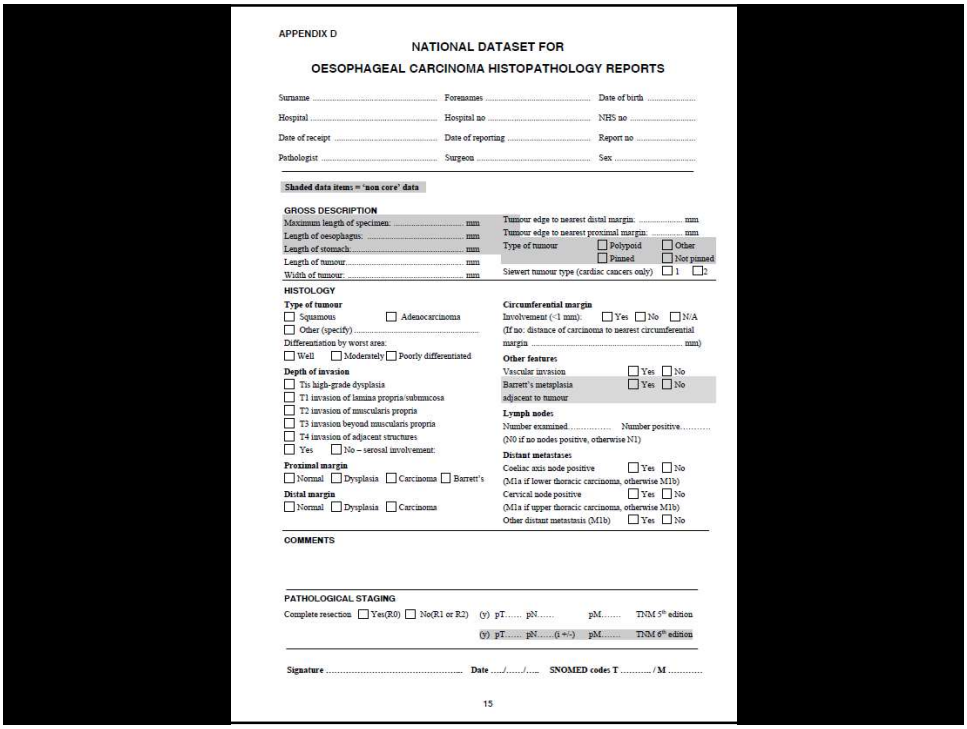
Upper GI Datasets revisited

N.Mapstone

oesophagus: core old

- maximum tumour diameter
- Siewert tumour type
- maximum depth of invasion
- polypoid or other morphology
- histological type
- grade
- serosal involvement
- resection margins (x3)
- vascular invasion
- lymph node state



APPENDIX D

NATIONAL DATASET FOR

OESOPHAGEAL CARCINOMA HISTOPATHOLOGY REPORTS

Surname ..... Forenames ..... Date of birth .....

Hospital ..... Hospital no ..... NHS no .....

Date of receipt ..... Date of reporting ..... Report no .....

Pathologist ..... Surgeon ..... Sex .....

Shaded data items = 'non core' data

GROSS DESCRIPTION

Maximum length of specimen: ..... mm

Length of oesophagus: ..... mm

Length of stomach: ..... mm

Length of tumour: ..... mm

Width of tumour: ..... mm

Tumour edge to nearest distal margin: ..... mm

Tumour edge to nearest proximal margin: ..... mm

Type of tumour ☐ Polypoid ☐ Other ☐ Pinned ☐ Not pinned

Siewert tumour type (cardiac cancers only) ☐ 1 ☐ 2

HISTOLOGY

Type of tumour

☐ Squamous ☐ Adenocarcinoma

☐ Other (specify) .....

Differentiation by worst area:

☐ Well ☐ Moderately ☐ Poorly differentiated

Depth of invasion

☐ Tis high-grade dysplasia

☐ T1 invasion of lamina propria/submucosa

☐ T2 invasion of muscularis propria

☐ T3 invasion beyond muscularis propria

☐ T4 invasion of adjacent structures

☐ Yes ☐ No – serosal involvement:

Proximal margin

☐ Normal ☐ Dysplasia ☐ Carcinoma ☐ Barrett's

Distal margin

☐ Normal ☐ Dysplasia ☐ Carcinoma

Circumferential margin

Involvement (<1 mm): ☐ Yes ☐ No ☐ N/A

(If no. distance of carcinoma to nearest circumferential margin ..... mm)

Other features

Vascular invasion ☐ Yes ☐ No

Barrett's metaplasia adjacent to tumour ☐ Yes ☐ No

Lymph nodes

Number examined..... Number positive.....

(N0 if no nodes positive, otherwise N1)

Distant metastases

Coeliac axis node positive ☐ Yes ☐ No

(M1a if lower thoracic carcinoma, otherwise M1b)

Cervical node positive ☐ Yes ☐ No

(M1a if upper thoracic carcinoma, otherwise M1b)

Other distant metastasis (M1b) ☐ Yes ☐ No

COMMENTS

PATHOLOGICAL STAGING

Complete resection ☐ Yes(R0) ☐ No(R1 or R2) (y) pT..... pN..... pM..... TNM 5th edition

(y) pT..... pN.....(i +/-) pM..... TNM 6th edition

Signature ..... **Date** ..../...../..... **SNOMED codes T** ..... / **M** .....

15

oesophagus: core new

- specimen preparation
- maximum tumour diameter 3 dimensons
- Siewert tumour type more details on location
- maximum depth of invasion
- polypoid or other morphology
- histologial type
- grade
- serosal involvement
- resection margins (x3)
- vascular invasion and perineural invasion
- lymph node state
- peritoneal seedlings
- neoadjuvant effect / regression grade

Oesophagus non core:old

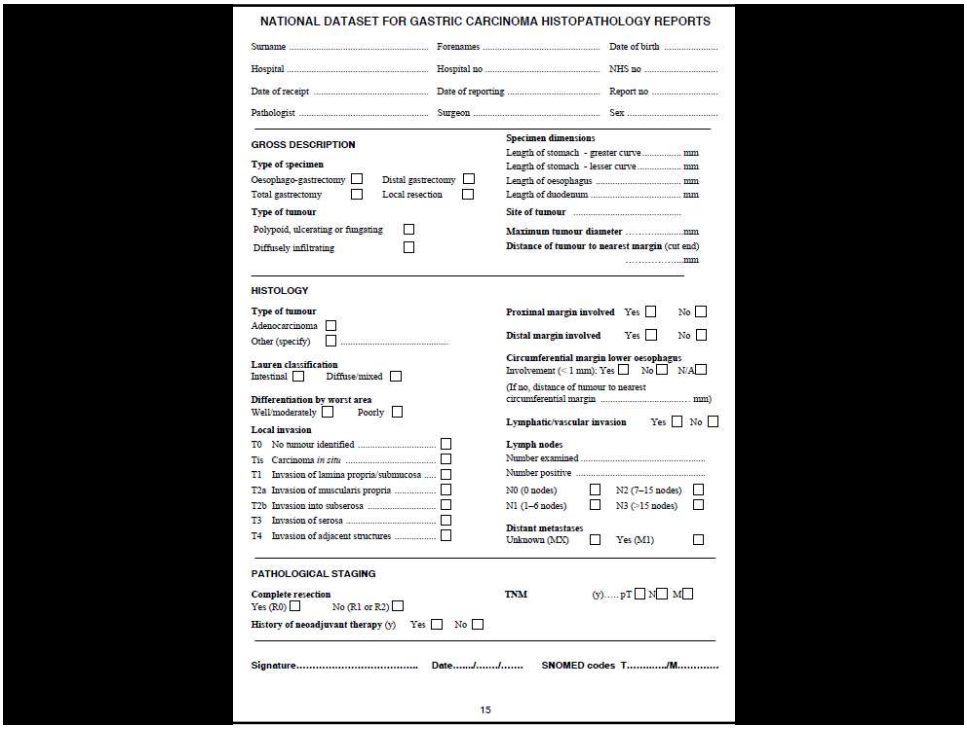
- specimen preparation
- overall dimensions
- Barrett's
- neoadjuvant effect
- molecular data

Oesophagus non core:new

- ~~specimen preparation~~
- overall dimensions
- dysplasia
- Barrett's
- ~~neoadjuvant effect~~
- molecular data
- block key

stomach core: old

- tumour site, size, morphology
- maximum depth of invasion
- histological type
- grade
- resection margins (x3)
- lymph nodes
- vascular invasion



NATIONAL DATASET FOR GASTRIC CARCINOMA HISTOPATHOLOGY REPORTS

Surname ..... Forenames ..... Date of birth .....

Hospital ..... Hospital no ..... NHS no .....

Date of receipt ..... Date of reporting ..... Report no .....

Pathologist ..... Surgeon ..... Sex .....

GROSS DESCRIPTION

Type of specimen

Oesophago-gastrectomy ☐ Distal gastrectomy ☐

Total gastrectomy ☐ Local resection ☐

Type of tumour

Polypoid, ulcerating or fungating ☐

Diffusely infiltrating ☐

Specimen dimensions

Length of stomach - greater curve ..... mm

Length of stomach - lesser curve ..... mm

Length of oesophagus ..... mm

Length of duodenum ..... mm

Site of tumour .....

