

## DREAMS TRIAL

### END OF TRIAL REPORT

<b>Title</b>	Dexamethasone Reduce Emesis after Major Gastrointestinal Surgery
<b>EudraCT number</b>	2010-022894-32
<b>Sponsor protocol code</b>	RG_10-209
<b>ISRCTN number</b>	21973627
<b>Sponsor details</b>	University of Birmingham Edgbaston Birmingham B15 2TT
<b>REC reference number</b>	10/H0402/77
<b>Details of IMP</b>	Dexamethasone
<b>Arms</b>	This was a two-arm trial. Patients were randomised in a 1:1 ratio to receive a single dose of 8 mg IV dexamethasone or not.
<b>Analysis stage</b>	Final
<b>Date of end of trial declaration</b>	16 <sup>th</sup> February 2015
<b>Primary completion date</b>	28 <sup>th</sup> January 2014
<b>Global end date of trial reached?</b>	Yes

<b>Chief Investigator</b>	Professor Dion Morton
<b>Signature</b>	
<b>Date</b>	

**This report was prepared by the Chief Investigator on behalf of the Sponsor.**

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## GENERAL INFORMATION ABOUT THE TRIAL

### Background and Rationale

Postoperative nausea and vomiting (PONV) is one of the most common complications affecting patients after surgery. The pathophysiology of PONV is multifactorial, but as patients undergoing colorectal surgery are exposed to various causative agents in addition to the physical factors of bowel manipulation predisposing to ileus, they are at a substantially higher risk of this problem. Following surgical intervention, patients view PONV as a very undesirable outcome, even more unpleasant than pain [1]. It causes significant morbidity, delays nutrition and increases the length of stay in hospital. Given that over 60,000 colorectal operations are performed annually in the UK alone, PONV has significant medical and cost implications to healthcare.

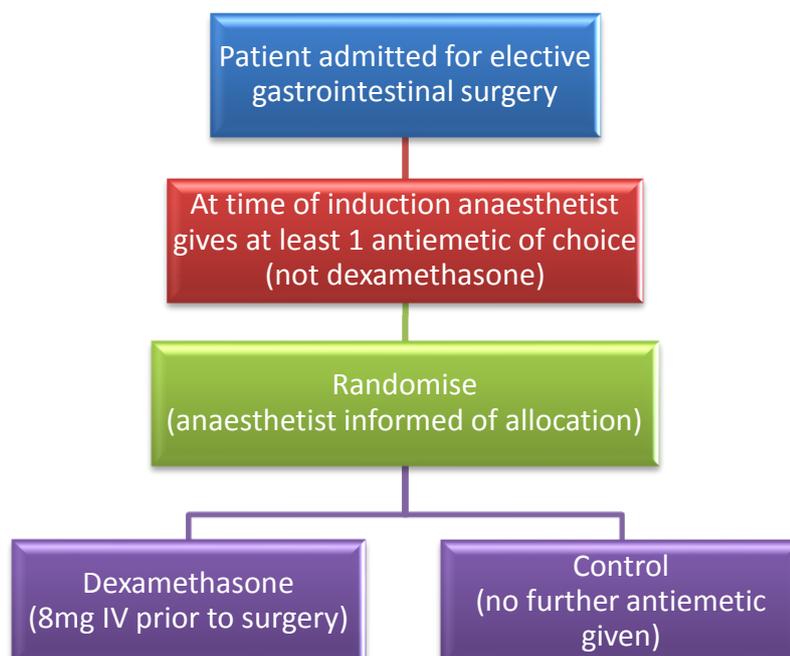
Dexamethasone is a potent corticosteroid that has been reported to influence a variety of patient and clinician-based recovery outcome measures [2, 3]. Dexamethasone has been carefully assessed in the prevention of PONV in low and intermediate risk surgery, and shown to have a substantial benefit. In a trial of over 4,000 patients that assessed 64 different combinations of anaesthetic measures, dexamethasone was identified as effective in reducing PONV [3]. However, only 11% of patients underwent abdominal procedures and only a small fraction underwent major gastrointestinal surgery [4].

In this study, the efficacy of the addition of a single dose of 8mg of IV dexamethasone, given at induction of anaesthesia, on reducing PONV and on recovery after gastrointestinal surgery was assessed.

### Main Objective

DREAMS is a phase IV, double blind multicentre randomised controlled trial (RCT) with the primary objective of determining whether preoperative dexamethasone reduces postoperative vomiting in patients undergoing major elective gastrointestinal surgery.

### Trial Schema



## Trial Design

DREAMS is a two-stage trial: i) a pilot study and ii) a phase IV RCT. The pilot study assessed recruitment rates, the randomisation process, the patient pathway and piloted the case report forms. The aim of the pilot was to inform the processes used in the main trial.

The pilot trial completed successfully and the main trial followed on directly. It is a large, phase IV, double-blind multi-centre randomised controlled trial comparing the effects of a single dose of 8mg IV dexamethasone on patient recovery after major gastrointestinal surgery.

## Background Therapy

All patients were required to be administered one additional anti-emetic at the time of induction. This anti-emetic was anaesthetist choice but could not be dexamethasone. The anti-emetic had to be administered following induction of anaesthesia but prior to commencement of surgery.

## SUBJECT DISPOSITION

### Eligibility Criteria

All patients undergoing elective open and laparoscopic gastrointestinal surgery for malignant or benign pathology, including small and large bowel resections, defunctioning stomas and closures of stomas, were eligible for entry into the study.

The exclusion criteria were obstructed patients; pregnant patients; those with a known adverse reaction to dexamethasone; patients currently taking any form of steroid medication except steroid inhalers, suppositories, pessaries, eye-drops, one-off local injections to a joint, and topical preparations; diabetes (including diet controlled)/ hyperglycaemic patients (blood glucose level >10mmol/l); an active gastric ulceration confirmed endoscopically; glaucoma; patients under the age of 18 and those patients unable or unwilling to give written informed consent for the study.

### Recruitment

The first patient was recruited and randomised into the trial on the 17-Jul-2011 and the last patient was randomised into the trial on 31-Jan-2014.

The study was open in the UK only and was open 48 centres.

### Population of Trial Subjects

A total of 1350 patients were randomised into the study.

**Table 1: Age breakdown for the trial**

Age Group	Number of participants
18 – 64	631
65 – 84	690
85 years and over	29

<b>TOTAL</b>	<b>1350</b>
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### Allocation Method and Blinding

Patients were randomised into the trial on a 1:1 ratio. A minimisation procedure using a computer-based algorithm was used. The stratification variables were:

- Gender
- Smoking status
- Open and laparoscopic surgery
- Intended post-operative analgesia
- ASA grade
- Patients within and outside of the Enhanced Recovery Pathway (ERAS).

The operating surgeon, the subject and the assessor were blinded to treatment allocation.

### Withdrawals, Deaths and Losses to Follow-Up

A total of 1350 patients entered the trial, with 676 patients entered into the 'Dexamethasone' arm and 674 in the 'No Dexamethasone' arm.

Of these 1350 patients, 99.6% have contributed data to primary outcome and 0.4% are missing any primary outcome data.

<b>Dexamethasone Arm</b>	<b>No Dexamethasone Arm</b>
1 patient died on Day 2	1 patient withdrew consent for all follow at Day 2
1 patient died on Day 4	1 patient died on Day 4
1 patient died on Day 5	2 patients died on Day 5
6 patients died post-Day 5 and prior to Day 30.	1 patient withdrew from all follow up on Day 6
	5 patients died post-Day 5 and prior to Day 30.

## BASELINE CHARACTERISTICS

**Table 2: Patient characteristics at baseline**

	Dexamethasone (N=674)	No Dexamethasone (N=676)	Total (N=1350)
<b>Stratification Factors</b>			
Gender			
Female	283 (42%)	284 (42%)	567 (42%)
Male	391 (58%)	392 (58%)	783 (58%)
Is the patient a smoker?			
No	574 (85%)	576 (85%)	1150 (85%)
Yes	100 (15%)	100 (15%)	200 (15%)
Type of surgery			
Laparoscopic	429 (64%)	427 (63%)	856 (63%)
Open	245 (36%)	249 (37%)	494 (37%)
Epidural or PCA			
Epidural	307 (46%)	308 (46%)	615 (46%)
PCA	238 (35%)	238 (35%)	476 (35%)
Not known	68 (10%)	70 (10%)	138 (10%)
Other	50 (7%)	49 (7%)	99 (7%)
None	11 (2%)	11 (2%)	22 (2%)
ASA grade			
P1 normal healthy patient	157 (23%)	155 (23%)	312 (23%)
P2 mild systemic disease	402 (60%)	405 (60%)	807 (60%)
P3 severe systemic disease	113 (17%)	113 (17%)	226 (17%)
P4 severe life threatening disease	2 (<0.5%)	3 (<0.5%)	5 (<0.5%)
Enhanced recovery after surgery program			
No	54 (8%)	53 (8%)	107 (8%)
Yes	611 (91%)	615 (91%)	1226 (91%)
Not known	9 (1%)	8 (1%)	17 (1%)
<b>Other Baseline Variables</b>			
Age at randomisation			
Mean (SD)	63.6 [13.4]	63.4 [13.5]	63.5 [13.4]
Median (IQR)	66 {56-74}	65 {56-73}	65 {56-74}
Range	19 - 93	18 - 90	18 - 93
Pack years (smokers only)			
Mean (SD)	27.4 [17.6]	22.9 [19.8]	25.1 [18.8]
Median (IQR)	25 {15-37.5}	16.5 {8-35}	20.5 {11-35.5}
Range	0.5-80	0.04 - 114	0.04 - 114

## END POINTS

### Primary End Point

The primary endpoint of the DREAMS trial was the proportion of patients experiencing vomiting within the first 24 hours post-surgery. Patients who had vomiting episodes recorded by either themselves or their medical care team were counted as having experienced vomiting.

