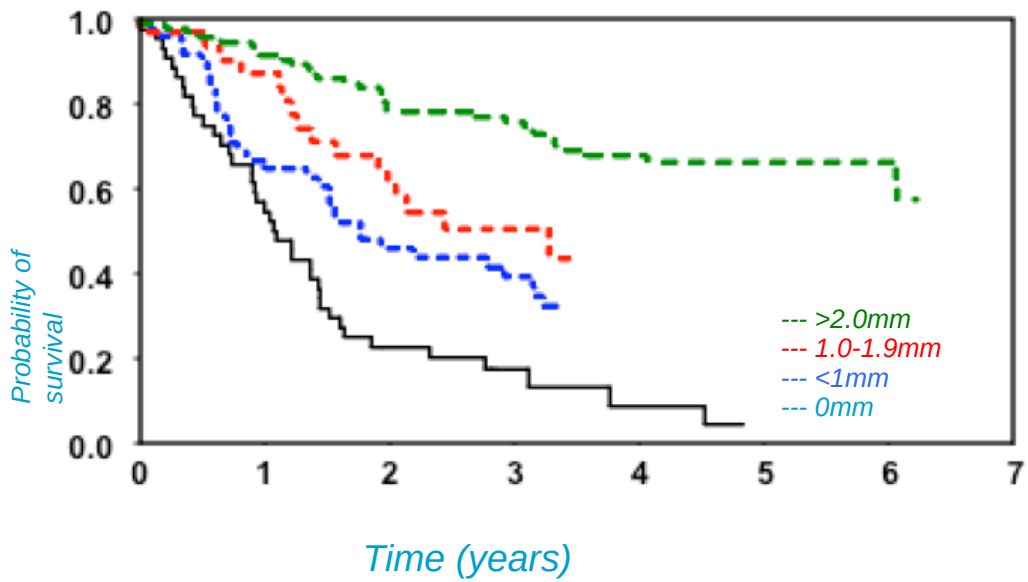
Resection Margin and Survival



Barbour et al. Ann Surg 246: 1-8

Circumferential resection margin (CRM) size correlates with overall survival

Prospective database, single institution study, N = 229



CRM	n	Median Survival (95% CI)
Positive	45	1.2 yrs (0.9-1.4)
<1mm	48	1.9 yrs (1.4-3.2)
1.0-1.9mm	31	3.5 yrs (2.0–no upper CI)
≥ 2.0mm	105	Not reached

- *CRM size is a significant prognostic factor for overall survival*
- *40.6% of patients in this study had a CRM <1mm*
- *Post operative chemoradiation did not alter survival in patients with CRM <1mm*
- *BUT smaller CRM may just reflect a larger tumour*

Landau et al., ESMO 2010 (Abstract 711PD)