Maximum tumour diameter ..... mm

Distance of tumour to nearest margin (cut end) ..... mm

HISTOLOGY

Type of tumour

Adenocarcinoma ☐

Other (specify) ☐ .....

Lauren classification

Intestinal ☐ Diffuse/mixed ☐

Differentiation by worst area

Well/moderately ☐ Poorly ☐

Local invasion

T0 No tumour identified ..... ☐

Tis Carcinoma *in situ* ..... ☐

T1 Invasion of lamina propria/submucosa .... ☐

T2a Invasion of muscularis propria ..... ☐

T2b Invasion into subserosa ..... ☐

T3 Invasion of serosa ..... ☐

T4 Invasion of adjacent structures ..... ☐

Proximal margin involved Yes ☐ No ☐

Distal margin involved Yes ☐ No ☐

Circumferential margin lower oesophagus

Involvement (< 1 mm): Yes ☐ No ☐ N/A ☐

(If no, distance of tumour to nearest circumferential margin ..... mm)

Lymphatic/vascular invasion Yes ☐ No ☐

Lymph nodes

Number examined .....

Number positive .....

N0 (0 nodes) ☐ N2 (7–15 nodes) ☐

N1 (1–6 nodes) ☐ N3 (>15 nodes) ☐

Distant metastases

Unknown (MX) ☐ Yes (M1) ☐

PATHOLOGICAL STAGING

Complete resection

Yes (R0) ☐ No (R1 or R2) ☐

TNM (y)..... pT ☐ N ☐ M ☐

History of neoadjuvant therapy (y) Yes ☐ No ☐

Signature..... **Date**...../...../..... **SNOMED codes** T...../M.....

15

stomach core: new

- tumour site (detail) , size, morphology
- maximum depth of invasion
- histological type
- grade
- resection margins (x3)
- lymph nodes
- vascular invasion and depth
- peritoneal seedlings
- neoadjuvant effect / regression grade

stomach non-core: old

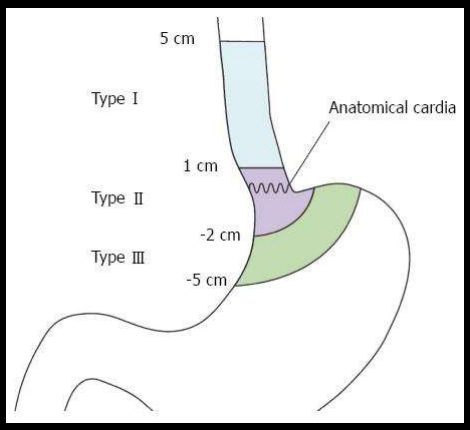
- specimen dimensions
- atrophy
- intestinal metaplasia
- dysplasia
- helicobacter infection
- regression grade
- molecular data

stomach non-core: new

- type of resection
- specimen dimensions
- Bormann classification
- atrophy
- intestinal metaplasia
- dysplasia
- helicobacter infection
- ~~regression grade~~
- molecular data

timescales

- 2007 v2 oesophagus and stomach datasets
- 2009 TNM 7
- 2016 v3 oesophagus and stomach datasets
- 2017 TNM 8



international union against cancer

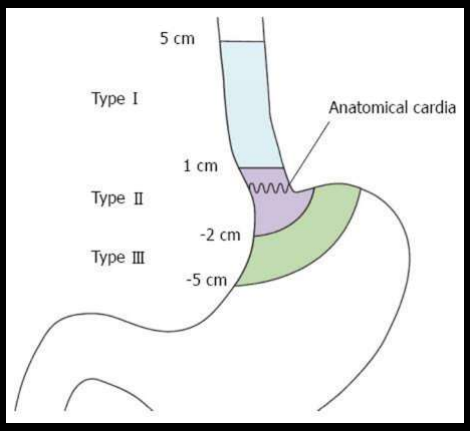
uicc global cancer control

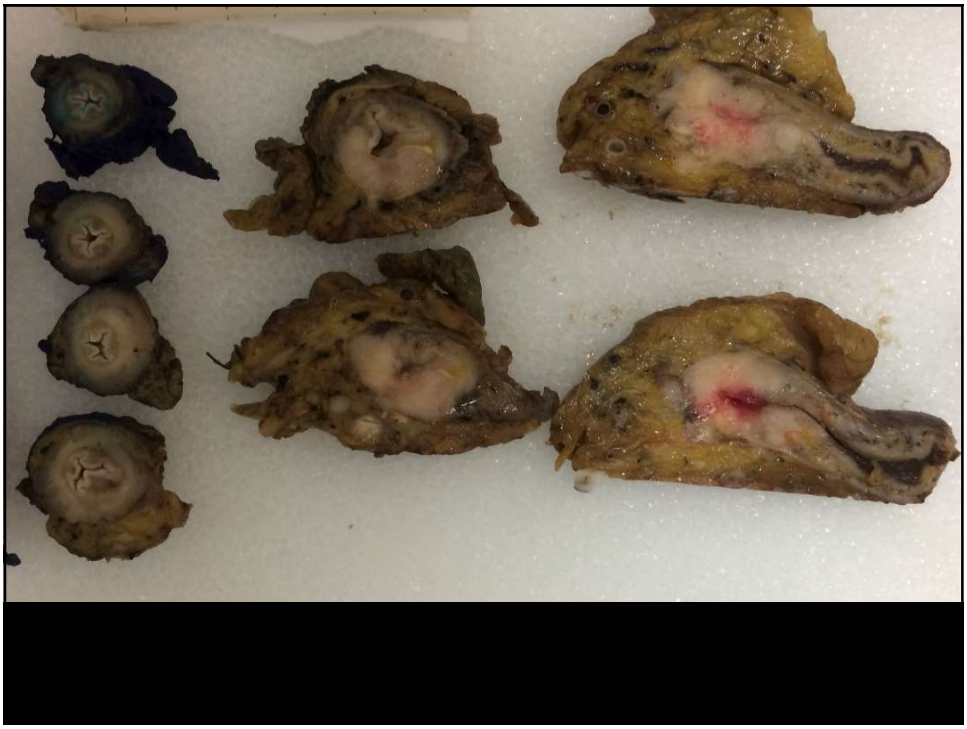
TNM-7
Oesophagogastric junction tumours

A tumour the epicenter of which is within 5 cm of the esophagogastric junction and also extends into the oesophagus is classified and staged according to the **oesophageal** scheme

All other tumours with an epicenter in the stomach greater than 5 cm from the oesophagogastric junction or those within 5 cm of the EGJ *without* extension into the oesophagus are staged using the **gastric** carcinoma scheme

INTERNATIONAL UNION AGAINST CANCER
www.uicc.org


5 cm
Type I
Anatomical cardia
1 cm
Type II
-2 cm
Type III
-5 cm



Adenocarcinoma

Clinical Stage

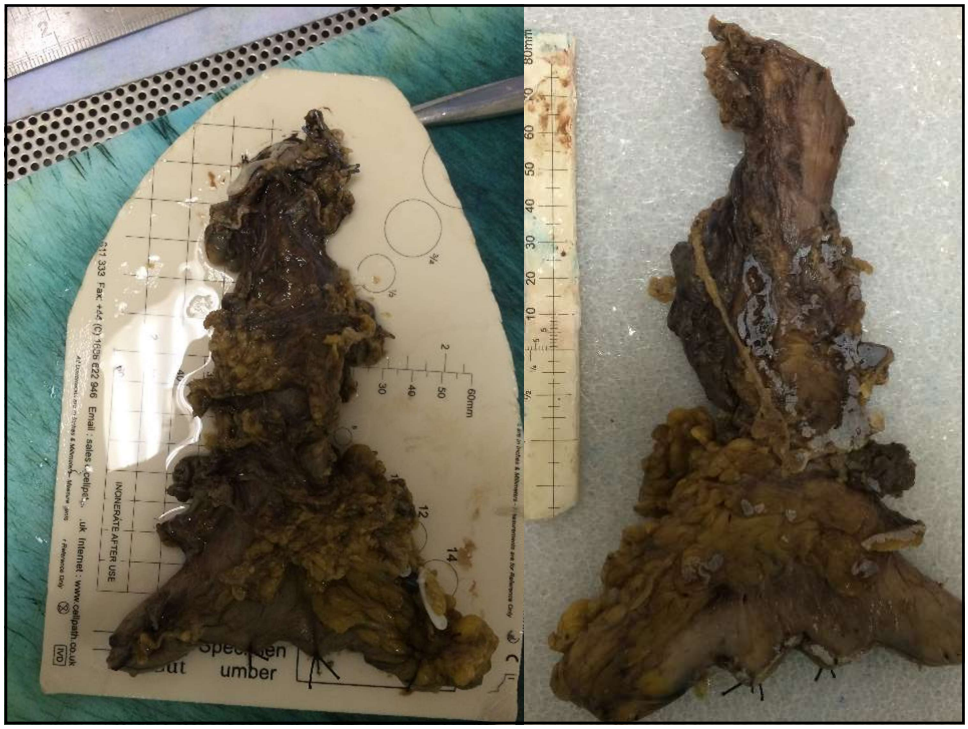
	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N0	M0
Stage III	T1	N2	M0
	T2	N1, N2	M0
	T3,T4a	N0, N1, N2	M0
Stage IVA	T4b	N0, N1, N2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