All patients with available data were included in the analyses and was analysed in the group to which they were randomised. The overall proportion of patients experiencing vomiting was compared between treatment arms by using a chi-squared test. The denominator for the proportion of patients was the number of patients randomised in each arm.

### Secondary End Points

Secondary endpoints in DREAMS were:

- vomiting/nausea up to 120 hours post-surgery
- use of PRN post-operative anti-emetics
- nausea measured using a validated PONV intensity scale
- fatigue measured using the FACIT-F questionnaire
- time to tolerating oral diet
- length of hospital stay
- health related quality of life measured using the EuroQol Eq-5D
- infection rates and healing complications within 30 days of surgery

### Statistical Analyses

#### Other vomiting / nausea

The primary endpoint considers vomiting data within the first 24 hours post-surgery. Similar data was also collected up to 5 days post-surgery or discharge (if earlier than 5 days). These data was analysed using the same methods employed for the primary outcome.

Patient reported nausea was collected on the patient-completed forms via a 0-100 scale where the patient indicated the severity of their nausea since the operation. An independent two-sample t-test was used to compare the treatment arms at each time point post-randomisation (24 hours, 72 hours and 5 days).

#### Use of post-operative anti-emetics

Data regarding use of anti-emetics post-surgery were collected on the staff-completed nausea and vomiting form completed at 24 hours, 3 days and 5 days post-surgery. At each separate time point the proportion of patients receiving post-operative anti-emetics was compared using a chi squared test.

#### Oral diet

Data regarding patients commencing an oral diet were collected on the staff-completed nausea and vomiting form completed at 24 hours, 3 days and 5 days post-surgery. At each separate time point the proportion of patients was compared using a chi squared test.

*Health related quality of life and Fatigue*

Quality of life and Fatigue will be measured using the EuroQol EQ-5D / FACIT-F questionnaires at three time points – immediately prior to surgery, 5 days post-surgery and 30 days post-surgery. These questionnaires will be scored by the original validated method. An independent two-sample t-test will be used to compare the treatment arms at each time point post-randomisation. Two analyses will be carried out – firstly a comparison of the absolute data, and secondly a comparison of the within patient change from baseline.

*Length of Hospital Stay*

Length of hospital stay was analysed using standard logrank methods.

*Infection rates and Healing Complications with 30 days of surgery*

Data on surgical complications were collected via the 30 day telephone questionnaire. The proportion of patients experiencing surgical complications was analysed using chi squared tests.

## ADVERSE EVENTS

### Adverse event information

SAEs were collected for all patients in the study from the first trial treatment until 30 days after the last treatment.

Trial outcome data were collected at Days 1, 3, 5 and 30 post-operatively, data collected included both staff completed forms and patient completed questionnaires. At these time-points, patients were either seen as inpatients or contacted by telephone. Data was collected on nausea and vomiting at each of these time-points. SAE data were collected until 30 days post-operatively.

**Table 3: Line Listing of Serious Adverse Reactions**

Trial (Subject) Number	Country; Gender; Age	SARs*	Outcome**	Time to onset***	Suspect Investigational Drug (If blinded, state 'blinded')	Daily dose; Route; Formulation	Dates of treatment	Narrative (i.e. comments describing the case and actions)
1005	UK; F; 71	Leaking ileostomy bag	Recovered	75 days	blinded	8mg dexamethasone IV	17-Aug-2011	Leaking ileostomy bag & high output stoma. Probably related to surgery, unrelated to IMP
1017	UK; M; 23	Abdominal pain & vomiting. Partial small bowel obstruction. Wound infection.	Recovered	19 days	blinded	8mg dexamethasone IV	08-dec-2011	Abdominal pain & vomiting. Raised white cells & inflammatory markers, stool culture negative. Partial small bowel obstruction – laparotomy with adhesionolysis performed. Infection of laparotomy wound. Related to surgery. NOT related to IMP.
1032	UK; M; 55	Erythematous wound	Recovered	5 days	blinded	8mg dexamethasone	22-Feb-2012	Painful erythematous wound, wound opened and swelling reduced with co-amoxiclan.

						IV		Related to surgery, not related to IMP. Expected
1042	UK; M; 58	Prolonged ileus, high stoma output	Recovered	3 days	blinded	8mg dexamethasone IV	05-Mar-2012	Prolonged ileus, high stoma output. Related to surgery, not related to IMP
1048	UK; M; 42	WOUND INFECTION	Recovered	03-Apr-12	27 days	blinded	07-Mar-12	WOUND INFECTION.Treated with flucloxacillin 500mg QDS for 7 days. Event ceased 10/04/12. Probably related to surgery. Possibly related to IMP. Expected.
1059	UK	Rectal haemorrhage	Recovered	26 days	blinded	8mg dexamethasone IV	14-Mar-2012	Rectal haemorrhage, known diverticular disease of bowel. Probably related to surgery BUT unrelated to dexamethasone.
1064	UK; M; 71	Anastomotic leak	Recovered	0 days	blinded	8mg dexamethasone IV	20-Mar-2012	Anastomotic leak. Related to surgery; probably unrelated to IMP. Expected
1066	UK; M; 62	Prolonged ileus	Recovered	4 days	blinded	8mg dexamethasone IV	21-Dec-2011	Prolonged ileus, anastomotic hold-up, treated conservatively. Related to surgery, not related to IMP. Expected
1088	UK; M; 80	Wound breakdown and infection.	Continuing	12 days	blinded	8mg dexamethasone IV	26-Apr-2012	Wound breakdown after laparotomy and infection. Possibly related to surgery; possibly related to IMP. Expected.
1089	UK;	Intra-abdominal sepsis, small bowel perforation	Recovered	5 days	blinded	8mg dexamethasone	30-Apr-2012	Intra-abdominal sepsis secondary to multiple small bowel perforations.

						IV		Related to surgery, not related to IMP.
1099	UK; M; 59	Emergency laparoscopy	Recovered	1 day	blinded	8mg dexamethasone IV	10-may- 2012	Emergency diagnostic laparoscopy and washout, refashioning of stoma. Related to surgery not related to IMP.
1194	UK; M; 52;	WOUND INFECTION	Recovered	14-Aug-12	15	blinded	30-Jul-12	WOUND INFECTION- Flucloxacillin 250mg QDS for 5 days. Related to surgery, possibly related to dexamethasone. Expected.
1221	UK; F; 50;	WOUND INFECTION	Recovered	03-Sep-12	21	blinded	13-Aug-12	WOUND INFECTION- At 30 day follow up telephone contact patient stated that they had a wound infection following discharge from hospital. Seen by GP prescribed antibiotics. Related to surgery, possibly related to dexamethasone. Expected.
1222	UK; M; 64;	WOUND INFECTION	Recovered	18-Aug-12	5	blinded	13-Aug-12	WOUND INFECTION-Patient reported at 30 day follow up. Related to surgery, possibly related to dexamethasone. Expected.
1229	UK; F; 18	WOUND INFECTION	Recovered	15-Aug-13	days tbc	blinded	15-Aug-12	WOUND INFECTION-awaiting further information regarding treatment. Probably related to surgery. Possibly related to surgery. Possibly related to IMP. Expected.
1241	UK; F; 61	? WOUND INFECTION	Recovered	22-Aug-13	days tbc	blinded	22-Aug-12	? WOUND INFECTION. Dressed daily at GP surgery. No antibiotics given.