CRM in Neoadjuvant Trials

	CS	S	CF	ECX	CXRT	S
OEO2	25%	28%				
OEO5			41%	33%		
CROSS					8%	30%

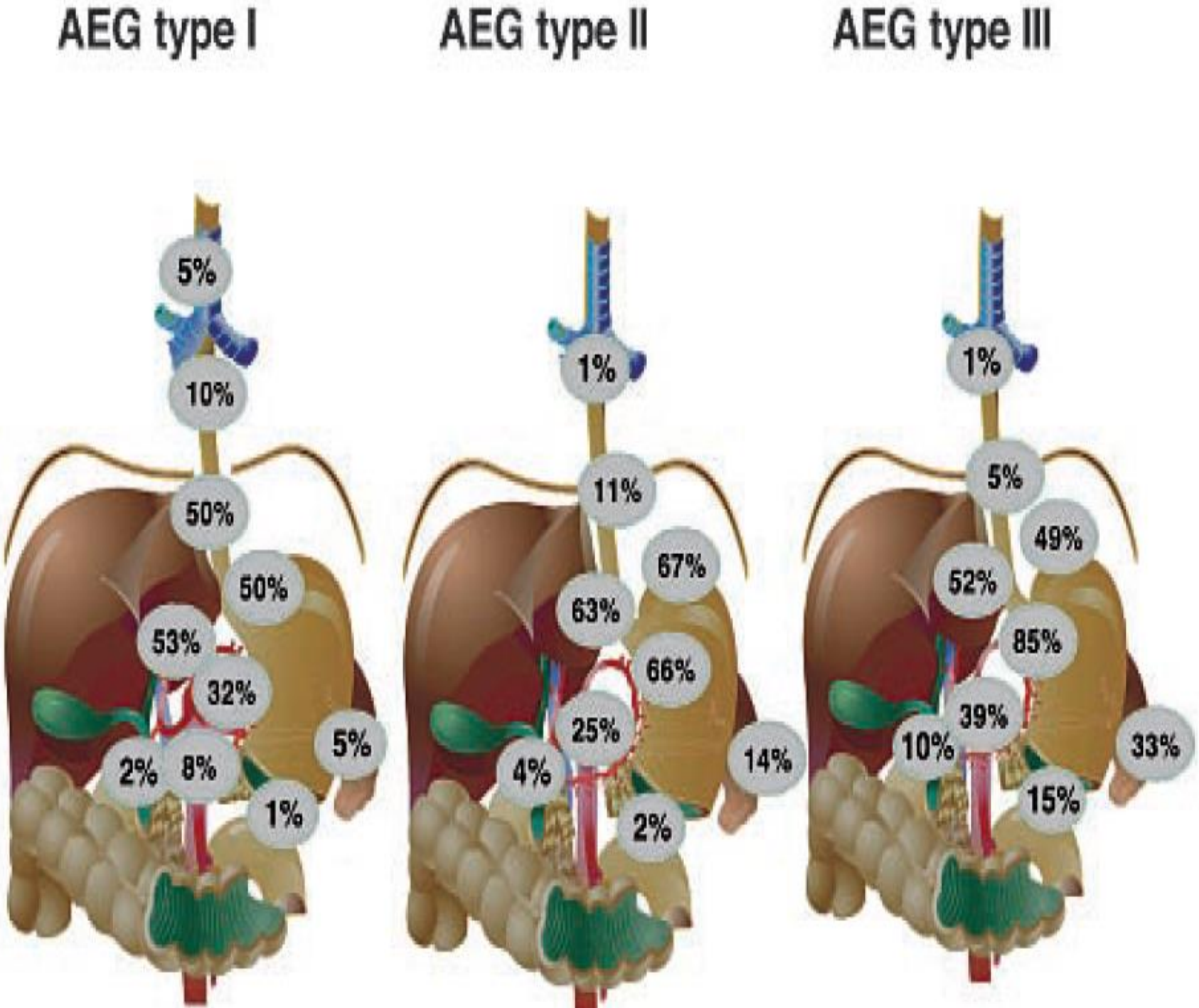
Radical Surgery – 13% - 2/62

Operation Selection

Surgical Approach

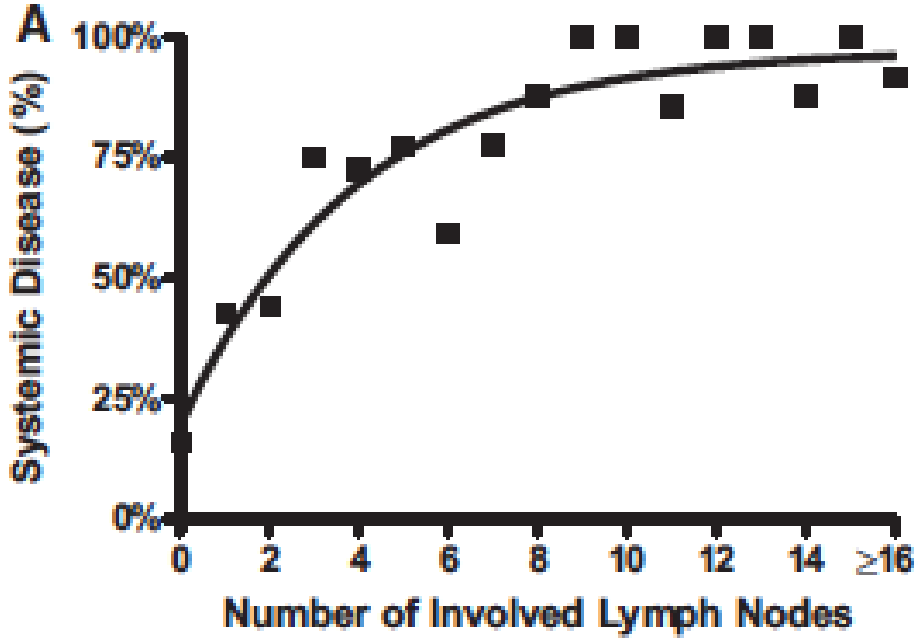
Margins

Lymphadenectomy


AEG type I
AEG type II
AEG type III
5%
10%
50%
50%
53%
32%
2%
8%
5%
1%
1%
11%
67%
63%
66%
25%
4%
14%
2%
1%
5%
49%
52%
85%
39%
10%
33%
15%

