THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Reinforcement of Closure of Stoma Site (ROCSS) Collaborative and West Midlands Research Collaborative. Prophylactic biological mesh reinforcement versus standard closure of stoma site (ROCSS): a multicentre, randomised controlled trial. *Lancet* 2020; **395:** 417–26.

Appendix

Multicentre randomised controlled trial of prophylactic biologic mesh reinforcement versus standard closure of stoma site

Reinforcement of Closure of Stoma Site (ROCSS) Collaborative and *West Midlands Research Collaborative*

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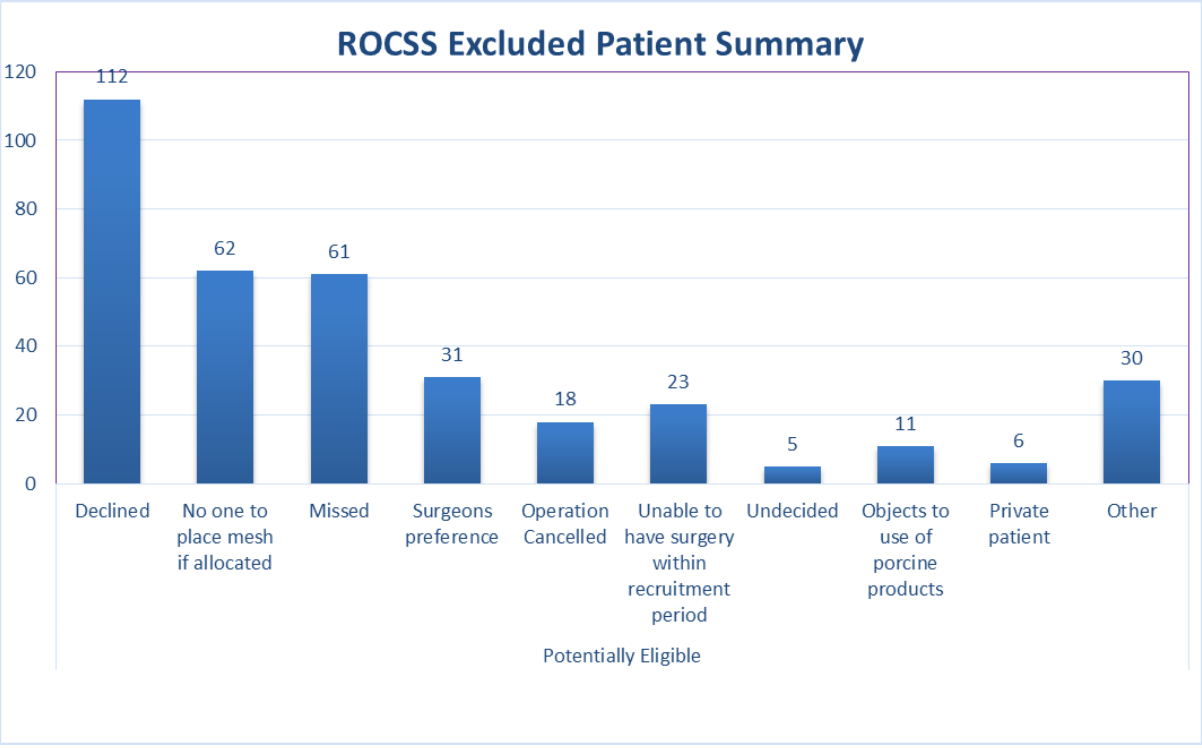
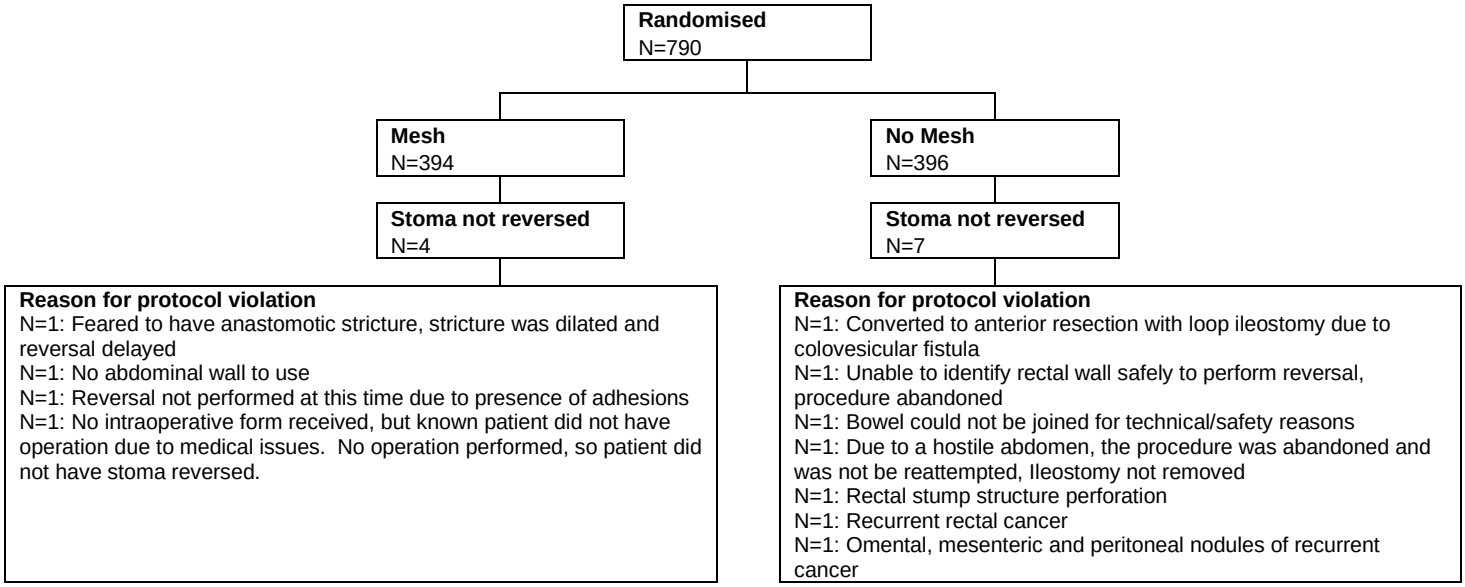
Supplemental Figure 1: Reasons eligible patients were not randomised