								Probably related to surgery. Possibly related to IMP. Expected.
1314	UK; M; 58	WOUND DEHISCENCE	Recovered	02-Oct-12	10	blinded	12-Oct-12	WOUND DEHISCENCE. Patient admitted with wound dehiscence (superficial - no bowel visible, clean and dry wound). Discharged with algosterol dressing and being packed alternate days by district nurse. Healed 27th December 2012.
1355	UK; F; 68;	SMALL BOWEL OBSTRUCTION	Recovered	07-Nov-12	13	blinded	25-Oct-12	SMALL BOWEL OBSTRUCTION-Related to surgery, not related to dexamethasone. Expected.
1372	UK; M; 71;	ANASTOMOTIC LEAK	Fatal	12-Nov-12	7	blinded	05-Nov-12	ANASTOMOTIC LEAK-Post mortem showed anastomotic leak, developed peritonitis and died. Patient found unresponsive with vomit in nebuliser mask-no output, not breathing. CPR given for 30 minutes. Related to surgery, possibly related to dexamethasone. Expected.
1385	UK; M; 80	WOUND DEHISCENCE, WOUND INFECTION	Recovered	23-Nov-12	11 days	blinded	12-Nov-12	WOUND DEHISCENCE, WOUND INFECTION. Small opening noted at bottom of wound noted beaded suture removed 23/11/12 - full thickness dehiscence seen. Area re-sutured and base of wound placed by consultant on ward. Referred to Tissue Viability Team. At time of 30-

								day follow-up patient no longer requiring wound packing, only simple dressing from district nurse. Event ceased 11/12/12. Related to surgery, possibly related to IMP. Expected.
1388	UK; M 51	VOMITING, ABDOMINAL PAIN	Recovered	17-Nov-12	5 days	blinded	12-Nov-12	VOMITING, ABDOMINAL PAIN. Re admitted on 17/11/13 with vomiting and abdominal pain-discharge letter sent. Event ceased 20/11/12. Likely related to surgery unlikely related to IMP. Expected.
1398	UK; M; 51	WOUND INFECTION, CLOTTED BLOOD AROUND WOUND	Recovered	06-Dec-12	16 days	blinded	20-Nov-12	WOUND INFECTION, CLOTTED BLOOD AROUND WOUND. Admitted via A&E with wound problems - clotted blood around wound. Wound clean and no further evidence of blood after admission. Event ceased 07/12/12. Related to surgery, possibly related to IMP. Expected.
1421	UK; M; 56	WOUND INFECTION AND ANASTOMOTOC LEAK FOLLOWING SURGERY.	Recovered	05-Dec-12	7 days	blinded	28-Nov-12	WOUND INFECTION AND ANASTOMOTIC LEAK FOLLOWING SURGERY. Taken back to theatre to fill the leaking section. The nature of surgery, low anterior resection has a risk of anastomosis leak. Event ceased 20/12/12. The complication of anastomotic leak and wound infection

								probably related to surgery. It is probably unrelated to IMP. Expected.
1438	UK; F; 58;	URINARY TRACT INFECTION	Recovered	04-Jan-13	30	blinded	05-Dec-12	URINARY TRACT INFECTION-Confirmed by dipstick. Related to surgery, probably not related to surgery. Expected.
1438	UK; F; 58;	WOUND INFECTION	Recovered	05-Dec-12	0	blinded	05-Dec-12	WOUND INFECTION-Required packing by district nurse. Related to surgery, possibly related to dexamethasone. Expected.
1440	UK; F; 74;	WOUND INFECTION	Recovered	17-Dec-12	11	blinded	06-Dec-12	WOUND INFECTION-wound infection treated by GP 19th December 2012, antibiotics. Wound noted to be infected by GP. No swab result available. Treated with 5 day course of antibiotics. Wound healed at 30 day follow up telephone call. Related to surgery, possibly related to dexamethasone. Expected.
1442	UK; M; 68;	WOUND INFECTION	Recovered	24-Dec-12	17	blinded	07-Dec-12	WOUND INFECTION-patient stated on Day 30 post-operative that had a course of antibiotics for wound infection after discharge and completed course. Related to surgery, possibly related to dexamethasone. Expected.
1464	UK; M; 66	SUPERFICIAL DEHISCENCE ON LOWER PART OF ABDOMINAL WOUND.	Recovered	07-Jan-13	17 days	blinded	21-Dec-12	SUPERFICIAL DEHISCENCE ON LOWER PART OF ABDOMINAL WOUND. Related to surgery, possibly related IMP.

## DREAMS END OF TRIAL REPORT

								Expected
1488	UK; F; 65	WOUND INFECTION	Recovered	12-Feb-13	34 days	blinded	09-Jan-13	WOUND INFECTION - swab result scanty growth of coliform bacilli. Event ceased 19/02/13. Probably related to surgery. Possibly related to IMP. Expected.
1509	UK; M; 76	RESPIRATION ARREST DUE TO ASPIRATION IB RECTAL CANCER AND PELVIC EXENTERATION	Fatal	22-Jan-13	5	blinded	17-Jan-13	RESPIRATION ARREST DUE TO ASPIRATION IB RECTAL CANCER AND PELVIC EXENTERATION-Extensive surgery, sudden vomiting-aspiration. Irreversible hypoxia. Unresponsive to advanced life support. Related to surgery, unlikely to be related to dexamethasone. Expected.
1536	UK; M; 58	DEVELOPED WOUND INFECTION	Recovered	08-Feb-13	10 days	blinded	29-Jan-13	DEVELOPED WOUND INFECTION post discharge from hospital treated with antibiotics. Event ceased 04/04/13. Related to surgery. Possibly related to IMP. Expected.
1574	UK; M; 74	WOUND OPENED	Recovered	21-Mar-13	31	Blinded	18-Feb-13	WOUND OPENING-At Day 30 telephone call patient reported wound had opened up. They reported that a course of antibiotics had been prescribed. District nurse was going to dress wound. Patient reports wound opened approximately one week ago. Related to surgery. Possibly related to dexamethasone.

								Expected.
1596	UK; M; 65	WOUND DEHISCENCE REQUIRING RE- LAPAROTOMY.	Recovered	06-Mar-13	5 days	blinded	01-Mar-13	WOUND DEHISCENCE REQUIRING RE-LAPAROTOMY. Two wound clips removed 05/03/13 wound began oozing and patient reported a 'pulling' sensation when moving in bed 06/03/13 02:00hrs. Deep dehiscence of wound noted. Patient returned to theatre 06/03/13 18:15 for laparotomy resuture of burst abdomen was checked and normal. Probably related to IMP definitely related to surgery. Expected.
1599	UK; M; 69	NEGATIVE SEPSIS	Recovered	15-Mar-13	14 days	blinded	01-Mar-13	NEGATIVE SEPSIS immediately after trial without catheter admitted to ITU. Event ceased 27/03/2013. Related to surgery, possibly related to IMP. Expected.
1627	UK; F; 77	ACUTELY CONFUSED	Recovered	19-Mar-13	1 day	blinded	18-Mar-13	ACUTELY CONFUSED- expected longer admission due to Parkinsons disease, patient became acutely confused. Delusional thoughts, contributed by parkinsons disease rivastigmine medication increased and patient improved and discharged home 24/04/14. Unlikely to be related to IMP or surgery. Expected.

1657	UK; F; 56	SEVERE PAIN VOMITING AND DIARRHOEA	Recovered	11-Apr-13	14 days	blinded	28-Mar-13	SEVERE PAIN VOMITING AND DIARRHOEA-emergency admission to hospital, further report to follow once notes obtained from outside hospital. Patient phoned today for 30 Day follow up and informed me of the event. Event ceased 17/04/13. Probably not related to treatment but awaiting confirmation regarding whether IMP or surgery. Expected.
1659	UK; M; 66	COLLECTION, ILEOSTOMY FLUX, PROLONGED ILEUS.	Recovered	08-Apr-13	6 days	blinded	02-Apr-13	COLLECTION, ILEOSTOMY FLUX, PROLONGED ILEUS. Pelvic collection due to deep operation. Stoma complications-stoma was formed at surgery. Event ceased 17/05/2013. Related to surgery, possibly related to IMP. Expected.
1662	UK; M; 73;	ATRIAL FIBULATION	Recovered	05-Apr-13	2	blinded	03-Apr-13	ATRIAL FIBULATION-Previous aortic valve replacement. Given two doses of 500 mg digoxin and a dose of 2.5 mg bisoprolol pm 5th April 2013. Recovered. Related to surgery, not related to dexamethasone. Expected.
1662	UK; M; 73;	COFFEE GROUND VOMIT AND X1 PROBABLE GI BLEED	Recovered	04-Apr-13	1	blinded	03-Apr-13	COFFEE GROUND VOMIT AND X1 PROBABLE GI BLEED-Had 2 units of blood (packed red cells) on 4th April 2013 and vitamin K injections on 4th