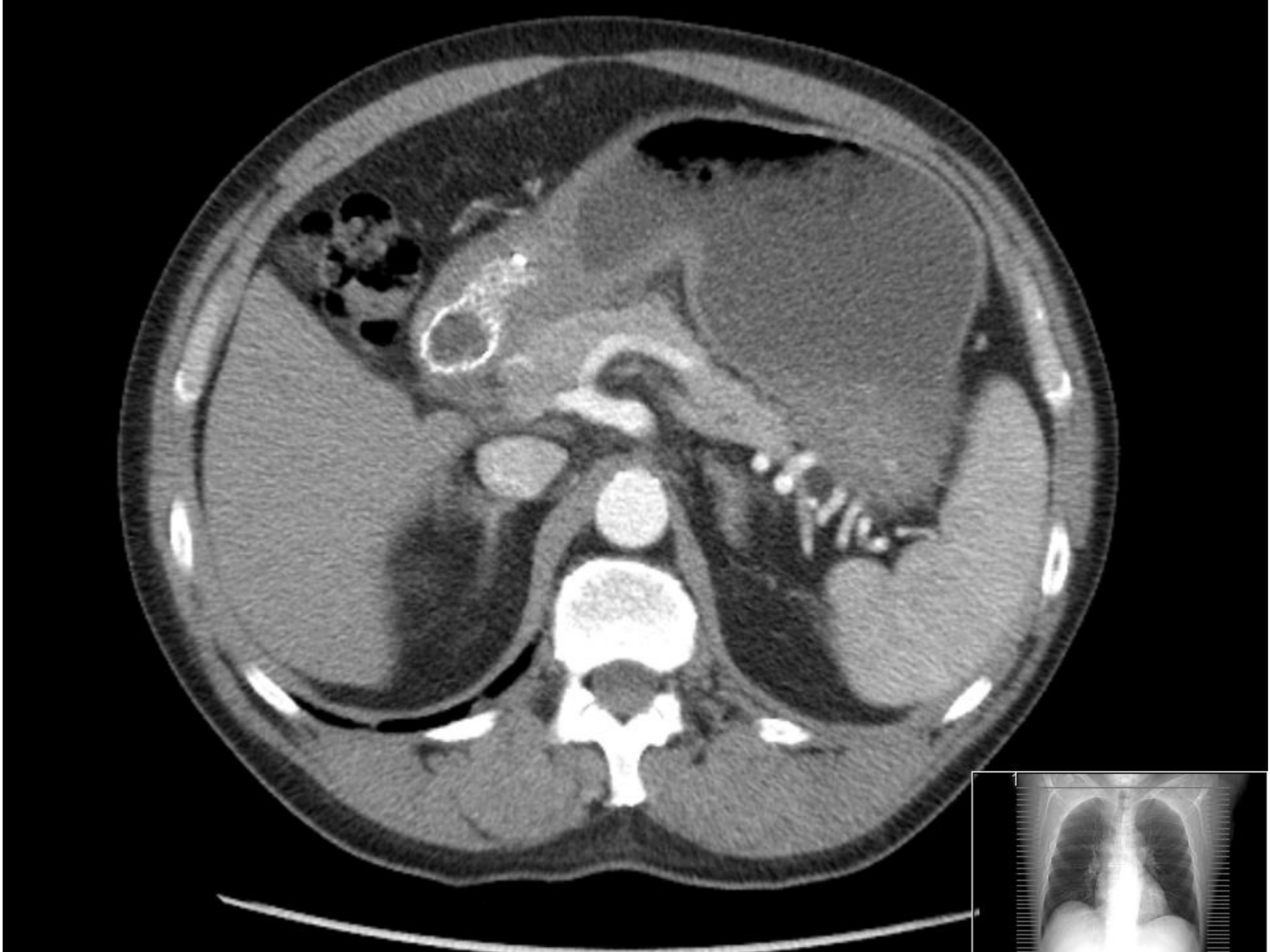
Risk of Systemic Disease and Number of Nodes Involved

Peyre et al 2008



# Involved Nodes	0	1	2	3	4	5	6	7	≥8
# Patients	183	54	34	32	29	22	22	9	67

Peyre et al 2008 Ann Surg 248: 979-985



INCURABLE DISEASE
Palliative Intent

Quality of life vs Quantity of life

Patient Wishes

Quality of Life

Resection vs Chemotherapy ?

Subtotal vs Total Gastrectomy ?

Palliative Resection

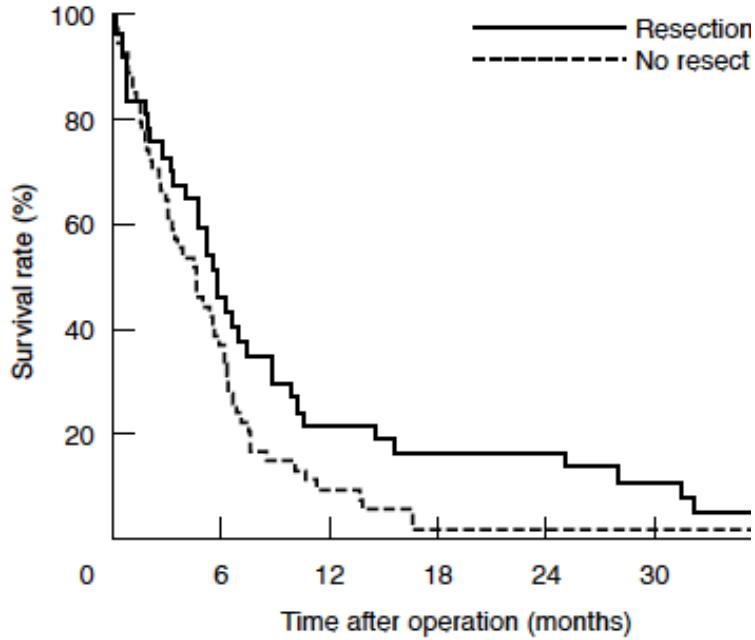
Dutch D1 vs D2 trial

295 / 996 (29%) incurable

T^+	macroscopically irresectable
H^+	liver metastasis
P^+	peritoneal metastasis
$N4^+$	distant lymph nodes