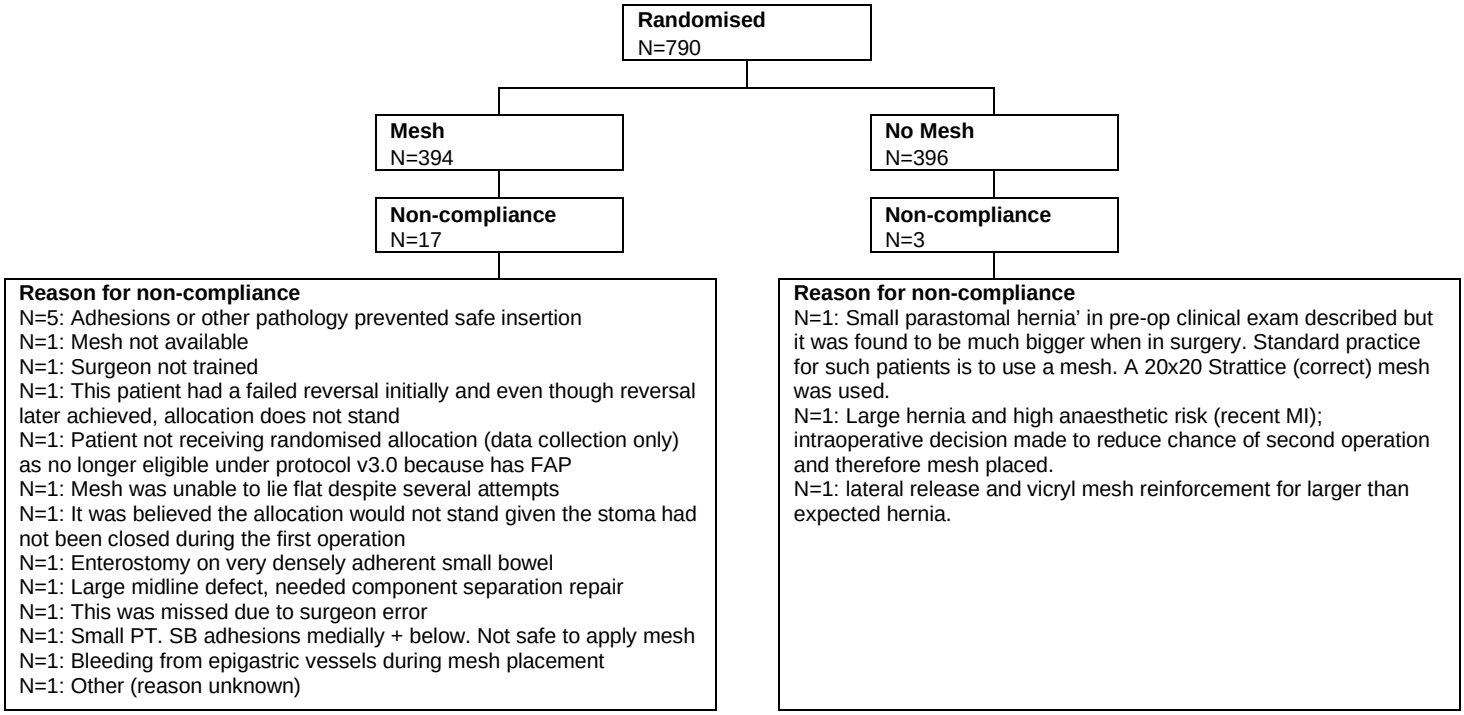


The acceptance rate was 68.8% (790/1149).
An additional 137 patients were screened but were