								April 2013. Related to surgery, probably related to dexamethasone. Expected.
1663	UK; F; 75	WOUND DEHISCENCE, WOUND OOZING	Recovered	15-Apr-13	12 days	blinded	03-Apr-13	WOUND DEHISCENCE, WOUND OOZING clips removed. Wound dehiscence to 2cm length. For 10/7 flucloxacillin only. Related to surgery, possibly related to IMP. Expected.
1677	UK; M; 59	WOUND INFECTION	Recovered	29-Apr-13	17 days	blinded	12-Apr-13	WOUND INFECTION-referred by GP for hospital review as evidence of infection in wound. Wound washed out and antibiotics started. Identified during 30 day follow up interview. Related to surgery. Probably related to IMP. Expected.
1691	UK; M; 26	WOUND INFECTION	Recovered	17-Apr-13	0	blinded	17-Apr-13	WOUND INFECTION. Treated with flucloxacillin. Event ceased 24/04/13. Probably related to surgery. Possibly related to IMP. Expected.
1697	UK; M; 47	WOUND INFECTION	Recovered	25-Apr-13	6 days	blinded	19-Apr-13	WOUND INFECTION-patient discharged with district nurse care 13/05/2013. Complication related to surgery. Probably related to IMP. Expected.
1716	UK; M; 65	SEVERE REFLUX OESOPHAGITIS DIAGNOSED FOR OGD.	Recovered	03-May-13	7 days	blinded	26-Apr-13	SEVERE REFLUX OESOPHAGITIS DIAGNOSED FOR OGD. patient had CT scan guided drainage of abdominal collection, infection treated by antibiotics. Event ceased

								13/05/13. Probably related to surgery (its unlikely that this patient was unwell with collection and sepsis post op and subsequently also developed oesophagitus) Probably not related to IMP probably related to surgery. Expected.
1718	UK; M; 41	WOUND INFECTION	Recovered	10-May-13	11 days	blinded	29-Apr-13	WOUND INFECTION-15/05/13 umbilicus dehisced abdominal wound. commenced on oral antibiotics. Pack cavity with gauze and apply suction continuous therapy. 20/05/13. Related to surgery. Probably related to IMP Expected.
1729	UK; F; 30	HEAVY STAPH AUREUS GROWTH IN WOUND.	Recovered	24-May-13	23 days	blinded	01-May-13	HEAVY STAPH AUREUS GROWTH IN WOUND. Flucloxacillin for 1/52. Event ceased 01/06/13. Probably related to surgery. Possibly related to IMP. Expected.
1739	UK; M; 57	UPPER GI BLEED 3 DUODENAL ULCERS	Recovered	25-May-13	18 days	blinded	07-May-13	UPPER GI BLEED 3 DUODENAL ULCERS INJECTED WITH ADRENALINE, IV omeprazole & transfusion 3 units of blood. Event ceased 28/05/13. Unrelated to surgery probably due to IMP. Expected.
1744	UK; F; 80	WOUND DIHISCENCE	Recovered	20-Jun-13	43	blinded	08-May-13	WOUND DIHISCENCE- Pereneal wound small dehiscence, packed with aquacel. Event ceased 03/09/14. Definitely related

								to surgery, possibly related to IMP. Expected.
1749	UK; F; 27	CHEST INFECTION	Recovered	13-May-13	4 days	blinded	09-May-13	CHEST INFECTION-given IV antibiotics. Event ceased 17/05/2013. Recognised post-op complication. Related to surgery and probably related to IMP. Expected.
1756	UK; M; 35	WOUND ABSESS	Recovered	27-May-13	13 days	blinded	14-May-13	WOUND ABSESS-patient re-admitted by GP due to wound abscess. Wound drained, oral antibiotics started. Event ceased 29/05/13. Related to surgery, probably related to IMP. Expected.
1756	UK; M; 35	WOUND INFECTION	Recovered	06-Jun-13	23 days	blinded	14-May-13	WOUND INFECTION. Previous pericolic abscess, abscess at port site post-op, wound improving, infection at bottom of wound currently. Probably unrelated to IMP. Complication of surgery. Expected.
1768	UK; F; 64	WOUND INFECTION	Recovered	24-May-13	7 days	blinded	17-May-13	WOUND INFECTION-taken back to theatre for laporotomy and resuturing of abdomen wound due to full dehiscence (snapped suture). Event ceased 04/06/13. Waiting for causality. Expected.
1770	UK; M; 64	WOUND INFECTION	Recovered	26-May-13	6 days	blinded	20-May-13	WOUND INFECTION-wound opened due to collection of puss. Wound swollen and cellulitic with puss discharging from wound. Wound opened

								26/05/13, swabs taken, wound packed with aquarel. Related to surgery. Possibly related to IMP. Expected.
1771	UK; M; 69	RAISED TROPININ AND MALAENA POST OP. OGD SHOWED RED AREA IN STOMACH. Not treated other than PPI.	Recovered	21-May-13	1 day	blinded	20-May-13	RAISED TROPININ AND MALAENA POST OP. OGD SHOWED RED AREA IN STOMACH. Not treatment other than PPI. Event ceased 28/05/13. Gastric inflammation probably due to IMP. Rise in troponin probably related to IMP and likely to be related to surgery. Expected.
1776	UK; F; 79	ABDOMIN PAIN, NAUSEA AND DIARRHOEA	Recovered	31-May-13	11 days	blinded	20-May-13	ABDOMIN PAIN, NAUSEA AND DIARRHOEA-chest xray showed right sided pneumonia. Treated with course of antibiotics. Even ceased 01/06/2013. Waiting causality. Expected.
1789	UK; M; 62	WOUND INFECTION	Recovered	26-May-13	3 days	blinded	23-May-13	WOUND INFECTION- Antibiotics commenced dressed by district nurse- given tricloxacillin by hospital on discharge given course of x2 of coamoxiclav on 27/05/13 and 05/06/13. Event ceased 2/06/13. Related to Surgery possibly related to IMP. Expected.
1790	UK; M; 62	PROLONGED HOSPITALISATION DUE TO WOUND DEHISCENCE	Recovered	23-May-13	0 days	blinded	23-May-13	PROLONGED HOSPITALISATION DUE TO WOUND DEHISCENCE. Vac therapy required. Complex

								surgery involving abdominal wall reconstruction for complex incisional hernia. Wound healed by 26/07/13. Related to surgery possibly related to IMP. Expected.
1808	UK; M; 66	URINE TRACT INFECTION	Recovered	10-Jun-13	6 days	blinded	04-Jun-13	URINE TRACT INFECTION- Retention catheterised. Event ceased 11/06/13. Related to surgery possibly related to IMP. Expected.
1823	UK; M; 76	WOUND DEHISCENCE	Recovered	16-Jun-13	9 days	blinded	07-Jun-13	WOUND DEHISCENCE- superficial wound dehiscence, 3 clips removed wound packed with aquagel. Discharged home under care of district nurse 19.06.13. Attended A&E with urinary retention. Bloods within normal limits. Catheterised. Discharged from A&E with catheter. Event ceased 18/06/13. Related to surgery possibly related to IMP. Expected.
1824	UK; F; 79	PORT SITE HERNIA	Recovered	13-Jun-13	3 days	blinded	10-Jun-13	PORT SITE HERNIA. Event ceased 14/06/13. Related to surgery. Probably unrelated to IMP. Expected.
1828	UK; M; 56	WOUND INFECTION- wound oozing GP prescribed antibiotics now healed.	Recovered	27-Jun-13	17 days	blinded	10-Jun-13	POSSIBLE WOUND INFECTION- wound oozing GP prescribed antibiotics now healed. Event ceased 10/07/13. Definitely related to surgery, possibly related to IMP. Expected.

1832	UK; F; 32;	WOUND INFECTION	Recovered	03-Jul-13	22	blinded	11-Jun-13	WOUND INFECTION-Patient saw GP on 3rd July 2013 and given 7 day course of antibiotics for the wound infection. Definitely related to surgery, possibly related to dexamethasone. Expected.
1839		POST OPERATIVE COLLECTION/HAEEMATOMA	Recovered	08-Jul-13	25 days	blinded	13-Jun-13	POST OPERATIVE COLLECTION/HAEEMATOMA-Previously admitted with UC with LIF and rectal pain and fresh red PR bleed 2011. Subtotal colectomy and ileostomy in 2011. Proctectomy on 13/6/2013 some discharge per wound since operation. A small amount of fluid collection in the anal canal and rectal stump. Event ceased 10/07/13. Related to surgery, unlikely related to IMP. Expected.
1845	UK; F; 55	WOUND INFECTION	Recovered	20-Jun-13	2 days	blinded	18-Jun-13	WOUND INFECTION-Patient spiked temperature of 38 at 17:30 20/06/13. IV antibiotics started 10:20 21/06/13. Wound site red and hot, some clips removed, wound packed and re-dressed 21/06/13 and 22/06/13. On 23/06/13 patient discharged with oral antibiotics. Related to surgery, possibly related to IMP. Expected.
1863	UK; F; 80	WOUND INFECTION	Recovered	3-Jul-2013	9	blinded	24-Jun-13	WOUND INFECTION- visited