Hartgrink et al Br J Surg 2002, 89:1438

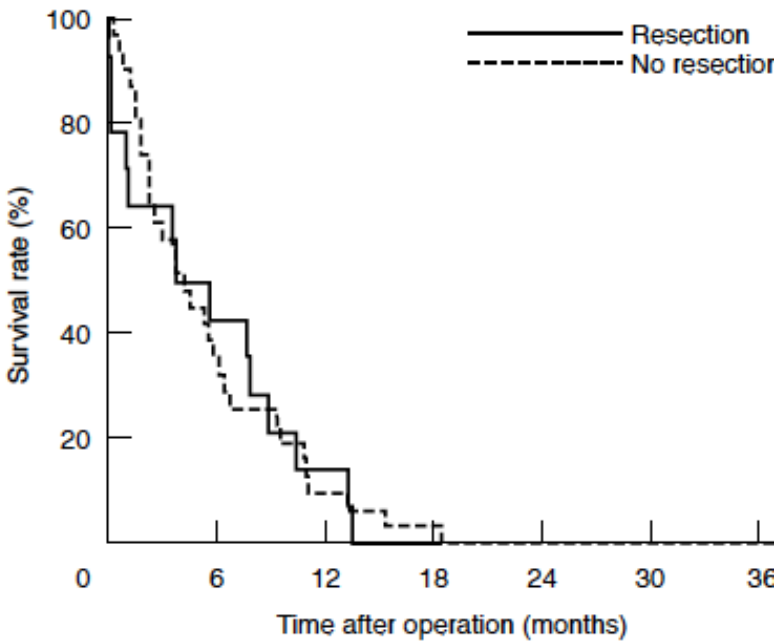
Palliative Surgery



No. at risk

Resection	37	8	6
No resection	54	5	1

Fig. 2 Survival following resection and no resection in patien
ıged 70 years or less and with two or more positive signs of
ncurability. $P = 0{\cdot}07$ (log rank test)



). at risk

Resection	14	2	0	0
No resection	31	3	0	0

ı. 4 Survival following resection and no resection in patients
ed more than 70 years and with two or more positive signs of
curability. $P = 0{\cdot}82$ (log rank test)

Palliative Surgery Selection

ASA I & II

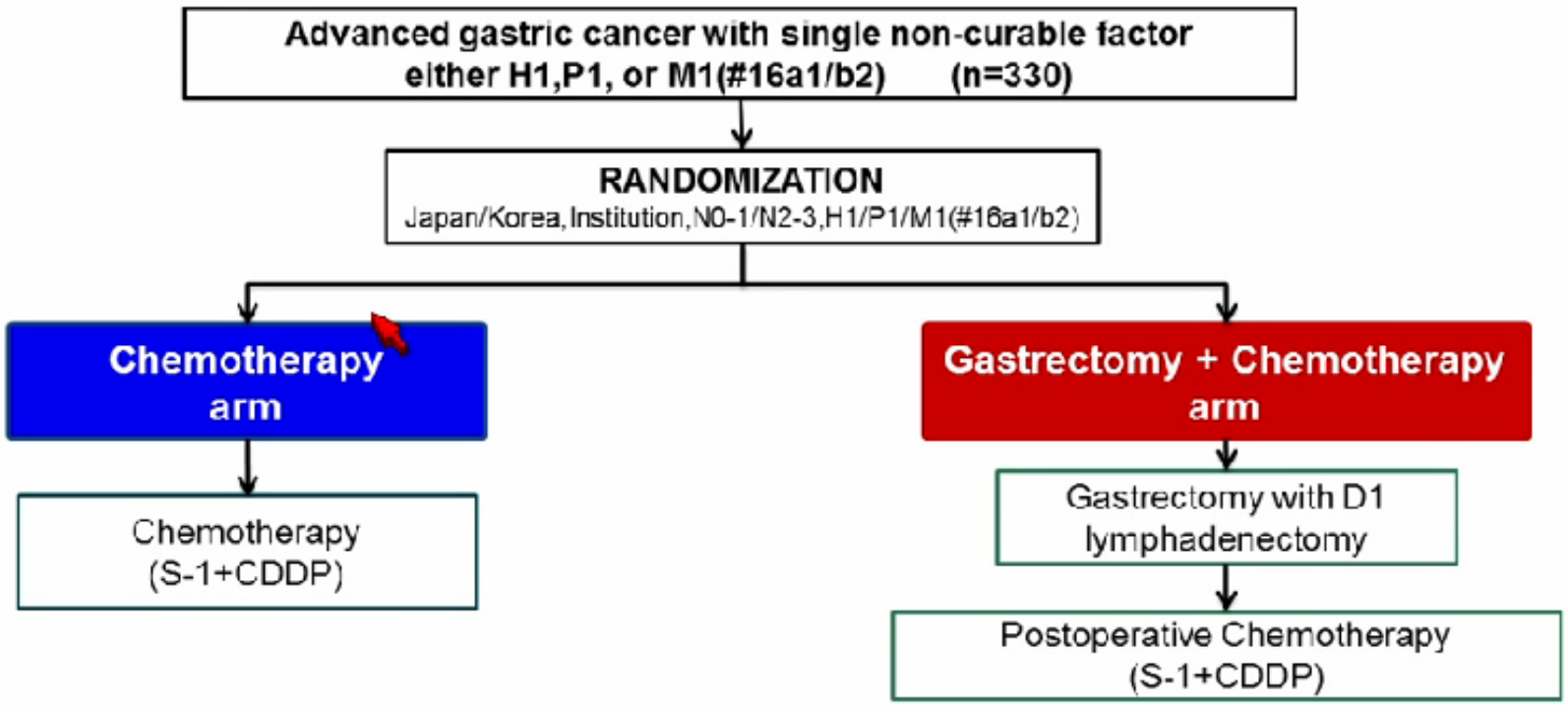
Non – R0 resection

Single site solid organ metastasis

Localised peritoneal disease without signet ring cancer

(Robb et al 2012)

REGATTA study design



- Primary endpoint: Overall survival
- Secondary endpoints: Progression-free survival, Adverse events