identified as being ineligible for this trial.

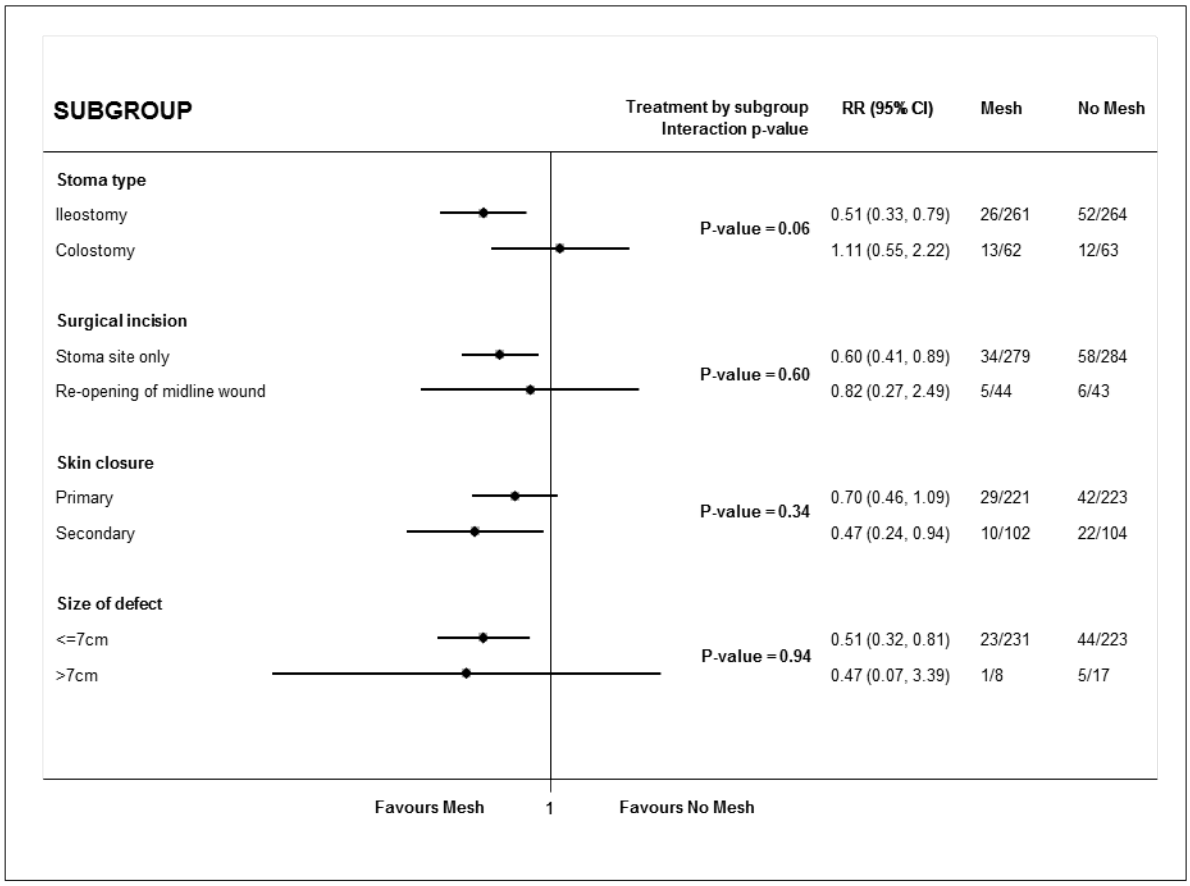
Supplemental Figure 2: Reasons for protocol violation