								GP, treated with oral antibiotics for one week. Related to surgery, possibly related to dexamethasone. Expected.
1868	UK; F; 76	DEHYDRATION DUE TO HIGH ILEOSTOMY OUTPUT	Recovered	11-Jul-13	15 days	blinded	26-Jun-13	DEHYDRATION DUE TO HIGH ILEOSTOMY OUTPUT- re-admission with dehydration due to high ileostomy output. End date to be confirmed. Related to surgery, possibly related to IMP. Expected.
1882	UK; F; 70	EMERGENCY ADMISSION WITH ABDOMINAL PAIN AND TEMPERATURE	Recovered	12-Sep-13	72 days	blinded	02-Jul-13	EMERGENCY ADMISSION WITH ABDOMINAL PAIN AND TEMPERATURE. Scan showed a 7x connection. Drained by CT guidance 16/09/13. Drain removed 23/09/13. Event ceased 24/09/13. Related to surgery possibly related to IMP. Expected.
1886	UK; F; 64	HEAVY GROWTH OF E.COLI	Recovered	14-Jul-13	11 days	blinded	03-Jul-13	HEAVY GROWTH OF E.COLI. Event ceased 21/07/13. Probably related to surgery. Possibly related to IMP. Expected.
1890	UK; M; 82	WOUND RE-OPENED. NO EVIDENCE OF ABDOMINAL SEPSIS.	Recovered	08-Jul-13	3 days	blinded	05-Jul-13	WOUND RE-OPENED. NO EVIDENCE OF ABDOMINAL SEPSIS. Originally admitted for cardiac respiratory failure. Excubated 15.07.13. Antibiotics commenced for wound infection whilst in hospital. Discharged home with district nurse care and to visit next week for

								assessment. Event ceased 06.08.13. Waiting causality. Expected.
1914	UK; M; 76	POST OP ABDOMINAL WALL DEHISCENCE AND BOWEL HERNIATION	Recovered	25-Jul-13	14 days	blinded	11-Jul-13	POST OP ABDOMINAL WALL DEHISCENCE AND BOWEL HERNIATION. 26/07/13 Rectus mesh inserted. 31/07/13 Small bowel fistula on CT scan, chronic abdominal sepsis. 4/08/13 open abdomen. Event ceased on 26/08/13. Related to surgery possibly related to IMP. Expected.
1914	UK; M; 76	LINE SEPSIS	Recovered	31-Aug-13	51	blinded	11-Jul-13	LINE SEPSIS due to infection. Re admitted to ICU line sepsis iv antibiotics new line inserted.. Related to surgery unlikely related to IMP. Expected.
1920	UK; M; 61	WOUND INFECTION	Recovered	19-Jul-13	3 days	blinded	16-Jul-13	WOUND INFECTION treated with oral antibiotics. Related to surgery, possibly related to IMP. Expected.
1935	UK; M; 71;	SUSPECTED WOUND INFECTION	Recovered	02-Aug-13	11	blinded	22-Jul-13	SUSPECTED WOUND INFECTION-swab negative- Had course of antibiotics from GP for suspected wound infection but wound swab negative. Related to surgery, possibly related to dexamethasone. Expected.
1951	UK; M; 70	PATIENT ADMITTED TO HOSPITAL FOR URINARY INFECTION.	Recovered	21-Aug-13	26 days	blinded	26-Jul-13	PATIENT ADMITTED TO HOSPITAL FOR URINARY INFECTION. Catheter insitu. Patient awaiting urology

								review. Discharged same day. Event ceased 21/08/13. Probably related to surgery. Probably unrelated to IMP. Expected.
1963	UK; F; 77	WOUND DIHISCENCE	Recovered	05-Aug-13	5 days	blinded	31-Jul-13	WOUND DIHISCENCE-MIDLINE AND LEFT ABDOMEN, Previous stoma site, now healed 01/10/13. Definitely related to surgery, probably related to IMP. Expected.
1964	UK; M; 42;	DIARRHOEA AND HIGH TEMPERATURE.	Recovered	03-Aug-13	3	blinded	31-Jul-13	DIARRHEA AND HIGH TEMPERATURE-Admitted to A&E. Probably related to surgery, probably not related to dexamethasone. Expected.
1982	UK; F; 64	WOUND DIHISCENCE	Recovered	24-Aug-13	15 days	blinded	09-Aug-13	WOUND DIHISCENCE-Clips removed from wound by district nurse at home. Admitted to hospital on 28/08/13. Prior packing of wound but continued to leak. Sent to theatre 31/08/13 for application of vac therapy. Wound approximately 20cm x 10cm, 10cm deep. Large amount of exudate. Wound washed out during theatre. IV antibiotics given event, patient discharged 10/09/13. Vac discontinued on 17/10/13. District nurse care with aquacel and alleryn dressing, initially twice weekly then as required. Event

								ceased 03/01/14. Related to surgery, possibly related to IMP. Expected.
1987	UK; M; 77	WOUND INFECTION	Recovered	25-Aug-13	13 days	blinded	12-Aug-13	WOUND INFECTION RIF- awaiting further information regarding treatment. Event ceased 21/10/13. Wound infection post op. Related to surgery possibly related to IMP. Expected.
1987	UK; M; 77	FRANK CELLULITIS, WOUND RIF, DIHISCENSE	Recovered	10-Sep-13	29 days	blinded	12-Aug-13	FRANK CELLULITIS, WOUND RIF, DIHISCENSE being investigated. Patient recovered. Waiting causality. Expected.
1988	UK; M; 65	PATIENT DEVELOPED WOUND INFECTION. BEING TREATED WITH ANTIBIOTICS	Recovered	18-Aug-13	5 days	blinded	13-Aug-13	PATIENT DEVELOPED WOUND INFECTION. Treated with antibiotics. The complication of wound infection is related to surgery. It is probably unrelated to IMP. Although this is possible. Expected.
1991	UK; M; 69;	WOUND INFECTION	Recovered	21-Aug-13	8	blinded	13-Aug-13	WOUND INFECTION-Treated by tissue viability nurse in the community. Small area remains unhealed on 31/01/14. Related to surgery, possibly related to dexamethasone. Expected.
1992	UK; M; 68	PATIENT ADMITTED WITH ACUTE CONFUSION AND FALL (HIT HEAD).	Recovered	17-Aug-13	18 days	blinded	13-Aug-13	PATIENT ADMITTED WITH ACUTE CONFUSION AND FALL (HIT HEAD). CT scan head and commenced gentamycin for urosepsis. Confusion delirium improved. Discharged home with oral antibiotics. Event

								ceased 17/08/13. Possibly related to IP. Complication of surgery, Expected.
2020	UK; F; 72	CONSOLIDATION CHEST	Recovered	11-Sep-13	7 days	blinded	04-Sep-13	CONSOLIDATION CHEST, pleural effusion B.L. Intra-abdominal collections. Event ceased 01/10/13. Intra-abdominal collection and pneumonia related to surgery. Possibly related to IMP. Expected.
2023	UK; M; 59	WOUND SITE INFLAMMED	Recovered	11-Sep-13	5 days	blinded	06-Sep-13	WOUND SITE INFLAMMED. Some clips removed. Packed with alginate. IV antibiotics commenced. Event ceased 05/11/13. Probably related to surgery but also related to IMP. Expected.
2026	UK; M; 64	DEVELOPED RASH	Recovered	14-Sep-13	5 days	blinded	09-Sep-13	RASH. Seen by GP developed rash 5 days post op. Thought to be an allergic reaction. Given piriton. No further problems. Event ceased 28/09/13. Probably unrelated to IMP or surgery. Expected.
2028	UK; M; 50	WOUNDS OPENING	Recovered	20-Sep-13	11 days	blinded	09-Sep-13	WOUND OPENED. Clips were removed by practice nurse. Wound dressed. Same evening wound opened and bled. Attended A&E, steri strips applied. No further problems. Event ceased 20/09/13. Related to surgery. Possibly related to IMP. Expected.
2033	UK; M;	WOUND INFECTION	Recovered	20-Sep-13	10	blinded	10-Sep-13	WOUND INFECTION-Patient

	55;							reported wound infection when contacted for 30 Day follow up. Related to surgery, possibly related to dexamethasone. Expected.
2037	UK; M; 60	VOMITING & DIAGNOSED WITH URINARY TRACT INFECTION	Recovered	23-Sep-13	12 days	blinded	11-Sep-13	VOMITING & DIAGNOSED WITH URINARY TRACT INFECTION. Generally unwell, vomiting. Diagnosed with urinary tract infection. Diagnosed with AF. Discharged 15/10/13 on anticoagulant-warfarin. Related to surgery possibly related to IMP (UTI only). Expected.
2048	UK; F; 71	THRUSH on attending the day of the TWOC clinic (successful).	Recovered	30-Sep-13	13 days	blinded	17-Sep-13	THRUSH on attending the day of the TWOC clinic on 30/09/13 (successful). Event ceased 30/09/13. Definitely related to surgery possibly related to IMP. Expected.
2048	UK; M; 71;	UNCONFIRMED URINE INFECTION	Recovered	26-Sep-13	9	blinded	17-Sep-13	? URINARY TRACT INFECTION- had urinary catheter with retention which was sorted by flushing. No swab done or MSU to confirm urine infection. Definitely related to surgery, possibly related to dexamethasone. Expected.
2053	UK; M; 76	PSEUDOMONAS ABDOMINAL WOUND INFECTION	Recovered	20-Sep-13	3 days	blinded	17-Sep-13	PSEUDOMONAS ABDOMINAL WOUND INFECTION. Necessitating x3 lots of antibiotics. Event ceased 17/10/13. Definitely related to surgery. Possibly related to