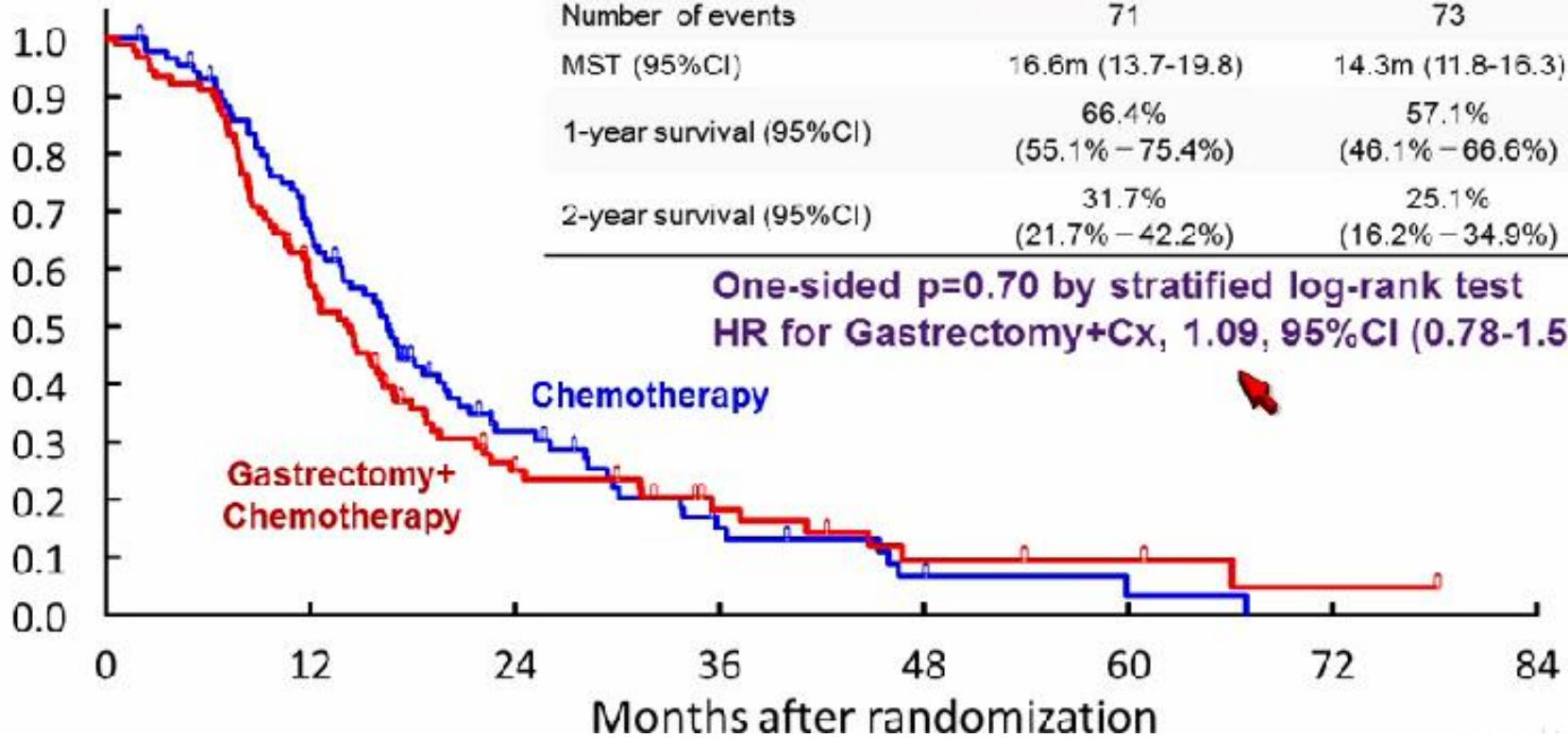
Recruitment: 330 patients

To detect an 10% improvement in 2-yr OS from 20-30%

HR = 0.75; 1-side αt= 0.05; 80% power

Yang et al ASCO 2015

Overall survival



	Chemotherapy n=86	Gastrectomy+Cx n=89
Number of events	71	73
MST (95%CI)	16.6m (13.7-19.8)	14.3m (11.8-16.3)
1-year survival (95%CI)	66.4% (55.1% – 75.4%)	57.1% (46.1% – 66.6%)
2-year survival (95%CI)	31.7% (21.7% – 42.2%)	25.1% (16.2% – 34.9%)

One-sided p=0.70 by stratified log-rank test
HR for Gastrectomy+Cx, 1.09, 95%CI (0.78-1.52)

Yang et al ASCO 2015

REGATTA

Metastasis Site	Chemotherapy	Gastrectomy + Chemotherapy
Liver	5 (6%)	11 (12%)
Peritoneum	66 (77%)	65 (73%)
Para-aortic node	11 (13%)	13 (15%)
Missing	4 (5%)	0