Supplemental Figure 3: Reasons for non-compliance



Supplemental Figure 4: Subgroup analysis forest plot



In addition, to planned subgroup analyses for the three minimisation variables (midline laparotomy planned; planned skin closure; type of stoma being closed), a pre-specified subgroup analysis was planned for the size of fascial defect.

Supplemental Table 1: Restrictions on 2 year follow-up for primary outcome data

Reason for loss to 2 year follow up for primary outcome data	Mesh (N=394)	No Mesh (N=396)	Total (N=790)
Stoma not reversed	4	7	11
Missing data in 24 month form	16	16	32
Outside +/- 3 months' time window	4	8	12
No 24 month follow-up form	47	38	85

Supplemental Table 2: Sensitivity analyses for primary outcome

Clinical hernia at 2 years	**Mesh**	**No mesh**	**Relative Risk (95% Confidence Interval)**	**P-value**
Primary Outcome Analysis*	39/323 (12.1)	64/327 (19.6)	0.62 (0.43-0.90)	0.012
Sensitivity Analyses				
Unadjusted intention to treat analysis	39/323 (12.1)	64/327 (19.6)	0.62 (0.43-0.89)	0.010
Adjusted† intention to treat analysis	39/323 (12.1)	64/327 (19.6)	0.63 (0.44-0.91)	0.013
Adjusted* intention to treat analysis (no time restrictions)	42/327 (12.8)	69/335 (20.6)	0.63 (0.44-0.90)	0.010
Adjusted* intention to treat analysis with stoma not reversed patients classified as no hernia	39/327 (11.9)	64/334 (19.2)	0.63 (0.44, 0.91)	0.013
Adjusted* per-protocol analysis	36/310 (11.6)	63/325 (19.4)	0.60 (0.41-0.88)	0.009
Adjusted* per-protocol analysis (no time restrictions)	39/314 (12.4)	68/333 (20.4)	0.61 (0.43-0.88)	0.008

*Adjusted for minimisation variables (midline laparotomy planned; planned skin closure; type of stoma being closed)

†Adjusted for minimisation variables (midline laparotomy planned; planned skin closure; type of stoma being closed), and age, gender, diabetes

Relative risk <1 favours Mesh

Analyses based on patients with outcome assessed within 3 months before or after the 2 year time point, unless recorded as having no time restrictions, in which case all patients with outcome data were included.

Supplementary Table 3: Characteristics of patients included in the analysis for the radiological hernia outcome at 1 year