								IMP. Expected.
2055		RETURNED TO THEATRE FOR LAPAROTOMY AND FORMATION OF STOMA.	Recovered	18-Sep-13	0	blinded	18-Sep-13	RETURNED TO THEATRE FOR LAPAROTOMY AND FORMATION OF STOMA. Returned to theatre for re-laparotomy and formation of end colostomy. Persistent bleeding in pelvic drain and episodes of hypotension with dropping HB. Event ceased 10/10/13. Related to surgery unlikely related to IMP. Expected.
2056	UK; M; 61	PERENIAL WOUND NOT HEALED YET	Recovered	14-Oct-13	26 days	blinded	18-Sep-13	PERENIAL WOUND NOT HEALED YET WITH INFECTION (Group G Streptococcus). Healed and required no further dressings/wound management. Event ceased 23/01/13. Definitely related to surgery. Possibly related to IMP. Expected.
2063	UK; F; 52;	WOUND INFECTION	Recovered	07-Oct-13	13	blinded	24-Sep-13	WOUND INFECTION-wound infection post op 1 week post discharge, 3x antibiotics given over 19 days. Wound healed on out-patient review on 11th November 2013. Related to surgery, possibly related to dexamethasone. Expected.
2065	UK; M; 86	WOUND INFECTION	Recovered	30-Sep-13	6 days	blinded	24-Sep-13	WOUND INFECTION-Patient had a wound infection on discharge. This required district nurse dressing. Event ceased on 10/10/13. Related to surgery. Probably related

								to IMP. Expected.
2073	UK; M; 67;	ANASTOMOTIC LEAK	Recovered	02-Oct-13	7	blinded	25-Sep-13	ANASTOMOTIC LEAK-patient admitted with nausea and vomiting. CT abdomen showed localised walled off anastomotic leak. Related to surgery, possibly related to dexamethasone. Expected.
2078	UK; M; 53;	LEAK FROM PERENIAL WOUND	Recovered	17-Oct-13	21	blinded	26-Sep-13	LEAK FROM PERENIAL WOUND-Fluoxacillin 500mg prescribed by GP for ten days due to leakage from wound, settled at 30 day phone call. Definitely related to surgery, possibly related to dexamethasone. Expected.
2083	UK; F; 83	WOUND DEHISCENCE	Recovered	14-Oct-13	13 days	blinded	01-Oct-13	WOUND DEHISCENCE healed on 13/01/14. Probably is unrelated to IMP as it is 30 day post-surgery, waiting clarification if IMP or surgery. Expected.
2107	UK; F; 81;	URINARY TRACT INFECTION-C-DIFFCILE INFECTION	Recovered	16-Oct-13	7	blinded	09-Oct-13	URINARY TRACT INFECTION-C-DIFFCILE INFECTION-Patient developed UTI and c-difficile infection resulting in prolongation of hospital stay. Related to surgery, possibly related to dexamethasone. Expected.
2111	UK; M; 66	DISTENDED ABDOMEN & VOMITING	Recovered	12-Oct-13	2 days	blinded	10-Oct-13	DISTENDED ABDOMEN & VOMITING. Drain smells of faeces. Distended abdomen and vomiting, ? minor anastomotic leak. Event ceased 25/10/13. Definitely

								related to surgery, possibly related to IMP. Expected.
2112	UK; F; 57;	WOUND NOT HEALING	Recovered	06-Nov-13	27	blinded	10-Oct-13	WOUND NOT HEALING-30 day telephone assessment completed-wound not completely healed. Related to surgery, probably related to dexamethasone. Expected.
2119	UK; M; 77;	URINARY TRACT INFECTION	Recovered	02-Nov-13	19	blinded	14-Oct-13	URINARY TRACT INFECTION-Patient was re-admitted to hospital for a urinary tract infection. Not related to surgery, unlikely to be related to dexamethasone. Expected.
2120	UK; M; 70	COMMENCED SEPSIS PATHWAY.	Recovered	17-Oct-13	2 days	blinded	15-Oct-13	COMMENCED SEPSIS PATHWAY. RR 24 HR T 37 deg. Creatinine 188 Urine output reduced. Event ceased 24/10/13. Related to surgery. Possibly related to IMP. Expected.
2127	UK; F; 62;	WOUND INFECTION	Recovered	28-Oct-13	11	blinded	17-Oct-13	WOUND INFECTION-Patient had a course of antibiotics. 2 week course of antibiotic from GP. Related to surgery, possibly related to dexamethasone. Expected.
2130	UK; F; 73	WOUND INFECTION	Recovered	23-Oct-13	5 days	blinded	18-Oct-13	WOUND INFECTION-top clips removed from wound, packed with aquagel oral antibiotics prescribed. Related to surgery. Possibly related to IMP. Expected
2142	UK; F; 57	WOUND INFECTION	Recovered	05-Nov-13	13 days	blinded	23-Oct-13	WOUND INFECTION. Related to surgery. Possibly related to IMP. Expected.

2155	UK; F; 66;	BLOOD CULTURE GREW CANDIDA	Recovered	17-Nov-13	19	blinded	29-Oct-13	BLOOD CULTURE GREW CANDIDA-two week course of casprofugin. Patient has known sensitivities allergies to penicillin which makes them susceptible to infection. Related to surgery, possibly related to dexamethasone. Expected.
2159	UK; M; 60;	URINE INFECTION	Recovered	07-Nov-13	9	blinded	29-Oct-13	URINE INFECTION-patient developed urine infection, they were treated with course of antibiotics to finish and home. Related to surgery, possibly related to dexamethasone. Expected.
2164	UK; M; 68	WOUND INFECTION	Recovered	14-Nov-13	15 days	blinded	30-Oct-13	WOUND INFECTION-patient stated that they had been treated for wound infection with antibiotics (flucloxacillin) and district nurse attending for dressing of wound - now healing and antibiotics finished. Event ceased 04/12/13. Related to surgery. Possibly related to IMP. Expected.
2165	UK; M; 64	WOUND NOT HEALING	Recovered	30-Oct-13	0 days	blinded	30-Oct-13	WOUND NOT HEALING- Wound not healing 30 days post op, improving slowly no sign of infection. reported by patient. Event ceased 16/12/13. Related to surgery possibly related to IMP. Expected.
2172	UK; M;	WOUND INFECTION	Recovered	06-Nov-13	5 days	blinded	01-Nov-13	WOUND INFECTION-Patient

	79							has infected wound, wound re-opened, Alginate pressure inserted, discharge delayed, antibiotic therapy. 14/11/2013 wound now healing well. Patient for discharge home. Waiting community social worker support. Event ceased 12/11/13. Related to surgery. Possibly related to IMP. Expected.
2175	UK; M; 68;	WOUND INFECTION	Recovered	16-Nov-13	12	blinded	04-Nov-13	WOUND INFECTION-patient re-admitted to hospital as had a wound infection that needed draining and required IV antibiotics. Related to surgery, probably related to dexamethasone. Expected.
2179	UK; F; 64;	WOUND INFECTION	Recovered	11-Nov-13	6	blinded	05-Nov-13	WOUND INFECTION on antibiotics for five days. Patient reported. Site emailed 12th June 2014. Results of swab received infection confirmed E coli. Related to surgery, possibly related to dexamethasone. Expected.
2180	UK; F; 51;	WOUND INFECTION	Recovered	26-Nov-13	21	blinded	05-Nov-13	WOUND INFECTION-Superficial wound infection to the extraction site incision. Wound swab taken 3 weeks post-op which identified pseudomonas. Treated with antibiotics. Now completely healed. Microbiology report stated may present

								colonisation. Related to surgery, possibly related to dexamethasone. Expected.
2191	UK; F; 83	VOMITING	Recovered	14-Nov-13	7 days	blinded	07-Nov-13	VOMITING-Patient re-admitted due to vomiting when discharged on 12/11/2013. Once the bowels opened patient completely settled. Event ceased 16/11/13. Related to surgery and expected, unlikely to be related to IMP. Expected.
2207	UK; F; 70	NAUSEA AND VOMITING	Recovered	27-Nov-13	12 days	blinded	15-Nov-13	NAUSEA AND VOMITING-admitted to A&E with vomiting large amounts of bile? Cause unknown awaiting CT report. NGT inserted, NBM & IV antibiotics commenced. Event ceased 07/12/13. Related to surgery, probably not related to IMP. Expected.
2209	UK; F; 46	VANCOMUGIN RESISTENT INFECTION IN PERENIAL WOUND	Recovered	18-Nov-13	3 days	blinded	15-Nov-13	VANCOMUGIN RESISTENT INFECTION IN PERENIAL. ECOLEFAM. Followed infection control guidelines. Event ceased 09/12/13. Related to surgery, possibly related to IMP. Expected.
2213	UK; M; 72;	WOUND INFECTION	Recovered	28-Nov-13	10	blinded	18-Nov-13	WOUND INFECTION-Lower midline-required removal of some sutures treated with oral augmentin. Swab taken confirmed E-Coli and pseudomonas. Definitely related to surgery, possibly related to dexamethasone.