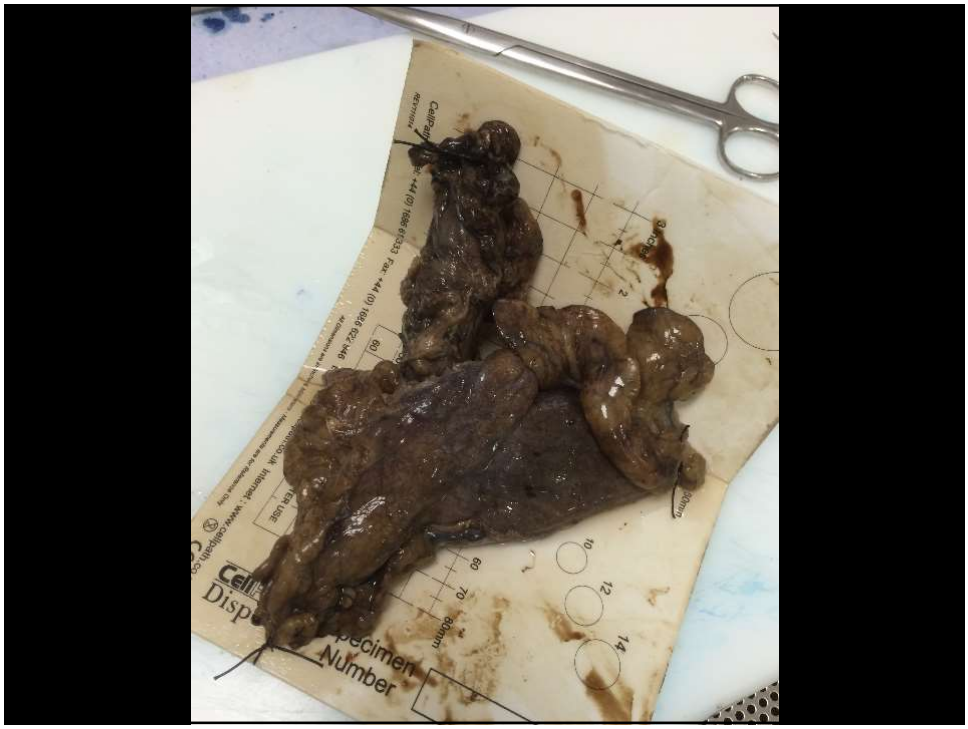
Pathological Stage

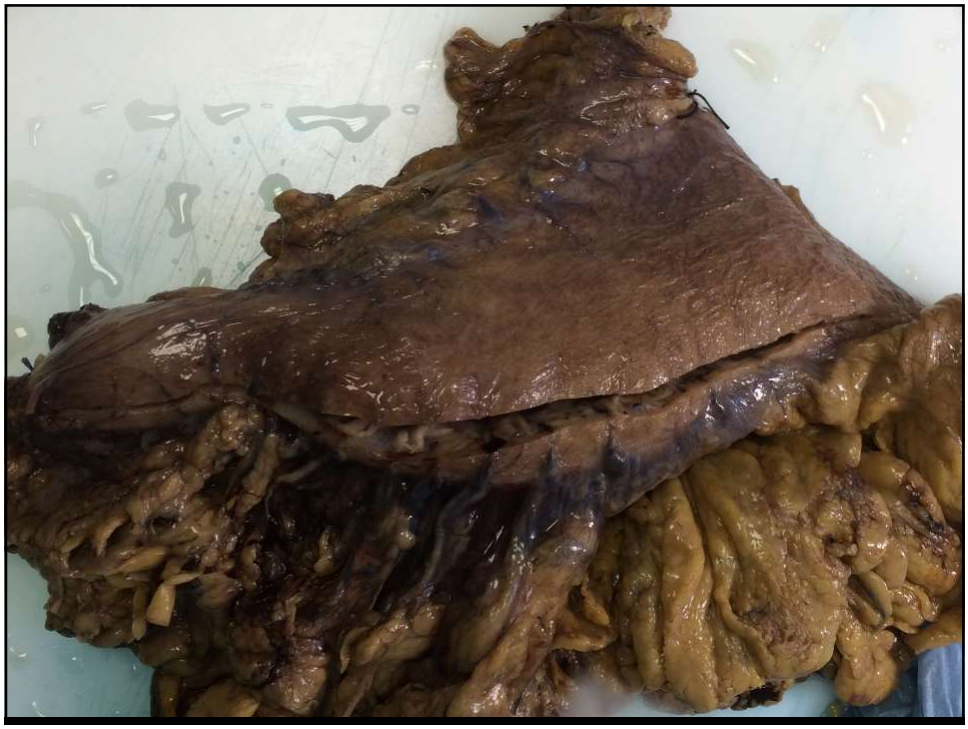
	T	N	M
Stage 0	Tis	N0	M0

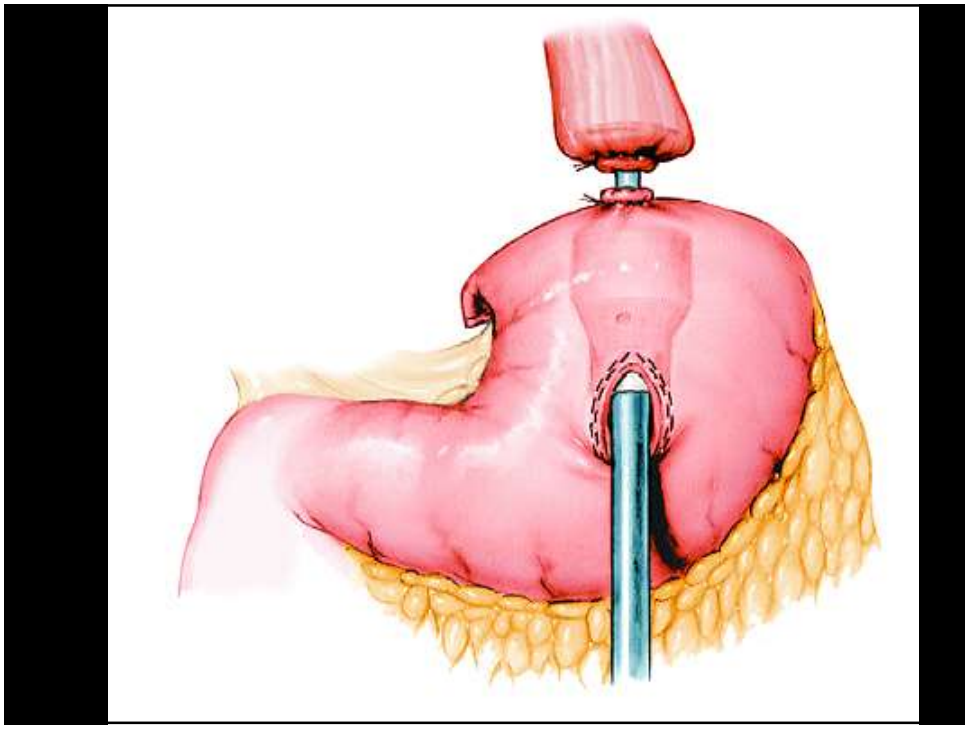
request form

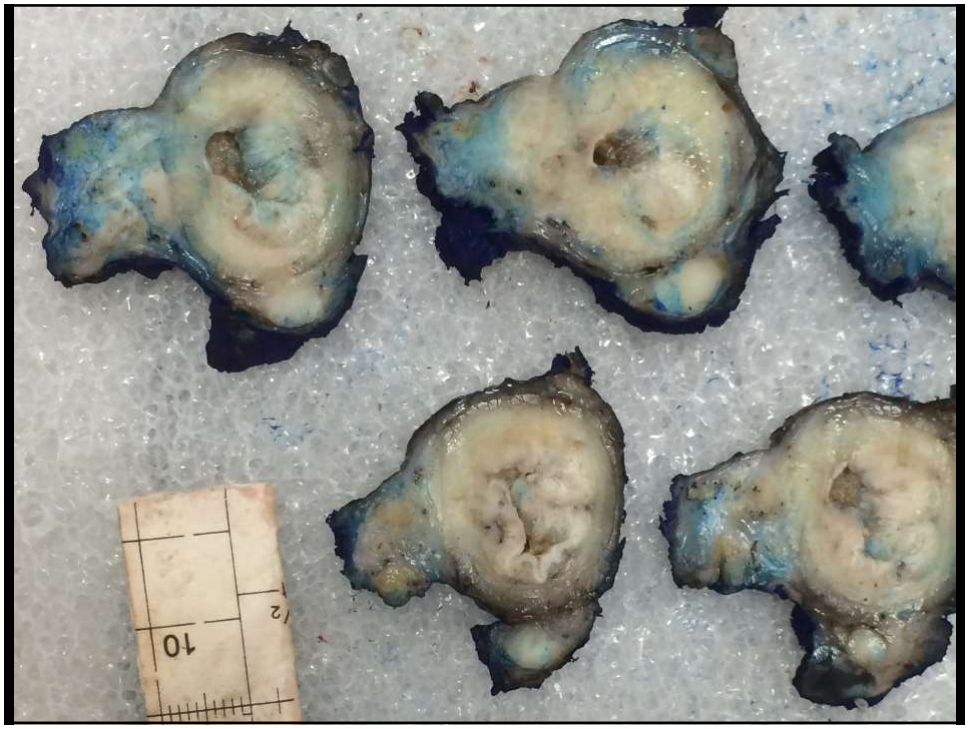
- site of tumour at diagnosis (mid or lower oesophagus; junctional; proximal/mid/distal stomach)
- tumour involvement of the OGJ
- pre-operative disease stage
- histological type of tumour
- previous histology (case number or name of the hospital where it was performed)
- history of neoadjuvant therapy
- type of resection
- whether the patient is enrolled in a clinical trial as a specific pathology procedure may need to be followed
- whether the patient is known to have hereditary gastric cancer as the pathology
- protocol for hereditary gastric cancer varies from that for sporadic gastric cancer. Details about specimen handling for hereditary gastric cancer are provided elsewhere.[9]