Baseline characteristics		Baseline data for all patients randomised to ROCSS			Baseline data for patients included in the analysis for rthe adiological hernia outcome at 1 year		
		Mesh (N=394)	No Mesh (N=396)	Total (N=790)	Mesh (N=229)	No Mesh (N=226)	Total (N=455)
Age	Mean (SD)	58.4 (16.0)	59.0 (16.0)	58.7 (16.0)	59.3 [15.5]	60.0 [15.0]	59.6 [15.3]
	Min-Max	18.0 - 89.0	19.0 - 89.0	18.0 - 89.0	18 - 89	19 - 87	18 - 89
Sex	Male	263 (67%)	251 (63%)	514 (65%)	150 (65.5%)	132 (58.4%)	282 (62%)
	Female	131 (33%)	145 (37%)	276 (35%)	79 (34.5%)	94 (41.6%)	173 (38%)
Body mass index	Mean (SD)	26.8 (4.8)	26.6 (5.2)	26.7 (5.0)	26.7 [4.9]	26.4 [5.0]	26.6 [4.9]
Diabetes	No	351 (89%)	357 (90%)	708 (90%)	205 (89.5%)	203 (89.8%)	408 (89.7%)
	Yes	42 (11%)	37 (9%)	79 (10%)	24 (10.5%)	22 (9.7%)	46 (10.1%)
	Missing	1 (<1%)	2 (<1%)	3 (<1%)	0 (0%)	1 (0.4%)	1 (0.2%)
Steroid medications	No	377 (96%)	382 (97%)	759 (96%)	219 (95.6%)	218 (96.5%)	437 (96%)
	Yes	15 (4%)	12 (3.0%)	27 (3%)	10 (4.4%)	7 (3.1%)	17 (3.7%)
	Missing	2 (<1%)	2 (<1%)	4 (<1%)	0 (0%)	1 (0.4%)	1 (0.2%)
Original indication for stoma	Cancer	227 (58%)	217 (55%)	444 (56%)	131 (57.2%)	120 (53.1%)	251 (55.2%)
	Non-cancer	167 (42%)	179 (45%)	346 (44%)	98 (42.8%)	106 (46.9%)	204 (44.8%)
Type of stoma opening	Loop	295 (75%)	310 (78%)	605 (77%)	172 (75.1%)	177 (78.3%)	349 (76.7%)
	End	99 (25%)	86 (22%)	185 (23%)	57 (24.9%)	49 (21.7%)	106 (23.3%)
Type of stoma being closed*	Ileostomy	315 (80%)	316 (80%)	631 (80%)	182 (79.5%)	181 (80.1%)	363 (79.8%)
	Colostomy	79 (20%)	80 (20%)	159 (20%)	47 (20.5%)	45 (19.9%)	92 (20.2%)
Side of stoma	Right side	307 (78%)	306 (77%)	613 (78%)	179 (78.2%)	175 (77.4%)	354 (77.8%)
	Left side	87 (22%)	90 (23%)	177 (22%)	50 (21.8%)	51 (22.6%)	101 (22.2%)
Parastomal hernia evident	No	284 (72%)	301 (76%)	585 (74%)	161 (70.3%)	174 (77%)	335 (73.6%)
	Yes	110 (28%)	95 (24%)	205 (26%)	68 (29.7%)	52 (23%)	120 (26.4%)
Midline incisional hernia evident	No	372 (94%)	380 (96%)	752 (95%)	215 (93.9%)	218 (96.5%)	433 (95.2%)
	Yes	22 (6%)	16 (4%)	38 (5%)	14 (6.1%)	8 (3.5%)	22 (4.8%)
Midline laparotomy planned*	No	339 (86%)	341 (86%)	680 (86%)	202 (88.2%)	199 (88.1%)	401 (88.1%)
	Yes	55 (14%)	55 (14%)	110 (14%)	27 (11.8%)	27 (11.9%)	54 (11.9%)
Planned skin closure*	Primary	274 (70%)	274 (69%)	548 (70%)	153 (66.8%)	154 (68.1%)	307 (67.5%)
	Secondary	120 (30%)	120 (30%)	240 (30%)	76 (33.2%)	71 (31.4%)	147 (32.3%)
	Missing	0 (0.0%)	2 (1%)	2 (<1%)	0 (0%)	1 (0.4%)	1 (0.2%)