Journal of Surgical Oncology 2015;111:1021–1027

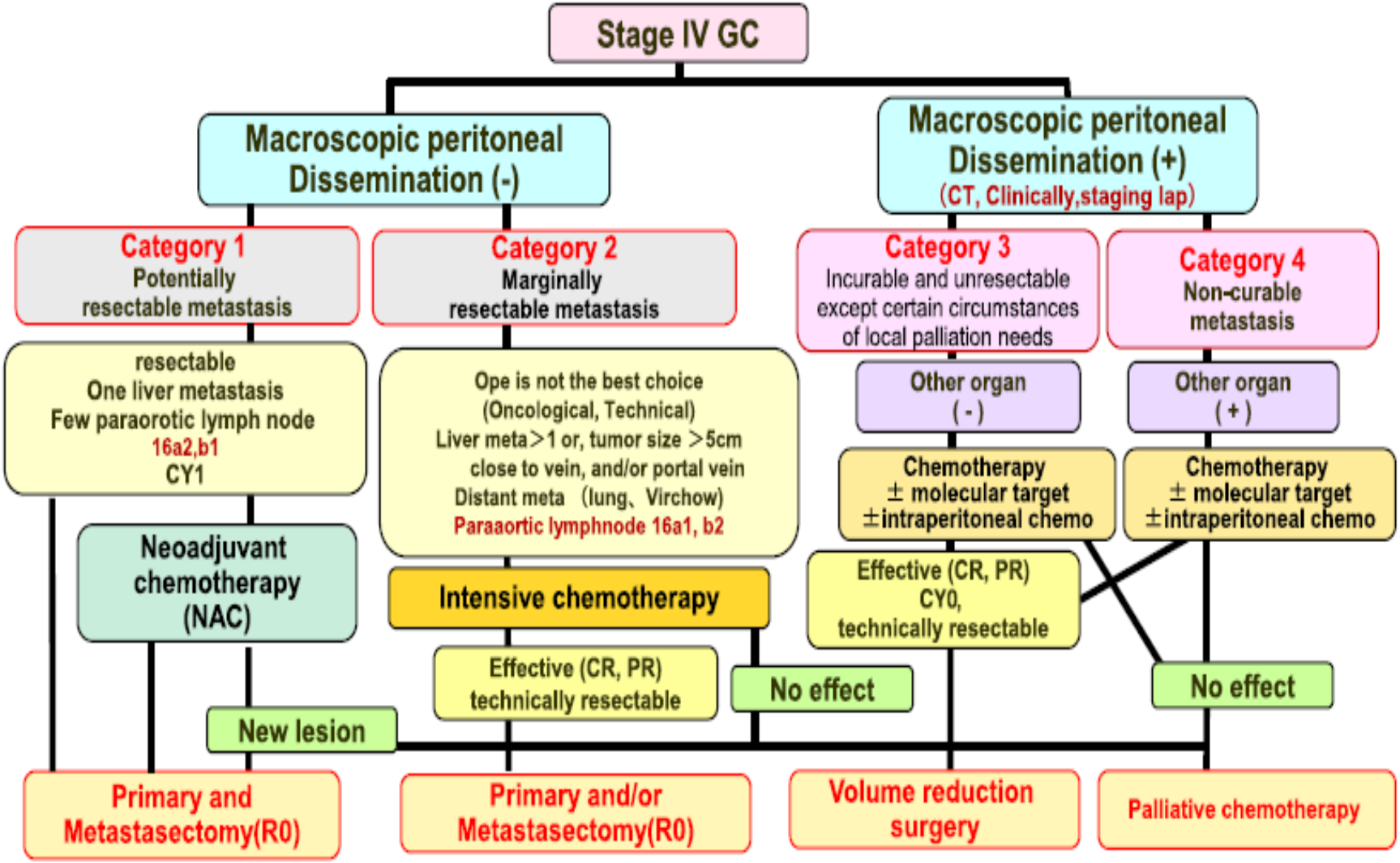
Hepatic Resection for Gastric Cancer Liver Metastases: A Systematic Review and Meta-Analysis

FAUSTO PETRELLI, MD, ANDREA COINU, MD, MARY CABIDDU, MD, MARA GHILARDI, MD, KAREN BORGONOVO, MD, VERONICA LONATI, AND SANDRO BARNI, MD
Department of Oncology, Division of Medical Oncology, Azienda Ospedaliera Treviglio, Treviglio (BG), Italy