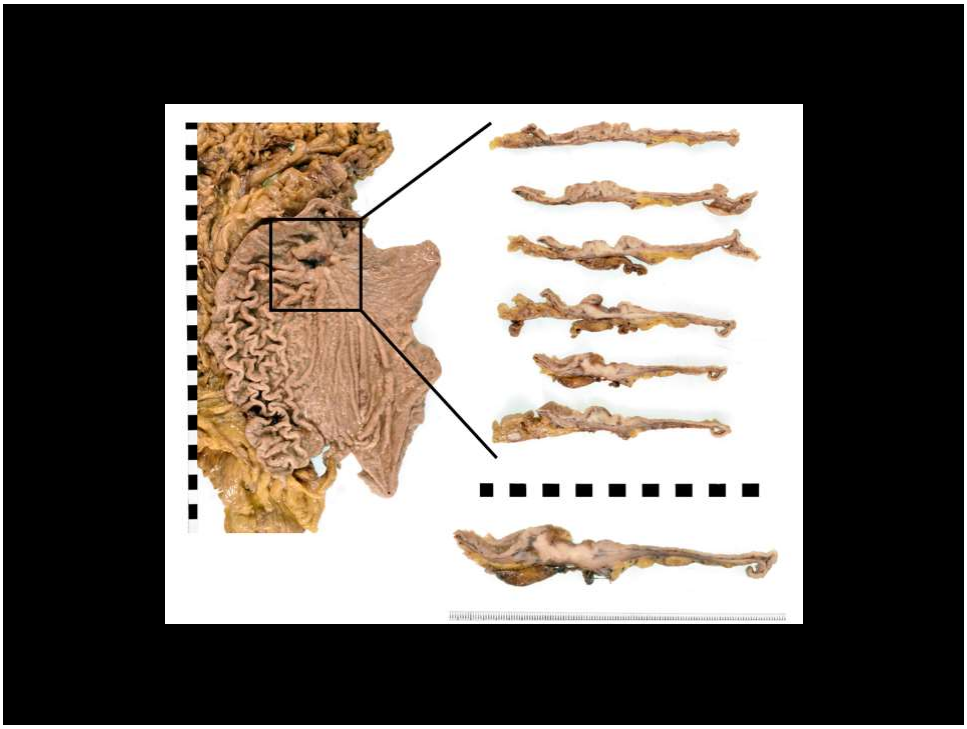



Specimen
Number

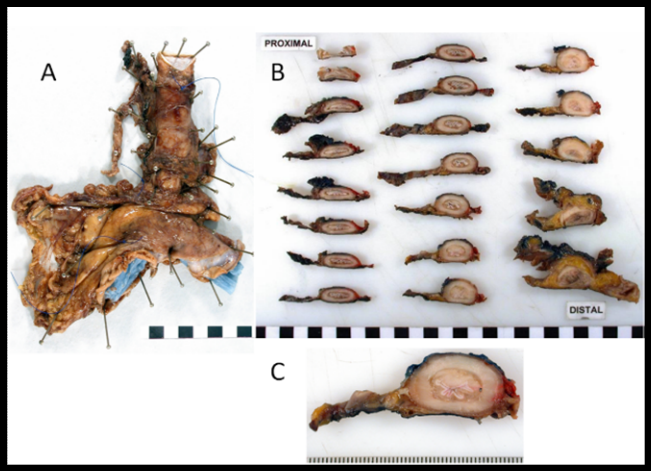









A
B



Tumour type

- Laurén,[12] Ming,[34] World Health Organisation,[1] Nakamura,[35] Mulligan,[36] Goseki[37] and Carneiro

Grade

In conformity with most other RCPath datasets, differentiation is recorded as being that of the highest (worst) grade in the tumour. Note, that according to the 'TNM helpdesk' grading of differentiation after pre-operative treatment should not be performed.

Resection margins

- R0
- R1
- R2

Resection margins

- Proximal
- Distal
- Radial

Table 1 Characteristics of studies included in the meta-analysis

Reference	Country	Definition of CRM	Total no. of patients	Tumour at CRM	Tumour ≤ 1 mm of CRM	No. with stage ≥ T3	Neoadjuvant therapy	Survival related to CRM positivity in multivariable analysis	Mean follow-up (months)	NO
Chao *et al.*[23] (2011)	Taiwan	CAP* and RCP	151	26 (17·2)	51 (33·8)	151 (100)	CRT	No	50·0	7
Deeter *et al.*[6] (2009)	USA	CAP* and RCP	135	16 (11·9)	83 (61·5)	135 (100)	CRT	Yes	37·2	8
Dexter *et al.*[7] (2001)	UK	RCP	135	NA	64 (47·4)	95 (70·4)	None	Yes	19·0	8
Griffiths *et al.*[11] (2006)	UK	RCP	249	NA	79 (31·7)	145 (58·2)	CT	Yes	70·0	9
Harvin *et al.*[8] (2012)	USA	CAP* and RCP	160	8 (5·0)	42 (26·3)	160 (100)	CRT	No	NA	7
Khan *et al.*[9] (2003)	UK	RCP	329	NA	67 (20·4)	267 (81·2)	None	No	60·0	9
Pultrum *et al.*[16] (2010)	The Netherlands	CAP and RCP*	98	25 (26)	47 (48)	58 (59)	None	Yes	37·0	9
Rao *et al.*[24] (2012)	UK	CAP and RCP*	115	17 (14·8)	57 (49·6)	80 (69·6)	CT	No	38·0	8
Saha *et al.*[25] (2009)	UK	RCP	105	NA	38 (36·2)	70 (66·7)	CT	Yes	26·0	8
Salih *et al.*[18] (2012)	UK	CAP and RCP*	232	38 (16·4)	89 (38·4)	171 (73·7)	CT	No	18·0	8
Scheepers *et al.*[17] (2009)	The Netherlands	CAP and RCP*	110	17 (15·5)	42 (38·2)	86 (78·2)	CT	Yes	NA	8
Sujendran *et al.*[26] (2008)	UK	RCP	242	NA	56 (23·1)	151 (62·4)	CT and CRT	Yes	NA	8
Thompson *et al.*[27] (2008)	Australia	RCP	240	NA	85 (35·4)	127 (52·9)	CRT	No	NA	8
Verhage *et al.*[19] (2011)	The Netherlands	CAP* and RCP	132	26 (19·7)	89 (67·4)	132 (100)	None	Yes	28·4	8

