

# The CREST Trial

A randomised phase III study of stenting as a bridge to surgery in obstructing colorectal cancer. Results of the UK ColoRectal Endoscopic Stenting Trial (CREST).

Funded by Cancer Research UK and developed by the National Cancer Research Institute



# Current acute oncological problem

## NBOCA audit report 2015

- Emergency admission with colorectal cancer remains at a stubborn 21 % of all cases.
- Over 5,000 cases per year
- 16 per cent of patients having major surgery had an urgent or emergency procedure
- 90 day mortality
  - 13.3% for patients having emergency surgery
  - 2% for elective surgery

# Rationale of CREST – Converting emergency into elective surgery

- Pre-operative correction of fluid and electrolyte balance
- Reduction of diaphragmatic splinting and pain with improvement in respiratory function
- Treatment of medical co-morbid disease
- Accurate pre-operative staging
- Referral to a specialist colorectal surgeon
- Major surgery may be avoided for patients with:
  - Rapidly progressive cancer
  - Unstable comorbid disease

Stenting needs to be properly evaluated in a randomised controlled trial addressing two key questions:

- \* Is there a worthwhile net benefit (in reduced operative mortality and morbidity, reduced stoma formation and better quality of life adjusted survival) from endoluminal stenting for patients presenting with an obstructing colonic cancer?

- \* If a benefit exists, is this identifiable in patients undergoing attempted curative treatment, palliative treatment, or both?

# Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Endoscopy 2014; 46: 990–1002

- SEMS placement is recommended as the preferred treatment for palliation of malignant colonic obstruction (strong recommendation, high quality evidence).
- SEMS placement as a bridge to elective surgery is not recommended as a standard treatment of symptomatic left-sided malignant colonic obstruction (strong recommendation, high quality evidence).
- For patients with potentially curable disease, stent placement may be considered in those who have an increased risk of postoperative mortality (weak recommendation, low quality evidence).

# CREST – Primary Objectives

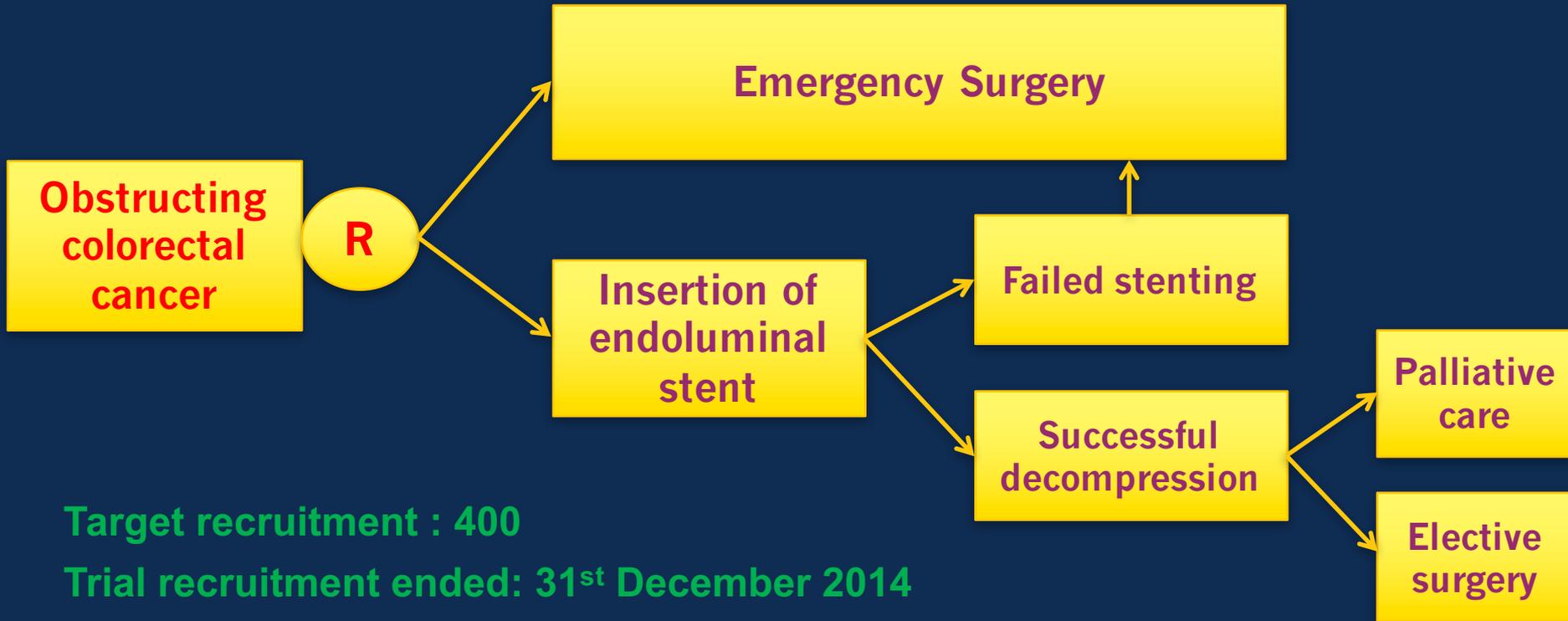
A phase III, multi-center randomised controlled trial to determine if endoluminal stenting for obstructing colonic cancers can result in:

- Reduced perioperative morbidity as assessed by length of hospital stay
- Reduced 30-day mortality

# CREST – Secondary outcome measures

- Stenting completion and complication rate
- Presence and duration of a stoma/anastomosis rate
- 6-month survival
- Proportion disease-free at 3 years
- Quality of life
- Perioperative morbidity

# The CREST Trial Design



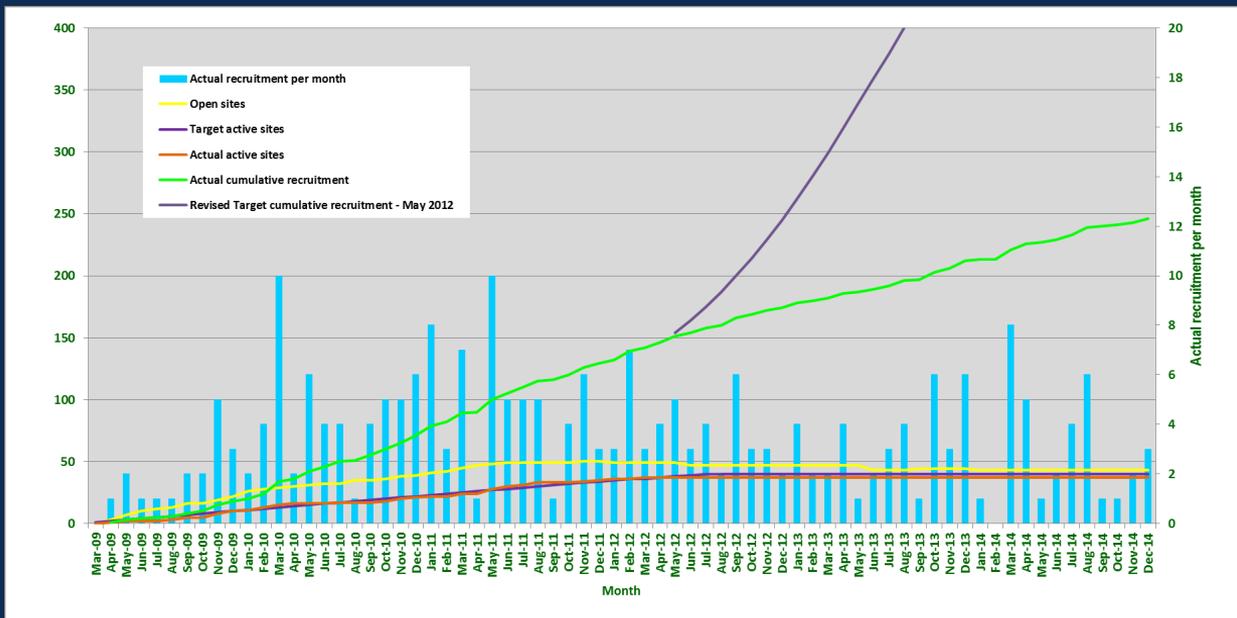
Target recruitment : 400

Trial recruitment ended: 31<sup>st</sup> December 2014

# CREST – Eligibility Criteria

- Left-sided colorectal cancer
- Radiological evidence of obstruction
- Patient fit for surgery
- No evidence of peritonitis and/or perforation
- Patient able and willing to give written informed consent
- Patients stratified by palliative or potentially curative