23 trials including 870 patients

Median survival 22 months

5-y-surv.	*all*	*23,9 %*
	synchronous	*22,6 %*
	metachronous	*30,0 %*



OLIGOMETASTATIC DISEASE

Yoshida, Kodera et al Gastric Cancer 2016

Surgery

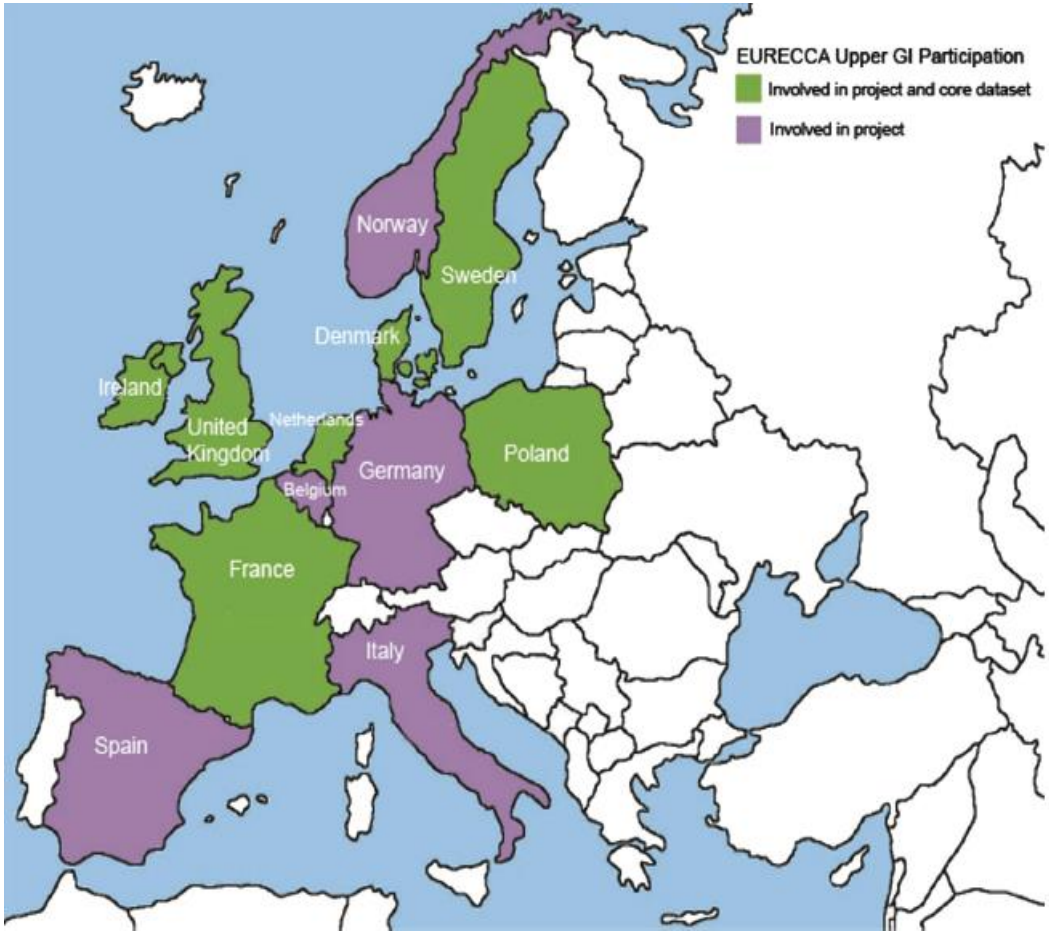
Quality Assurance

EUREGA
EUROPEAN REGISTRATION OF CANCER CARE

- *13 countries affiliated to EURECCA upper GI group*

Data source

- *Registry*
- *National audit*
- *National society*
- *National audit*

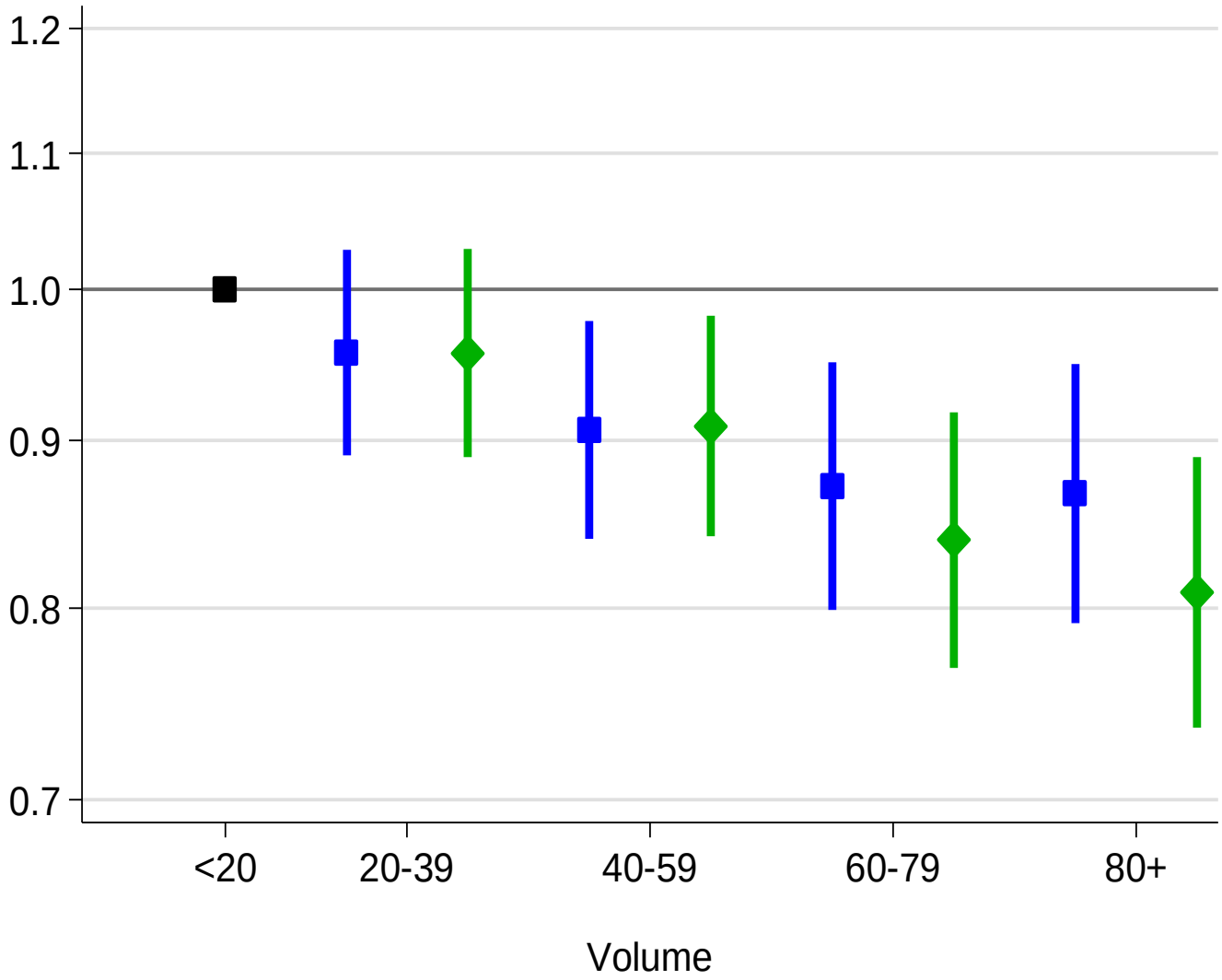


ECCO ESSENTIAL REQUIREMENTS FOR QUALITY CANCER CARE