Supplementary Table 4: Pain scores

Pain	Time point	Mesh	No Mesh	Total	Linear regression model Adjusted mean difference[$] (95% Confidence Interval) P-value	Repeat measures model Effect Size[$] (95% CI) P-value
Pain score*						
N Mean [SD] Min – Max	Baseline	347 15.1 [25.7] 0 – 100	346 15.5 [25.5] 0 – 100	693 15.3 [25.6] 0 – 100	-	0.438 (-1.965, 2.841) 0.72 **Treatment by Time Interaction** **P-value** 0.67
N Mean [SD] Min – Max	30 day	336 17.5 [22.1] 0 – 100	334 18.2 [22.3] 0 – 100	670 17.8 [22.2] 0 – 100	-0.808 (-4.214, 2.598) 0.64	
N Mean [SD] Min – Max	12 months	338 15.5 [26.6] 0 – 100	335 14.1 [24.0] 0 – 100	673 14.8 [25.3] 0 – 100	2.283 (-1.594, 6.159) 0.25	
N **Mean [SD]** **Min – Max**	**24 months**	**316** **12.9 [24.6]** **0 – 100**	**309** **12.5 [23.4]** **0 – 100**	**625** **12.7 [24.0]** **0 – 100**	**0.123 (-3.895, 4.140)** **0.95**	

*Pain score ranges from 0-100, with higher scores indicating worse outcome

[$]adjusted for all minimisation variables (stoma type, surgical incision, skin closure type) and baseline score. Estimates from the repeated measures analyses are based on model without the treatment by time interaction term.

Differences <0 favour Mesh.

The pain score at the 2 year time-point (shown in bold) is the primary analysis.

Supplementary Table 5: Quality of life (EQ-5D EuroQol score and VAS score)

EQ-5D	Time point	Mesh	No Mesh	Total	Linear regression model Adjusted mean difference[$] (95% Confidence Interval) P-value	Repeat measures model Effect Size[$] (95% Confidence Interval) P-value
EQ-5D EuroQol score[*]						
N Mean [SD] Min – Max	Baseline	384 0.87 [0.20] -0.59 – 1.00	385 0.87 [0.18] -0.14 – 1.00	769 0.87 [0.19] -0.59 – 1.00	-	-0.004 (-0.026, 0.018) 0.74 **Treatment by Time Interaction P-value** 0.31
N Mean [SD] Min – Max	30 day	361 0.79 [0.23] -0.48 – 1.00	360 0.81 [0.23] -0.59 – 1.00	721 0.80 [0.23] -0.59 – 1.00	-0.018 (-0.050, 0.014) 0.27	
N Mean [SD] Min – Max	12 months	338 0.86 [0.19] -0.18 – 1.00	337 0.84 [0.21] -0.18 – 1.00	675 0.85 [0.20] -0.18 – 1.00	0.006 (-0.022, 0.035) 0.66	
N Mean [SD] Min – Max	**24 months**	**314 0.85 [0.22] -0.08 – 1.00**	**314 0.85 [0.23] -0.08 – 1.00**	**628 0.85 [0.23] -0.08 – 1.00**	**0.006 (-0.027, 0.039) 0.72**	
EQ-5D VAS score[†]						
N Mean [SD] Min – Max	Baseline	385 80.2 [16.6] 6 – 100	386 79.7 [17.2] 0 – 100	771 79.9 [16.9] 0 – 100	-	-0.866 (-2.770, 1.037) 0.37 **Treatment by Time Interaction P-value** 0.94
N Mean [SD] Min – Max	30 day	362 76.2 [18.1] 10 – 100	364 76.3 [18.3] 0 – 100	726 76.2 [18.2] 0 – 100	-0.396 (-2.882, 2.090) 0.75	
N Mean [SD] Min – Max	12 months	345 78.2 [19.8] 0 – 100	339 79.4 [17.8] 0 – 100	684 78.8 [18.8] 0 – 100	-1.606 (-4.207, 0.996) 0.23	
N Mean [SD] Min – Max	**24 months**	**321 80.0 [19.0] 0 – 100**	**314 80.0 [17.6] 1 – 100**	**635 80.0 [18.3] 0 – 100**	**-0.179 (-2.883, 2.525) 0.90**	

*EQ-5D EuroQol Score ranges from -0.59 – 1, with higher scores indicating better outcome

[†]EQ-5D VAS ranges from 0 – 100, with higher scores indicating better outcome

[$]adjusted for all minimisation variables (stoma type, surgical incision, skin closure type) and baseline score. Estimates from the repeated measures analyses are based on model without the treatment by time interaction term.

Differences >0 favour Mesh.

The EQ-5D scores at the 2 year time-point (shown in bold) are the primary analyses.