# CReST Recruitment

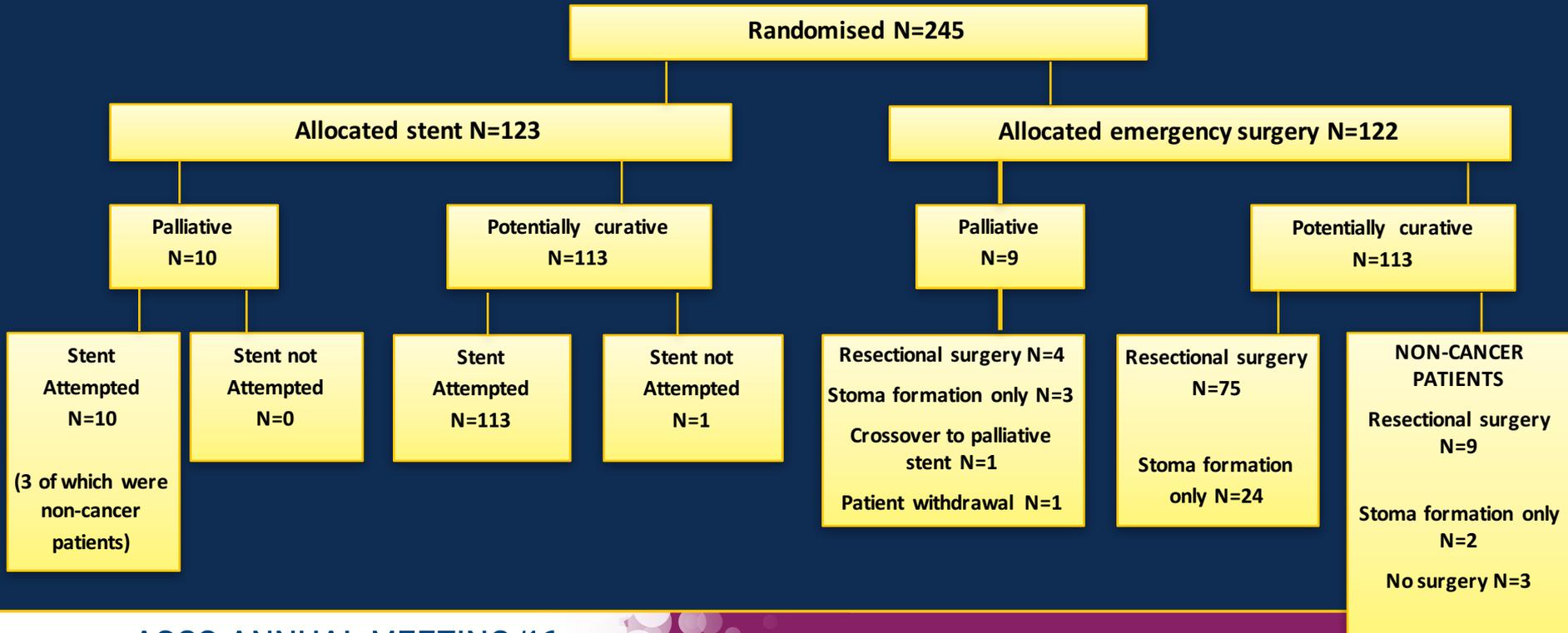


**70% acceptance**

Recruitment ended: 31<sup>st</sup>  
December 2014  
Revised Target recruitment:  
400  
Actual recruitment: 245



# Compliance with Randomised Treatment Allocation



# CREST Patient Demographics

	Stenting (N=123)	Surgery (N=122)
Gender: Male	72 (59%)	77 (63%)
Mean Age: (sd)  range	69.9 (12.2) 34 - 94	69.1 (11.2) 36 - 89
Age group: <50	7 (6%)	7 (6%)
	17 (14%)	15 (12%)
50-59	30 (24%)	38 (31%)
60-69	69 (56%)	62 (51%)
70+		