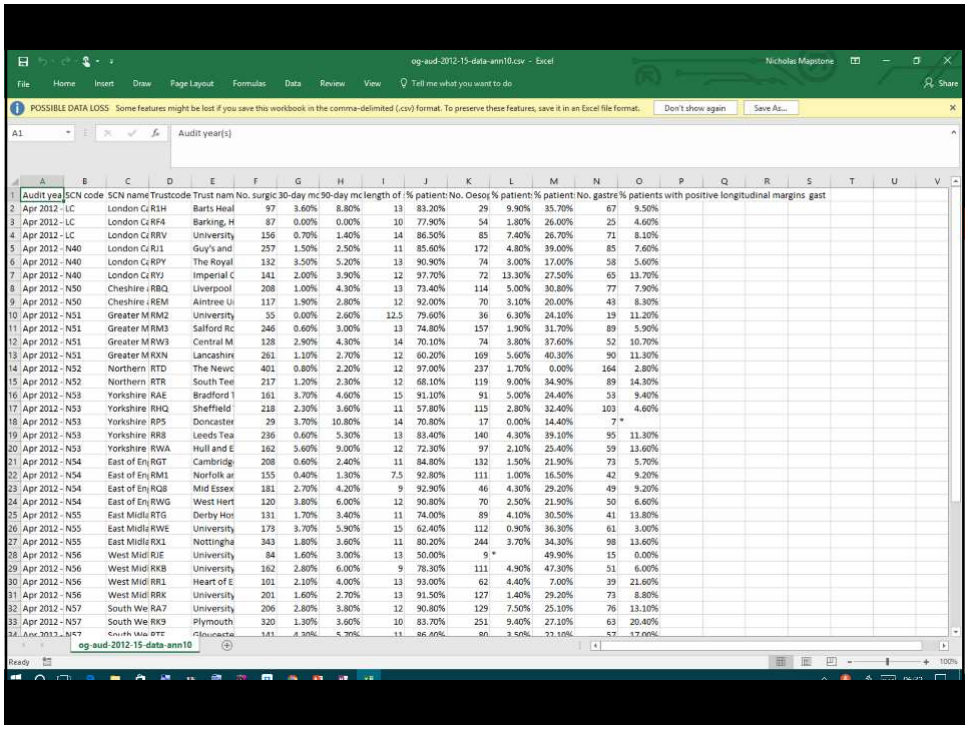
Values in parentheses are percentages. *Indicates the definition that was more prognostically significant in studies that used both definitions of circumferential resection margin (CRM) involvement. NO, Newcastle–Ottawa study quality score; CAP, College of American Pathologists (tumour at CRM); RCP, Royal College of Pathologists (tumour within 1 mm of CRM); CRT, neoadjuvant chemoradiotherapy; NA, data not available; CT, neoadjuvant chemotherapy.

Chan 2013

NOGCA 2014

Table 6-10
Percentage of patients with positive resection margins after a curative resection, in England and Wales

	Oesophagectomy		Gastrectomy		Total	
	n	Overall %	n	Overall %	n	Overall %
Positive longitudinal (proximal or distal) resection margin	98	3.7	144	9.1	242	5.7
Positive circumferential margin	685	27.7	113	10.5	798	22.5

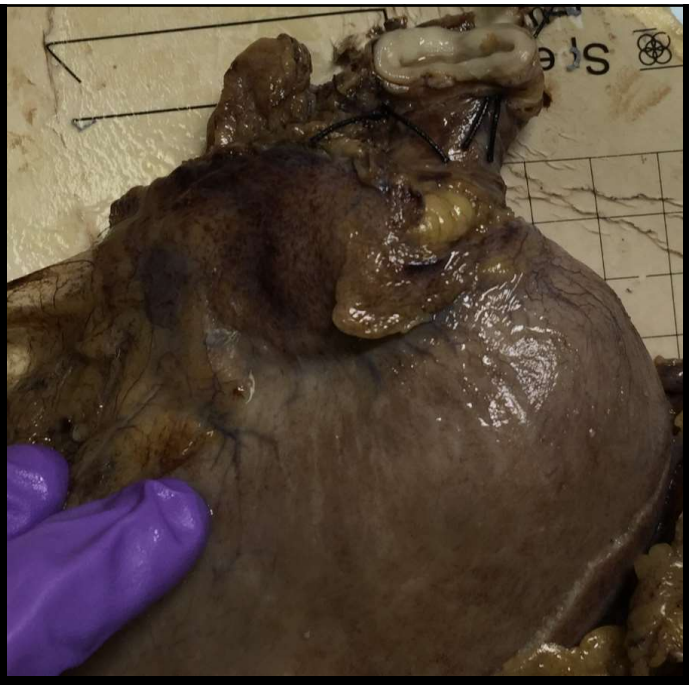


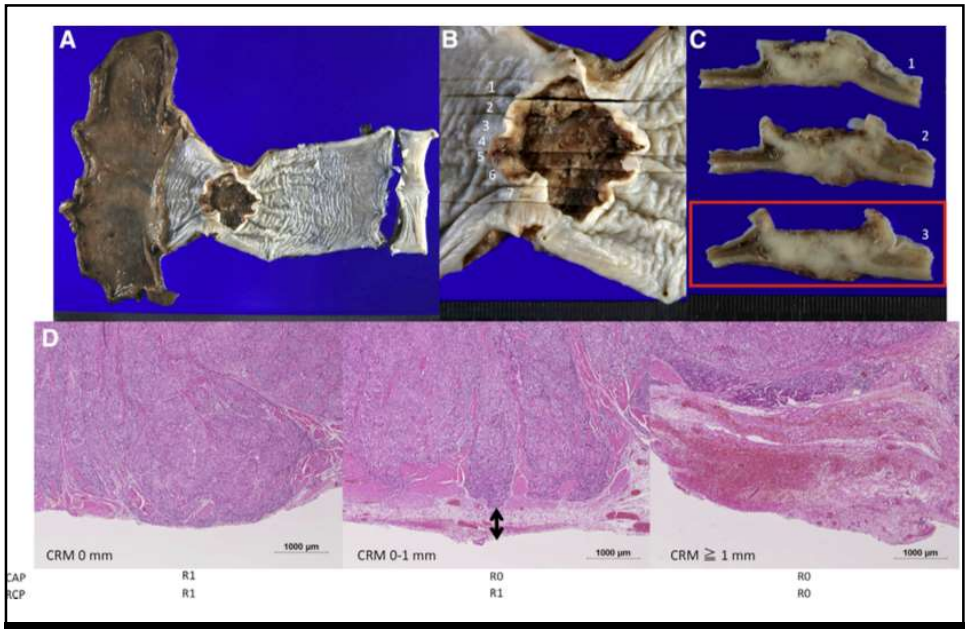
NOGCA 2016

Number of lymph nodes examined and positive resection margins

Annex 10 reports the metrics reported in England for the Clinical outcomes publication (COP) 2016 (volume, 30-day mortality, 90-day mortality) for both England and Wales, as well as the proportion of patients with adequate lymph nodes examined and proportion of patients with positive margins at the trust/health board level.

Guidelines suggest that the minimum number of lymph nodes required for staging the disease is at least 15 for both oesophagectomies and gastrectomies. Adequate lymph node resection enables more accurate staging, which may offer a survival benefit. This indicator will allow the surgical units to monitor their process of care and adherence to published standards of surgical care. We provide some initial figures on the number of lymph nodes examined, and will be undertaking further development work next year. This will focus on clarifying the most appropriate definition of the measure and the creation of a risk adjustment algorithm with adequate performance.





Okada 2016

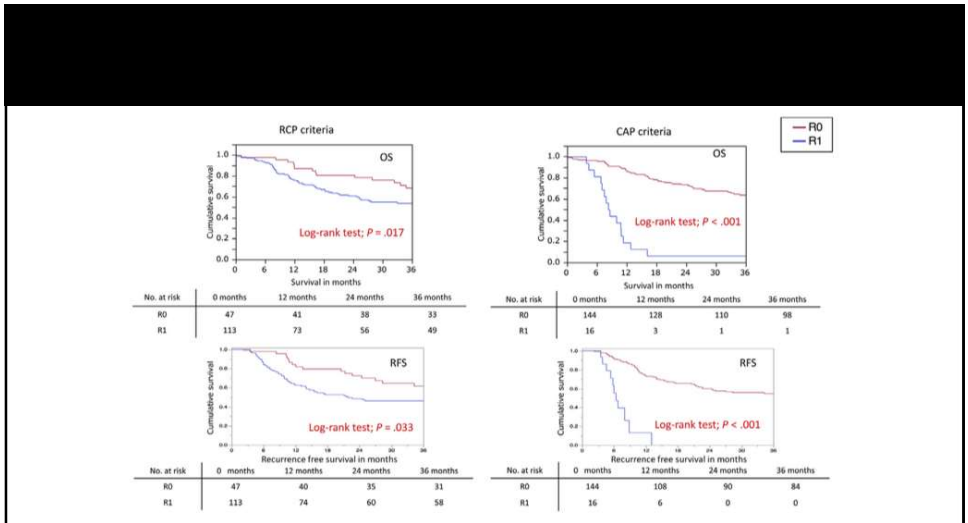


Fig 2. Cumulative overall survival (OS) and recurrence-free survival (RFS) curves of all 160 patients with pT3 or ypT3 and were diagnosed as R0 and R1, respectively, according to the College of American Pathologists (CAP) or the Royal College of Pathologists (RCP) criteria.

Okada 2016

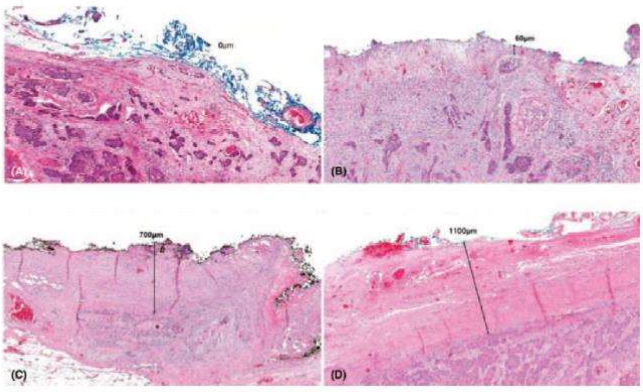


FIGURE 2. Representative examples of tumor distance from CRM: (A) CRM: 0 μm, (B) CRM: 60 μm, (C) CRM: 700 μm, and (D) CRM: 1100 μm.