								Expected.
2215	UK; F; 52;	WOUND INFECTION	Recovered	03-Dec-13	14	blinded	19-Nov-13	WOUND INFECTION-Post operative. Definitely related to surgery, possibly related to dexamethasone. Expected.
2222	UK; F; 81;	CHEST INFECTION	Recovered	22-Nov-13	2	blinded	20-Nov-13	CHEST INFECTION-patient developed chest infection following surgery in the hospital. Treated with antibiotics and chest physio, recovered before discharged home on 2nd December 2013. Definitely related to surgery, possibly related to dexamethasone. Expected.
2225	UK; F; 80;	WOUND INFECTION	Recovered	01-Dec-13	10	blinded	21-Nov-13	WOUND INFECTION-treated with oral antibiotics. Related to surgery, possibly related to dexamethasone. Expected.
2226	UK; M; 56;	WOUND INFECTION/GREEN MUCUS	Recovered	28-Nov-13	7	blinded	21-Nov-13	WOUND INFECTION/GREEN MUCUS-which recovered and healed in community setting and had green mucus coming out of the rectum. Antibiotics given for both problems. Patient recovered with antibiotics. Related to surgery, possibly related to dexamethasone. Expected.
2229	UK; F; 38;	WOUND INFECTION	Recovered	10-Dec-13	18	blinded	22-Nov-13	WOUND INFECTION-patient reported post discharge. Treated with GP with oral co amoxicillin, swabs taken on 10th December 2013 identified staphylococcus aureus and anaerobic cocci.

								Wound healed on 17th December 2013. Related to surgery, possibly related to dexamethasone. Expected.
2235	UK; M; 61	UNCONFIRMED URINE INFECTION	Recovered	21-Dec-13	7	blinded	26-Nov-13	? URINE INFECTION-Patient reported symptoms of hesitancy when attempting to pass urine and states he has had a urine infection, however no urine sample taken at this time and no antibiotics prescribed. Related to surgery, possibly related to dexamethasone. Expected.
2236	UK; M; 71;	WOUND INFECTION	Recovered	13-Dec-13	17	blinded	26-Nov-13	WOUND INFECTION-Related to surgery, possibly related to dexamethasone. Expected.
2244	UK; M; 58;	CHEST INFECTION/DEHYDRATION	Recovered	03-Dec-13	5	blinded	28-Nov-13	CHEST INFECTION/DEHYDRATION- whilst in patient due to high stoma output. Recovered before discharge. Related to surgery, unlikely to be related to dexamethasone. Expected.
2246	UK; M; 73;	CHEST INFECTION	Recovered	16-Dec-13	18	blinded	28-Nov-13	CHEST INFECTION-treated with antibiotics for 5 days. Related to surgery, possibly related to dexamethasone. Expected.
2258	UK; M; 64;	WOUND INFECTION	Recovered	17-Dec-13	13	blinded	04-Dec-13	WOUND INFECTION-potential wound infection, given 7 days antibiotics-flucloxacillin in clinic on 17th December 2013. Related to surgery, possibly related to

								dexamethasone. Expected.
2260	UK; M; 60	ABDOMIN PAIN & VOMITING	Recovered	12-Dec-13	6 days	blinded	06-Dec-13	ABDOMIN PAIN & VOMITING - Patient admitted with abdominal pain and vomiting. Event ceased 18/12/13. Definitely related to surgery, probably related to IMP. Expected.
2268	UK; M; 55;	CHEST INFECTION	Recovered	02-Jan-14	23	blinded	10-Dec-13	CHEST INFECTION-Related to surgery, possibly related to dexamethasone. Expected.
2268	UK; M; 55;	WOUND INFECTION	Recovered	13-Dec-13	3	blinded	10-Dec-13	WOUND INFECTION-Related to surgery possibly related to dexamethasone. Expected.
2268	UK; M; 55;	URINE INFECTION	Recovered	02-Jan-14	23	blinded	10-Dec-13	URINE INFECTION-Related to surgery possibly related to dexamethasone. Expected.
2273	UK; M; 64;	INTRA ABDOMINAL BLEED	Recovered	14-Dec-13	2	blinded	12-Dec-13	INTRA ABDOMINAL BLEED-patient had to be returned to theatre. Related to surgery, possibly related to dexamethasone. Expected.
2280	UK; M; 62;	WOUND INFECTION	Recovered	21-Jan-14	36	blinded	16-Dec-13	WOUND INFECTION-Patient reported wound infection and given antibiotic for a week. Related to surgery, possibly related to dexamethasone. Expected.
2281	UK; F; 73	CONFUSION	Recovered	17-Dec-13	1 day	blinded	16-Dec-13	CONFUSION-Patient became confused on 17/12/13 in the evening. Is now settled and lucid, though anxious. Event ceased 18/12/13. Related to surgery, possibly related to IMP. Expected.
2291	UK; M;	WOUND INFECTION/WEAPY	Recovered	27-Dec-13	9	blinded	18-Dec-13	WOUND INFECTION/WEAPY

	67;	WOUND						WOUND-weeping from drain site. Wound dressings: 30th December 2014-13 January 2014 and antibiotics given: 27th December 2013-23rd January 2014. Related to surgery, possibly related to dexamethasone. Expected.
2293	UK; M; 84;	UNCONFIRMED WOUND INFECTION	Recovered	29-Dec-13	10	blinded	19-Dec-13	? WOUND INFECTION-District Nurses dressings. Not confirmed no swab taken. Email received 24th July 2014 stating this. Related to surgery, possibly related to dexamethasone. Expected.
2299	UK; M; 50;	URINE INFECTION	Recovered	31-Jan-14	22	blinded	09-Jan-14	URINE INFECTION-confirmed microbiology possibly infection. Probably related to surgery, possibly related to dexamethasone. Expected.
2300	UK; M; 60;	WOUND INFECTION	Recovered	31-Jan-14	22	blinded	09-Jan-14	WOUND INFECTION-possible wound infection wound oozing. GP prescribed antibiotics and daily dressings with the practice nurse/district nurse. Definitely related to surgery, possibly related to dexamethasone. Expected.
2307	UK; M; 68;	PROLONGED ILEUS	Recovered	17-Jan-14	4	blinded	13-Jan-14	PROLONGED ILEUS- Due to nature and length of initial surgery. Definitely related to surgery, possibly dexamethasone. Expected.
2308	UK; F; 64;	WOUND INFECTION	Recovered	20-Jan-14	7	blinded	13-Jan-14	WOUND INFECTION-required oral dose of antibiotics (at

								home) Wound healed by Day 30 follow up telephone Questionnaire 11th February 2014. Related to surgery, possibly related to dexamethasone. Expected.
2314	UK; F; 63;	WOUND INFECTION	Recovered	07-Feb-14	23	blinded	15-Jan-14	WOUND INFECTION-Patient developed wound infection-treated with antibiotics, packed/redressed alternate days. Related to surgery, possibly related to dexamethasone. Expected.
2314	UK; F; 63;	ABDOMINAL PAIN/FEVER	Recovered	13-Feb-14	29	blinded	15-Jan-14	ABDOMINAL PAIN/FEVER-Patient re-admitted with abdominal pain, fevers. Treated with IV antibiotics. CT scan report and discharge letter attached. Probably related to surgery and probably not related to dexamethasone. Expected.
2315	UK; F; 72;	DELAYED WOUND HEALING	Recovered	21-Jan-14	5	blinded	16-Jan-14	DELAYED WOUND HEALING-patient reported a delay in wound healing (some oozing from the wound-wound swabs taken-no antibiotics prescribed). No evidence of infection, no swab taken etc. Related to surgery, possibly related to dexamethasone. Expected.
2316	UK; M; 61;	PERENIAL WOUND SMALL SINUS	Recovered	12-Feb-14	27	blinded	16-Jan-14	PERENIAL WOUND SMALL SINUS-1.5 cm deep. Internal suture found chronic discharging sinus. Antibiotics