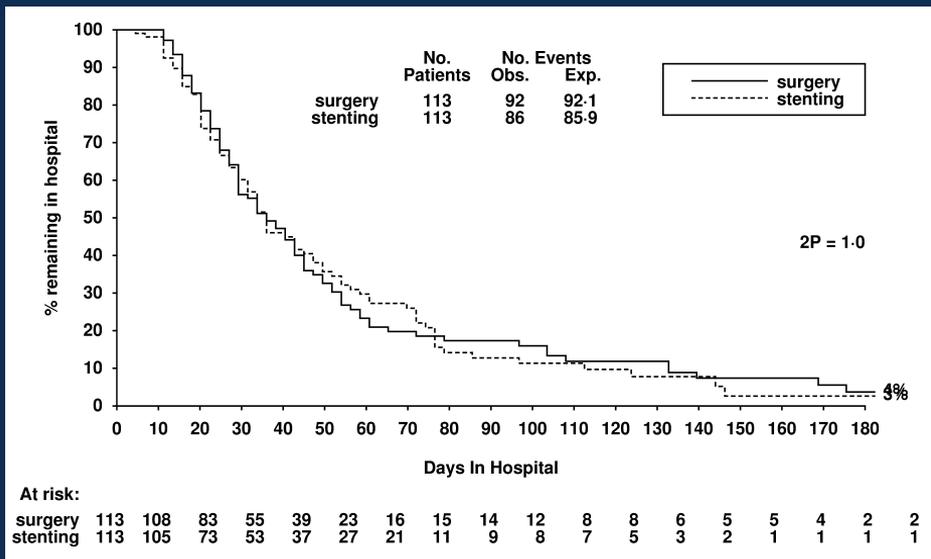
# CREST Patient Baseline Data

	Stenting (N=123)	Surgery (N=122)
Transverse Colon	4 (3%)	3 (2%)
Splenic Flexure	7 (6%)	7 (6%)
Descending Colon	28 (23%)	30 (25%)
Sigmoid	68 (55%)	67 (55%)
Rectosigmoid	15 (12%)	14 (11%)
Rectum	1 (1%)	1 (1%)
ASA Grade	24 (20%)	27 (22%)
P1	78 (63%)	75 (62%)
P2	21 (17%)	20 (16%)
P3		

# CREST Patient Baseline Data - Stratification

	Stenting (N=123)	Surgery (N=122)
Palliative	10 (8%)	9 (7%)
Potentially curative	113 (92%)	113 (93%)
Likelihood of cure:		
Probably not	3 (3%)	6 (5%)
Probably yes	78 (69%)	72 (64%)
Uncertain (possibly yes)	32 (28%)	35 (31%)

# Does stenting reduce length of stay and 30-day mortality?



	Stenting	Surgery
Days in hospital (curative patients with complete 1 year data)		
N	86	92
Median (IQR)	14.5 (9, 24)	13.5 (9.5, 22.5)
Deaths within 30 days of randomisation	5	6
Time to death for these patients (days from randomisation to death)		
Median (IQR)	7 (6, 15)	5 (3, 9)

# Stenting Completion and Immediate Complication Rate

	N = 123
Stent relieved the obstruction	98 (82%)
Endoscopic + fluoroscopic	91
Fluoroscopic only	3
Endoscopic only	4
Immediate complications	
None	92
Haemorrhage	-
Respiratory depression	-
Migration	4
Perforation	1
Hypotension	-
Other	2

- **Immediate complications defined as those within 24 hours from stent insertion.**
- **Stent technique only shown for those patients who stent was said to relieve the obstruction**

# Stenting Intermediate and Late Complication Rates

		N = 123
<b>Stent relieved the obstruction</b>	Yes	98
	No	16
	<i>Ineligible for stenting</i>	4
	<i>Stent not deployed</i>	4
	<i>Missing CRF</i>	1
<b>Intermediate (24 hours – 7 days after stenting)</b>		
	None	85
	Migration	2
	Haemorrhage	0
	Perforation	2
	Recurrent obstruction	4
	Other	7
<b>Late (7 – 28 days after stenting)</b>		
	None	78
	Haemorrhage	0
	Perforation	3
	Ongoing obstruction	3
	Any degree of sensation	10
	Other	3

Intermediate ‘other’ complications:

- Small bowel ileus retention - suprapubic catheter. pneumonia (n=1)
- Pt suffered cardiac arrest (n=1)
- Infection (n=2)
- Febrile illness (n=1)
- Pyrexia (n=1)
- Respiratory depression (n=1)

Late ‘Other’ complications:

- Eating difficulties (n=1)
- Infection / fluid collection (n=1)
- Abdominal pain (n=1)

# Stent related perforations

- N=6
- 5 resulted in an urgent surgery
- 1 stenting only
- 1 mechanical ventilation
- No post-operative deaths

# Does stenting reduce stoma rates?

	Stenting (N = 123)	Emergency surgery (N = 122)	P-value
No surgery	24	3	
Patients who have had surgery	99	119	
Has the procedure resulted in a stoma?	46 / 99 (46%)	82 / 119 (69%)	0.001
End	28	48	
Loop	18	33	
Unknown	-	1	

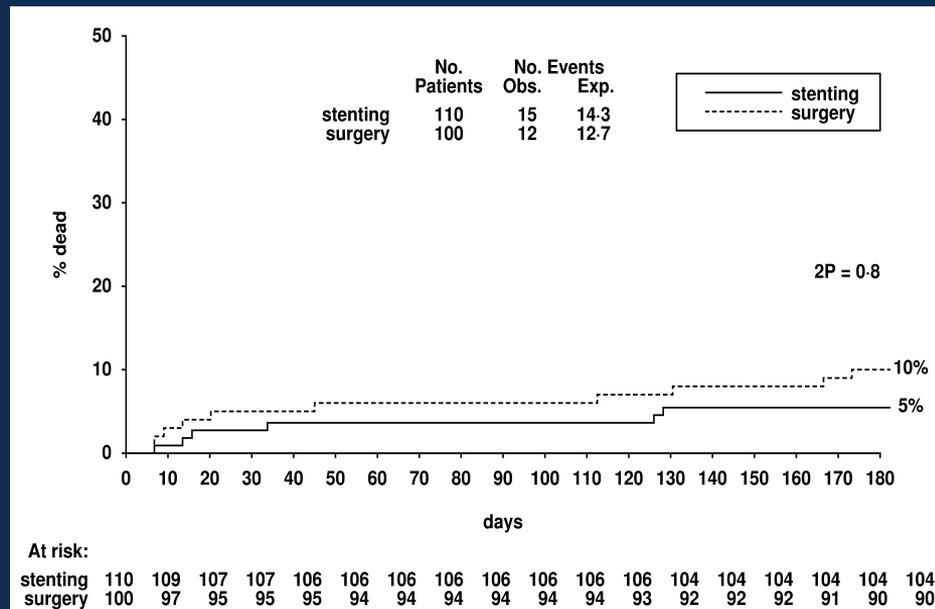
# CReST – Reasons patients did not have surgery

	<b>Stent (N=24)</b>
<b>Indication changed from potentially curative to palliative post stenting</b>	12
<b>Palliative at randomisation</b>	8
<b>Died post stenting prior to elective surgery (D=3, D=7)</b>	2
<b>Patient declined surgery</b>	2

	<b>Surgery (N=3)</b>
<b>Non-cancer patient</b>	1
<b>Crossover to stent + palliative chemo post stent (PI believed pt ineligible post rand.)</b>	1
<b>Patient withdrawal from trial prior to randomised intervention</b>	1

# 6-Month Survival Rates

	Stenting (N = 123)	Emergency Surgery (N = 122)
All deaths	59 / 123	47 / 122
<1 month	5	6
1-6 months	11	11
6months – 1 yr	16	7
1-2 yrs	15	11
2-3 yrs	7	10
3-4 yrs	2	1
4-5 yrs	3	1
All deaths (cancer patients only)	58 / 120	47 / 109
Deaths within 6 months	16	17
Deaths within 6 months (cancer patients, bridge to surgery)	15/110	12/100



# Severity of Surgical Complications (Clavien-Dindo Classification)

	Stenting	Surgery	P-value
Patients with Clavien Dindo classification	48	45	
CD 3+	22 (46%)	27 (60%)	0.20