Supplementary Table 6: Serious Adverse Events

SAE Category	Mesh (N=394)		No Mesh (N=396)		Total (N=790)	
	Patients	*Events*	*Patients*	*Events*	*Patients*	*Events*
WOUND						
Stoma Site wound infection/Midline Non Stoma wound infection	39 (10%)	41	43 (11%)	44	82 (10%)	85
Uncertain/Surgical Site Infection	12 (3%)	12	6 (2%)	6	18 (2%)	18
Seroma formation	2 (1%)	2	1 (<1%)	1	3 (<1%)	3
Excess Wound Pain	4 (1%)	5	2 (1%)	2	6 (1%)	7
Wound Haematoma	3 (1%)	3	7 (2%)	7	10 (1%)	10
CARDIAC						
Arrhythmia/Bradycardia	5 (1%)	6	3 (1%)	3	8 (1%)	9
Congestive Cardiac Failure	2 (1%)	2	0 (0%)	0	2 (<1%)	2
Hypotension	2 (1%)	2	2 (1%)	2	4 (1%)	4
Myocardial infarction	0 (0%)	0	1 (<1%)	1	1 (<1%)	1
INTRAOPERATIVE						
Iatrogenic Bowel Injury	5 (1%)	5	4 (1%)	5	9 (1%)	10
Iatrogenic Ureteric Injury	1 (<1%)	1	0 (0%)	0	1 (<1%)	1
GASTROINTESTINAL						
Anastomotic Leak	12 (3%)	13	9 (2%)	9	21 (3%)	22
Ileus	25 (6%)	25	19 (5%)	19	44 (6%)	44
Large Bowel Obstruction	2 (1%)	2	0 (0%)	0	2 (<1%)	2
Small Bowel Obstruction	15 (4%)	19	13 (3%)	18	28 (4%)	37
Staple Line Haematoma	1 (<1%)	1	2 (1%)	2	3 (<1%)	3
Gastrointestinal Bleeding	1 (<1%)	1	0 (0%)	0	1 (<1%)	1
Constipation	0 (0%)	0	7 (2%)	7	7 (1%)	7
Diarrhoea	4 (1%)	4	3 (1%)	5	7 (1%)	9
Dyspepsia	1 (<1%)	1	1 (<1%)	1	2 (<1%)	2
Enterocutaneous Fistula	4 (1%)	4	4 (1%)	5	8 (1%)	9
Acute Colitis Pouchitis	5 (1%)	5	6 (2%)	6	11 (1%)	11
C.Diff Infection	3 (1%)	3	4 (1%)	4	7 (1%)	7
Intraabdominal Abscess Only	2 (1%)	2	4 (1%)	4	6 (1%)	6
Pancreatitis	1 (<1%)	1	0 (0%)	0	1 (<1%)	1
RESPIRATORY						
Pulmonary Atelectasis	2 (1%)	2	0 (0%)	0	2 (<1%)	2
Pneumothorax	0 (0%)	0	1 (<1%)	1	1 (<1%)	1
Pneumonia	13 (3%)	14	5 (1%)	5	18 (2%)	19
NEOPLASMS						
Cancer Recurrence	7 (2%)	8	7 (2%)	8	14 (2%)	16
DeNovo Cancer	0 (0%)	0	5 (1%)	5	5 (1%)	5
METABOLIC/OTHER						
Sepsis/Infection	8 (2%)	8	3 (1%)	3	11 (1%)	11
Gout	0 (0%)	0	1 (<1%)	1	1 (<1%)	1
Dehydration/ Kidney Injury	7 (2%)	8	2 (1%)	2	9 (1%)	10
Retention	2 (1%)	2	2 (1%)	2	4 (1%)	4
Fall/Syncope	2 (1%)	2	3 (1%)	3	5 (1%)	5
Cerebrovascular Accident	1 (<1%)	1	3 (1%)	3	4 (1%)	4
Venous Thromboembolism	2 (1%)	2	0 (0%)	0	2 (<1%)	2
Metabolic	0 (0%)	0	1 (<1%)	1	1 (<1%)	1
Other	15 (4%)	15	9 (2%)	11	24 (3%)	26
Total		222		196		418

Of the 790 patients randomised, 274 (34.7%) experienced at least one SAE.