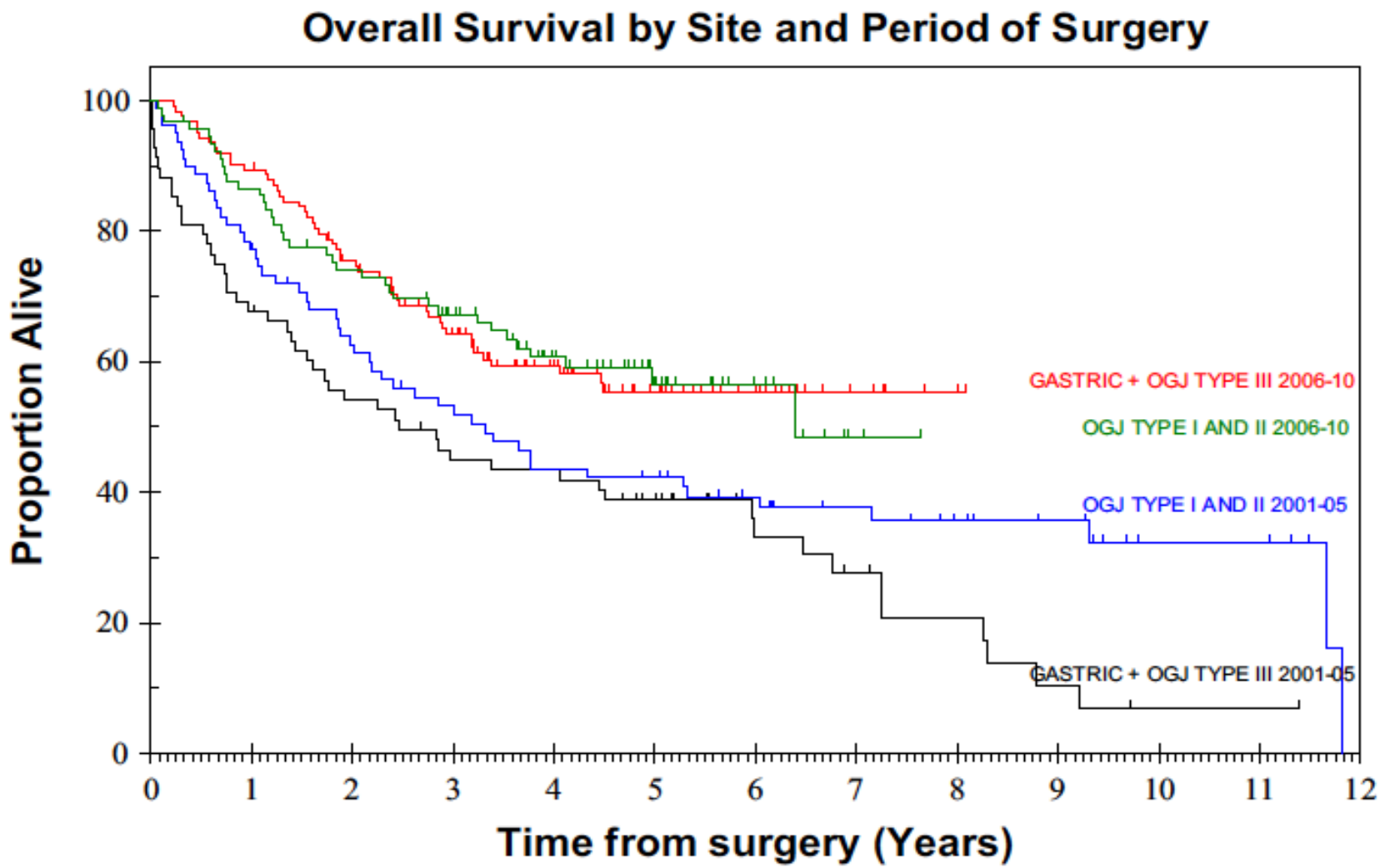
OESOPHAGEAL / GASTRIC CANCER

Multidisciplinary standards for service and management of oesophageal and gastric cancer

HR according to hospital volume



Adjusted for sex, age, deprivation, co-morbidity score, type of cancer and resection quintile



Fontana et al *Gastric Cancer* 2016

Nodal Yield
MAGIC vs ST03

MAGIC (2006)

< 15	15 - 20	20 - 25	> 25
104 (48%)	47 (22%)	24 (11%)	43 (19%)

ST03 (2017)

<15	15-24	>25
141 (17%)	277 (33%)	410 (50%)

Thank you for your attention