# Summary

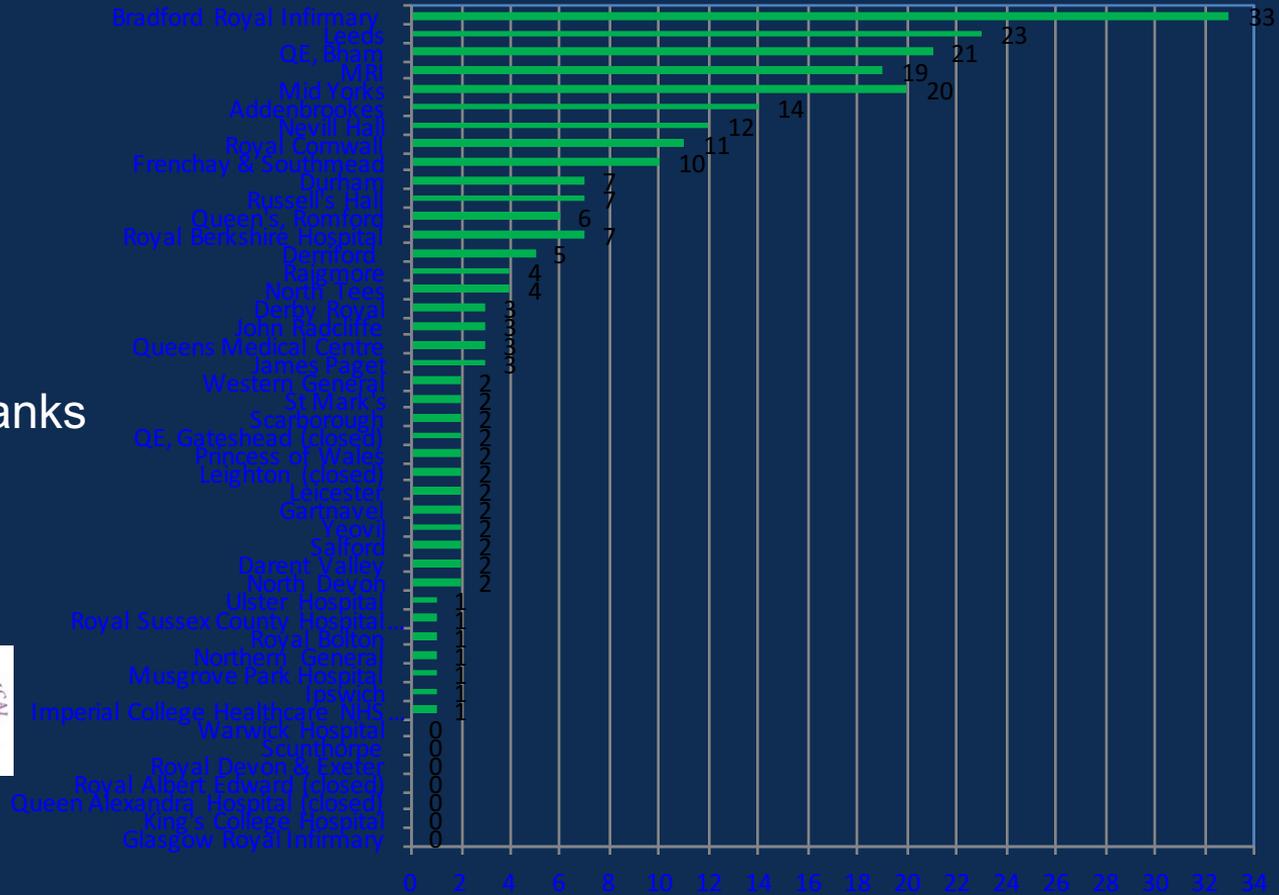
- Recruitment feasible in the emergency setting
- 5% will not have CRC
- Combined endoscopic fluoroscopic technique had good success rates & low complication rates across multiple hospital sites



# Conclusions – SEMS as a bridge to surgery

- Clinical success rate 80%
- Mortality and LoS unaffected
- Stoma rates significantly reduced
- Cancer specific survival not worse
- Reasonable alternative to emergency surgery

With special thanks  
to



# Learning Objectives for obstructing colorectal cancer

- Rates of urgent presentation of CRC
- Morbidity and mortality
- Current guidance on stenting in emergency setting
- Clinical success rate and complications of stenting
- Effect on stoma rates
- Effect on cancer survival



# With thanks to

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