TABLE 2. Comparison of the Results of Positive Circumferential Resection Margin According to 3 Different Criteria

	CRM Status	No. Patients	HR (95% CI)	P
RCP criteria (cutoff point: 1000 μm)				0.027
	Negative	104 (21.7%)		
	Positive	375 (78.3%)	1.384 (1.039–1.844)	
Present criteria (cutoff point: 500 μm)				<0.001
	Negative	231 (48.2%)		
	Positive	248 (51.8%)	1.696 (1.342–2.143)	
CAP criteria (cutoff point: 0 μm)				<0.001
	Negative	388 (81.0%)		
	Positive	91 (19.0%)	1.969 (1.501–2.584)	

Lee 2015

How to Define a Positive Circumferential Resection Margin in T3 Adenocarcinoma of the Esophagus

Roy J.J. Verhage, MD, Herman J.A. Zandvoort, MD,* Fiebo J.W. ten Kate, MD, PhD,† and Richard van Hillegersberg, MD, PhD**

Abstract: A positive circumferential resection margin (CRM+) prevalence of obesity and reflux disease, esophageal adeno-carcinoma (EAC) has become the most prevalent type

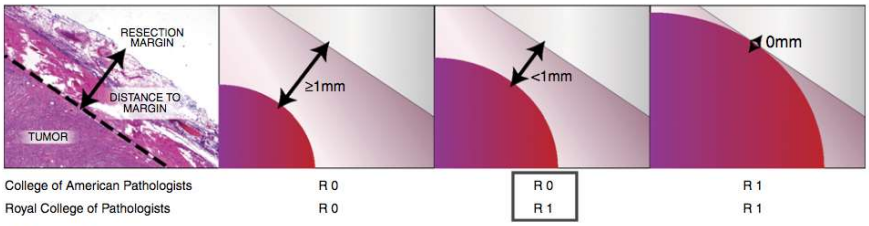


FIGURE 1. Definitions of the CRM according to the criteria of the CAP and the RCP. The corresponding R-classification is denoted; R0-no microscopic residual tumor; R1-microscopic residual tumor; R2-macroscopic residual tumor (not shown). EAC, Hematoxylin and eosin staining.

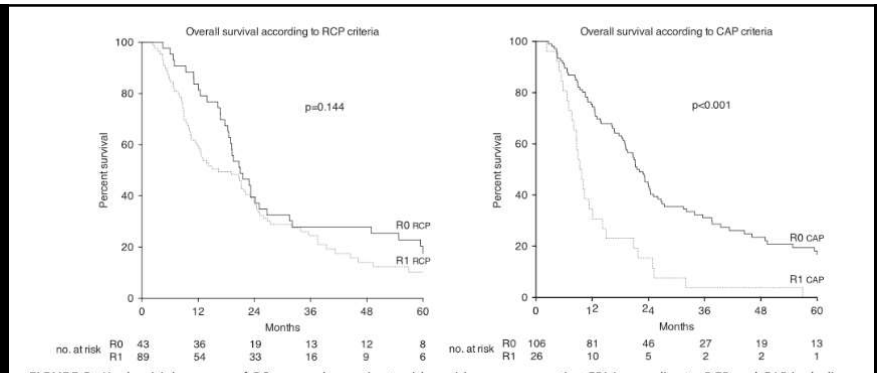


FIGURE 2. Kaplan-Meier curves of OS comparing patients with positive versus negative CRM according to RCP and CAP including log rank *P* value and numbers at risk.

Inclusion and Exclusion Criteria

As prognosis is highly influenced by disease stage and CRM involvement predominantly concerns advanced disease,[10] only patients with T3 adenocarcinoma of the esophagus were included. Exclusion criteria were inhospital mortality and the use of neoadjuvant chemotherapy or chemoradiotherapy. These criteria were applied to yield a homogenous study population.

Original article

Defining a positive circumferential resection margin in oesophageal cancer and its implications for adjuvant treatment

J. R. O'Neill[1], N. A. Stephens[1], V. Save[2], H. M. Kamel[4], H. A. Phillips[3], P. J. Driscoll[5] and S. Paterson-Brown[1]

Departments of [1]General Surgery and [2]Pathology, Royal Infirmary of Edinburgh, and [3]Department of Oncology, Western General Hospital, Edinburgh, [4]Department of Pathology, Wishaw General Hospital, Glasgow, and [5]Department of General Surgery, Victoria Hospital, Kirkcaldy, UK
Correspondence to: Mr J. R. O'Neill, Department of General Surgery, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA, UK (e-mail: roneill1@staffmail.ed.ac.uk)

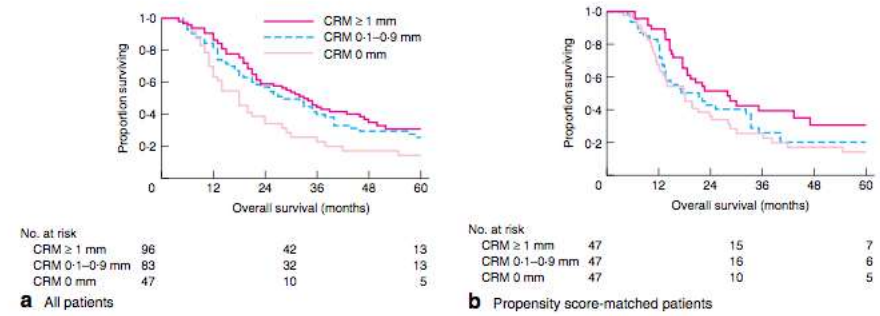


Fig. 1 Kaplan–Meier curves for **a** all patients and **b** propensity score-matched patients stratified by distance to the circumferential resection margin (CRM)

Systematic review and meta-analysis of the influence of circumferential resection margin involvement on survival in patients with operable oesophageal cancer

D. S. Y. Chan, T. D. Reid, I. Howell and W. G. Lewis

Department of Surgery, University Hospital of Wales, Heath Park, Cardiff CF14 4XN, UK
Correspondence to: Mr D. S. Y. Chan (e-mail: dcsy23@gmail.com)

Table 1 Characteristics of studies included in the meta-analysis

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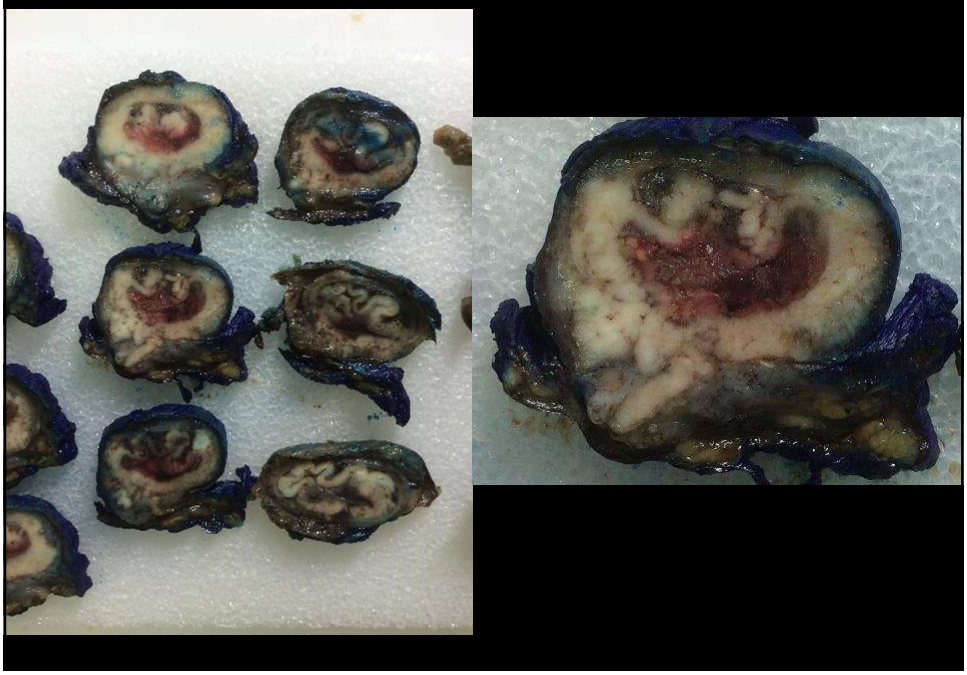
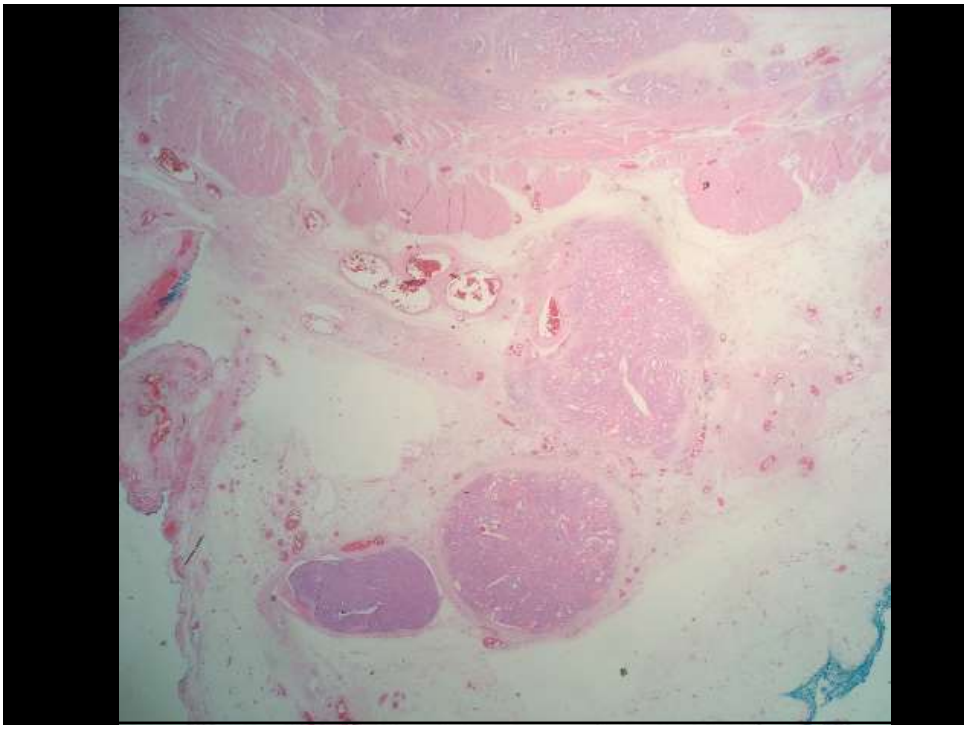
Khan *et al.*[9] (2003)	UK	RCP	329	NA	67 (20·4)	267 (81·2)	None	No	60·0	9
Pultrum *et al.*[10] (2010)	The Netherlands	CAP and RCP*	98	25 (26)	47 (48)	58 (59)	None	Yes	37·0	9
Rao *et al.*[24] (2012)	UK	CAP and RCP*	115	17 (14·8)	57 (49·6)	80 (69·6)	CT	No	38·0	8
Saha *et al.*[25] (2009)	UK	RCP	105	NA	38 (36·2)	70 (66·7)	CT	Yes	26·0	8
Salih *et al.*[18] (2012)	UK	CAP and RCP*	232	38 (16·4)	89 (38·4)	171 (73·7)	CT	No	18·0	8
Scheepers *et al.*[17] (2009)	The Netherlands	CAP and RCP*	110	17 (15·5)	42 (38·2)	86 (78·2)	CT	Yes	NA	8
Sujendran *et al.*[26] (2008)	UK	RCP	242	NA	56 (23·1)	151 (62·4)	CT and CRT	Yes	NA	8
Thompson *et al.*[27] (2008)	Australia	RCP	240	NA	85 (35·4)	127 (52·9)	CRT	No	NA	8
Verhage *et al.*[19] (2011)	The Netherlands	CAP* and RCP	132	26 (19·7)	89 (67·4)	132 (100)	None	Yes	28·4	8