								given-Augmentin. Silver nitrate cauterey applied. Related to surgery, possibly related to dexamethasone. Expected.
2328	UK; F; 53;	NAUSEA AND VOMITING	Recovered	29-Jan-14	6	blinded	23-Jan-14	NAUSEA AND VOMITING-persistent vomiting and nausea, improving condition discharge delayed. Discharged 1st February 2014. Definitely related to surgery, probably related to dexamethasone. Expected.
2329	UK; M; 60;	POST OP ILEUS/WOUND INFECTION/ANASTOMOTIC LEAK	Recovered	27-Jan-14	4	blinded	23-Jan-14	POST OP ILEUS/WOUND INFECTION/ANASTOMOTIC LEAK. Conservative management and antibiotics. Related to surgery, possibly related to dexamethasone. Expected.
2331	UK; M; 57;	COLLECTION AT PERENIAL STUMP	Recovered	30-Jan-14	7	blinded	23-Jan-14	COLLECTION AT PERENIAL STUMP-treated with IV antibiotics and drained (CT guided). Related to surgery, possibly related to dexamethasone. Expected.
2332	UK; F; 45;	PERSISTENT POST OPERATIVE ILEUS/PERFORATION	Recovered	28-Jan-14	5	blinded	23-Jan-14	PERSISTENT POST OPERATIVE ILEUS/PERFORATION-persistent post-operative ileus then perforation of ileus into subcutaneous tissue. Related to surgery, probably not related to dexamethasone. Expected.
2335	UK; M; 70;	URINARY TRACT INFECTION	Recovered	03-Feb-14	7	blinded	27-Jan-14	URINARY TRACT INFECTION-treated for UTI by GP. Given a

								course of oral antibiotics. Asymptomatic. Probably related to surgery, possibly related to dexamethasone. Expected
2341	UK; F; 52;	WOUND INFECTION	Recovered	07-Feb-14	10	blinded	28-Jan-14	WOUND INFECTION-patient developed wound infection-treated with oral antibiotics, packed/redressed alternate days. Swab taken from abdomen microbiology report stated Skin and faecal flora including: SAUR. Staphylococcus aureus. Erythromycin S. Flucloxacilli. Related to surgery, possibly related to dexamethasone. Expected.
2343	UK; M; 62;	WOUND BREAKDOWN/FISTULA FOLLOWING ANTERIOR RESECTION	Recovered	07-Feb-14	10	blinded	28-Jan-14	WOUND BREAKDOWN/FISTULA- following anterior resection-CT confirmed fistula 10th February 2014. Laparotomy and fistula repair, epidural leak following this pain relieved by analgesia. CT enclosed & electronic discharge summary. Discharged with vac dressing 21st February 2014. Related to surgery, possibly related to dexamethasone. Expected
2348	UK; M; 68;	SMALL LEAK NEXT TO ANASTOMOSIS	Recovered	02-Feb-14	3	blinded	30-Jan-14	SMALL LEAK NEXT TO ANASTOMOSIS-managed conservatively. Definitely related to surgery, probably

								not related to dexamethasone. Expected.
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**Table 4: Cumulative Summary Tabulation of Serious Adverse Events**

<b>System Organ Class Preferred Term</b>	<b>8mg IV dexamethasone – blinded trial, code unbroken for all patients, n=1350</b>
<b>Gastrointestinal disorders</b>	<b>Gastrointestinal disorders</b>
-abdominal pain	-23
-abscess	-5
-anal pain	-1
-ascites	-1
-biliary peritonitis	-1
-bowel leak	-1
-bowel obstruction	-15
-bowel perforation	-4
-bruising of stoma	-1
-constipation	-4
-diarrhoea	-7
-distended abdomen	-4
-faecal contamination	-1
-fistula	-3
-hemorrhage	-18
-High output stoma	-1
-ileus	-30
-Ileus haematoma	-1
-jejunal perforation	-1
-adhesions to small bowel	-2
-nausea	-15
-oesophagitis	-1
-collections	-4
-pseudo obstruction	-1
-relaporotomy	-2
-ileal obstruction	-1

-peritonitis	-1
-vomiting	-24
<b>TOTAL</b>	<b>-174</b>
<b>Infections and infestations</b>	<b>Infections and infestations</b>
-abdominal infection	-1
-sepsis	-5
-urosepsis	-1
-skin infection	-7
-stoma site infection	-2
-vaginal infection	-1
-urinary tract infection	-19
-viral gastroenteritis	-1
-wound infection	-85
-wound site inflamed	-1
-lung infection	-25
-other	-7
<b>TOTAL</b>	<b>-155</b>
<b>Investigations</b>	<b>Investigations</b>
-raised troponin	-1
<b>TOTAL</b>	<b>-1</b>
<b>Injury, poisoning and procedural complications</b>	<b>Injury, poisoning and procedural complications</b>
-anastomotic leaks	
-fall and facial trauma	-32
-hernia	-1
-ileocaecal resection	-5
-ileocolic bypass	-1
-wound dehiscence	-1
-wound leakage	-30
-wound breakdown	-1
-other	-1

<b>TOTAL</b>	-8 <b>-80</b>
<b>Metabolism and nutrition disorders</b> -low sodium -Raised potassium <b>TOTAL</b>	<b>Metabolism and nutrition disorders</b> -1 -1 <b>-2</b>
<b>Nervous system disorders</b> -dizziness TOTAL	<b>Nervous system disorders</b> -2 <b>-2</b>
<b>General disorders and administration site conditions</b> -epidural leak -fever -multi organ failure <b>TOTAL</b>	<b>General disorders and administration site conditions</b> -1 -1 -2 <b>-4</b>
<b>Cardiac</b> -acute coronary syndrome -atrial fibulation -cardiac arrest -cardiac problems -ischaemic heart disease/Peripheral vascular disease -myocardial infarction -ventricular tachycardia <b>TOTAL</b>	<b>Cardiac</b> -1 -3 -4 -1 -1 -2 -1 <b>-13</b>
<b>Renal and urinary disorders</b> -pain in catheter -renal failure -urinary retention	<b>Renal and urinary disorders</b> -1 -1 -2

-kidney infection	-1
<b>TOTAL</b>	<b>-5</b>
<b>Reproductive system and breast disorders</b>	<b>Reproductive system and breast disorders</b>
-epididymitis	-1
-perineal pain	-1
<b>TOTAL</b>	<b>-2</b>
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>Respiratory, thoracic and mediastinal disorders</b>
-acute respiratory distress syndrome	-1
-chest pain	-1
-emphysema	-1
-metabolic acidosis	-2
-pulmonary embolism	-3
-pulmonary edema	-2
-respiratory failure	-2
-shortness of breath	-1
<b>TOTAL</b>	<b>-13</b>
<b>Skin and subcutaneous tissue disorders</b>	<b>Skin and subcutaneous tissue disorders</b>
-rash	-1
<b>TOTAL</b>	<b>-1</b>
<b>Vascular disorder</b>	<b>Vascular disorder</b>
-hematoma	-2
-hypotension	-1
-blood pressure (low)	-1
<b>TOTAL</b>	<b>-4</b>
<b>Other</b>	<b>Other</b>
-abnormal bloods	-1
-apnoea	-1
-confusion	-1
-dehydration	-2

-deranged bloods	-4
-elevated temperature	-4
-Ischaemic colon to the point of anastomosis	-1
-laparotomy/formation of stoma	-1
-paranoid	-1
-refashioning of stoma	-1
-stoma failure	-2
-catheter in situ post 30 days	-1
-delayed wound healing	-2
-drowned	-1
<b>TOTAL</b>	<b>-23</b>

## MORE INFORMATION

### Substantial Amendments

**Table 3: List of substantial protocol amendments requiring approval by the competent authority.**

Date of protocol amendment approval by the Competent Authority	Amendment description
11-May-2011	Trial design amended to include a pilot phase.
20-Dec-2013	Sample size increased, addition of an exclusion criteria, clarification of primary outcome, addition of a secondary outcome.
20-Feb-2015	The definition of the end of trial was amended.

### Interruptions

There were no global interruptions to the trial.

### Conclusions

For published outcome data, please see the final trial publication.

### Publication and Dissemination

The final publication has been drafted and will be submitted in February 2016.

The paper will initially be submitted to the New England Journal of Medicine.

The trial protocol was published in 2013:

Hamilton E, Ravikumar R, Bartlett D, Hepburn E, Hwang MJ, Mirza N, Bahia S, Wilkey A, Bodenham-Chilton H, Handley K, Magill L, Morton D and on behalf of the West Midlands Research Collaborative: Dexamethasone reduces emesis after major gastrointestinal surgery (DREAMS). *Trials* 14:249, 2013. Link: <http://www.trialsjournal.com/content/14/1/249>

The preliminary results that have been presented to date are:

- **Joint National Institute of Academic Anaesthesia & Royal College of Surgeons Meeting, London** – “Collaborative working between anaesthetists and surgeons”.  
28<sup>th</sup> April 2014
- **Digestive Disorders Federation Tripartite Meeting, London** - Presentation of initial primary outcome measures - closed meeting.  
3<sup>rd</sup> June 2014
- **National Research Collaborative Meeting, Cardiff** - Presentation of initial primary outcome measures - closed meeting.  
5th December 2014

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