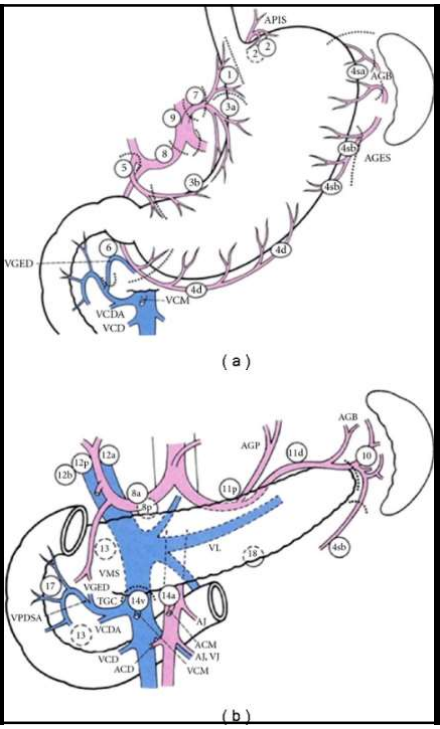
Values in parentheses are percentages. *Indicates the definition that was more prognostically significant in studies that used both definitions of circumferential resection margin (CRM) involvement. NO, Newcastle–Ottawa study quality score; CAP, College of American Pathologists (tumour at CRM); RCP, Royal College of Pathologists (tumour within 1 mm of CRM); CRT, neoadjuvant chemoradiotherapy; NA, data not available; CT, neoadjuvant chemotherapy.

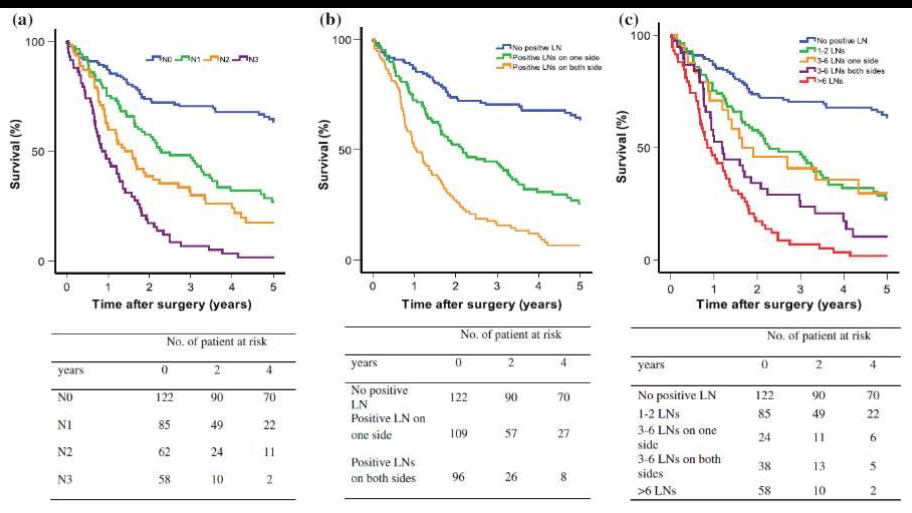
Conclusion: CRM involvement is an important predictor of poor prognosis. CAP criteria differentiate a higher-risk group than RCP criteria, but overlook a patient group with similar poor outcomes.





According to the UICC TNM classification, 6 and 16 lymph nodes are the minimum number of lymph nodes that should be retrieved from an oesophagectomy specimen and gastrectomy specimen, respectively.





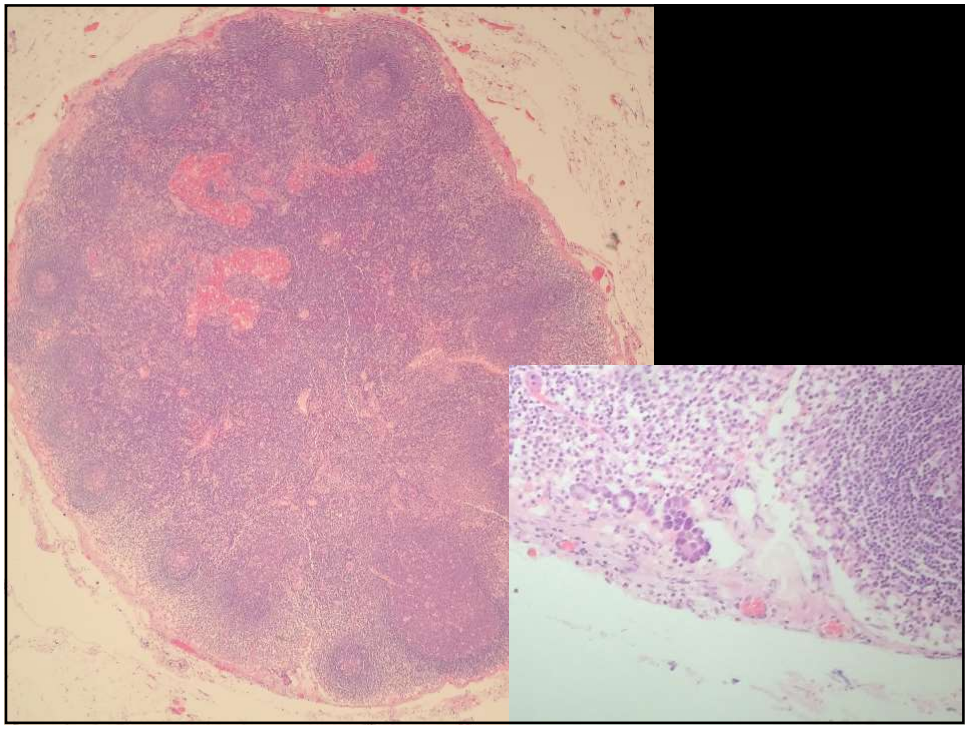
	No. of patient at risk		
years	0	2	4
N0	122	90	70
N1	85	49	22
N2	62	24	11
N3	58	10	2

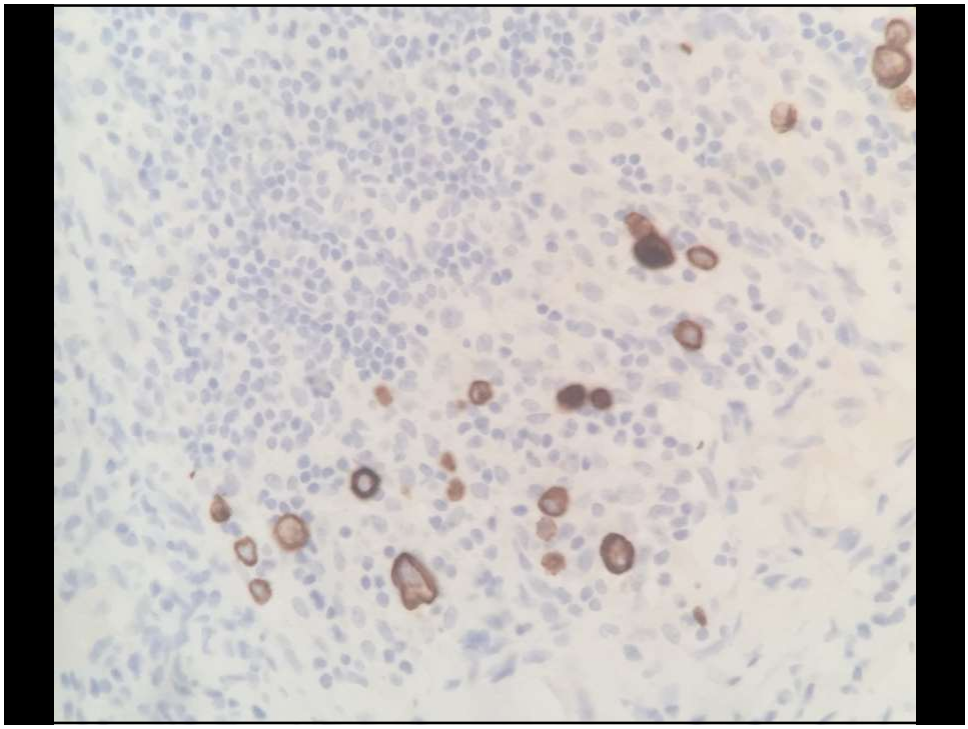
	No. of patient at risk		
years	0	2	4
No positive LN	122	90	70
Positive LN on one side	109	57	27
Positive LNs on both sides	96	26	8

	No. of patient at risk		
years	0	2	4
No positive LN	122	90	70
1-2 LNs	85	49	22
3-6 LNs on one side	24	11	6
3-6 LNs on both sides	38	13	5
>6 LNs	58	10	2

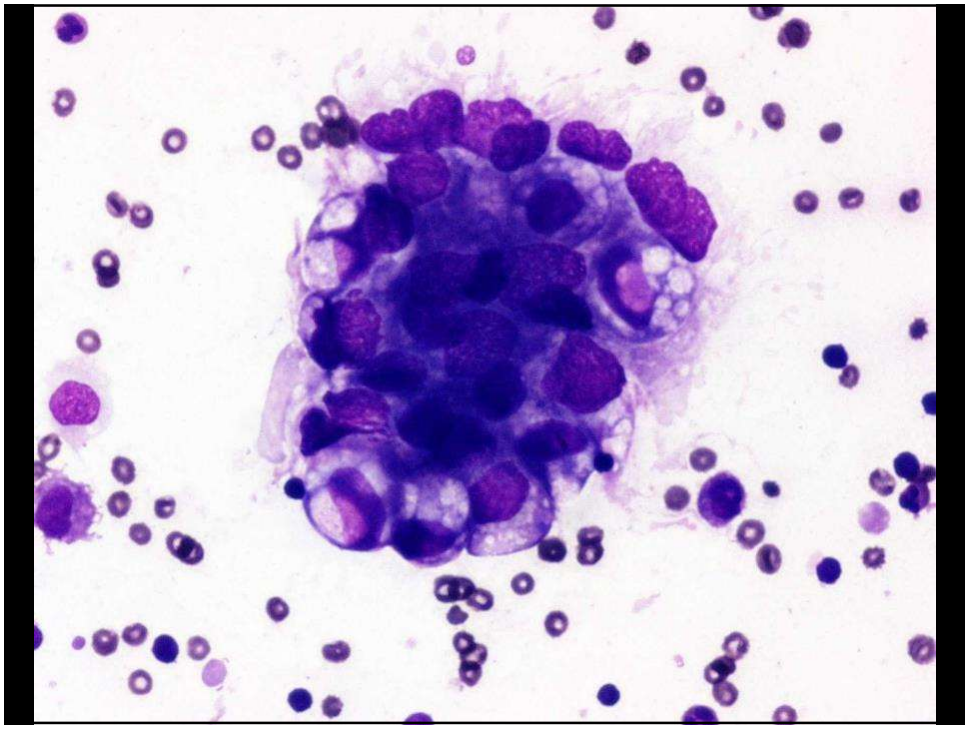
Fig. 1 Kaplan–Meier overall survival curves of 327 patients stratified by **a** N stage according to the seventh edition TNM staging system, **b** location of involved lymph nodes relative to the diaphragm, and **c** proposed combined lymph node staging system. Data are based on pathological findings as assessed in the resection specimens

Talsma 2014





pN0(i)
pM0(i)



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Perioperative Chemotherapy versus Surgery Alone for Resectable Gastroesophageal Cancer

David Cunningham, M.D., William H. Allum, M.D., Sally P. Stenning, M.Sc., Jeremy N. Thompson, M.Chir., Cornelis J.H. Van de Velde, M.D., Ph.D., Marianne Nicolson, M.D., J. Howard Scarffe, M.D., Fiona J. Lofts, Ph.D., Stephen J. Falk, M.D., Timothy J. Iveson, M.D., David B. Smith, M.D., Ruth E. Langley, M.D., Ph.D., Monica Verma, M.Sc., Simon Weeden, M.Sc., and Yu Jo Chua, M.B., B.S., for the MAGIC Trial Participants*

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JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Long-Term Results of a Randomized Trial of Surgery With or Without Preoperative Chemotherapy in Esophageal Cancer

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From the Department of Surgery, Royal Marsden National Health Services (NHS) Foundation Trust, London; Medical Research Council Clinical Trials Unit, London; Department of Surgery

A B S T R A C T

Purpose

OEO2 is a randomized, controlled trial of preoperative chemotherapy in patients undergoing radical

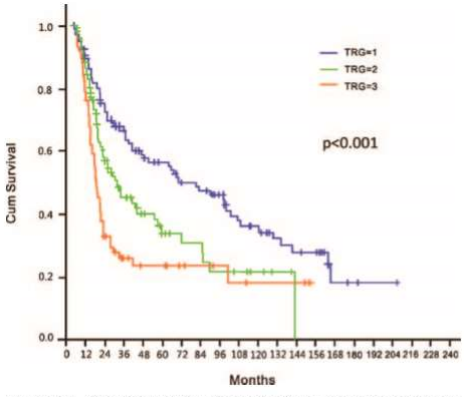

FIGURE 1. Overall survival in the entire study cohort according to the 3-point tumor regression grade (TRG).

list of the different regression grading systems

- Mandard
- Japanese
- Dworak
- Wheeler
- Becker
- Junker and Mueller
- Rubbia-Brandt
- Ryan
- Le Sodan
- Schneider
- Lowy
- Mansourd

Tumour regression grade

System used:	grade:

Table 2: Published tumour regression scoring systems for oesophageal cancer

Authors	Grading	Pathological features
Mandard et al 1994 (177)		
	TRG1	Complete regression (i.e. fibrosis without detectable residual cancer cells)
	TRG2	Few residual cancer cells scattered through the fibrosis
	TRG3	Fibrosis and tumour cells with predominance of fibrosis
	TRG4	Residual cancer outgrowing fibrosis
	TRG5	Absence of any regressive changes
Japanese Society of Esophageal Disease (184)		
	ypV0	Ineffective (i.e. no regression evidence)
	ypV1	Slightly effective: Viable cell more than 1/3 of tumour tissue, but with evidence of degeneration
	ypV2	Moderately effective: Viable cell less than 1/3 of tumour tissue and severely degenerated or necrotic
	ypV3	Markedly effective: No viable cell
Schneider et al 2005 (185)		
	I	>50% vital residual tumour cells
	II	10%–50% vital residual tumour cells
	III	<10% vital residual tumour cells
	IV	no vital residual tumour cells
Chirieac et al 2005 (179)		
	1	No evidence of residual tumour
	2	1-10% residual tumour
	3	11-50% residual tumour
	4	>50% residual tumour
***Becker et al 2003 (178) Swisher et al 2005 (186) Langer et al (175)**		
	CRT	no residual cell
	P1	1%–50% of residual viable cell
	P2	>50% residual viable cell in primary tumour
Brucher et al 2006 (176) Barbour et al 2008 (187)		
	Responders	<10% residual tumour cells
	Non responders	>10% residual tumour cells
Donington et al 2003 (188)		
	Complete responders	No evidence of residual tumour
	Residual tumour	Any evidence of residual tumour

*Becker et al original paper developed the system originally for gastric cancer and later used the same system for oesophageal cancer

Salih 2016