POP-I

Post-operative anaemia in adults

IMP ADMINISTRATION ONLY SLIDES

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The clinical benefits and cost effectiveness and safety of haematopoietic interventions for patients with anaemia following major emergency surgery: a phase IV, multi-site, multi-arm randomised controlled trial:

Peri-op Iron and Erythropoietin (EPO) Intervention Study (POP-I)

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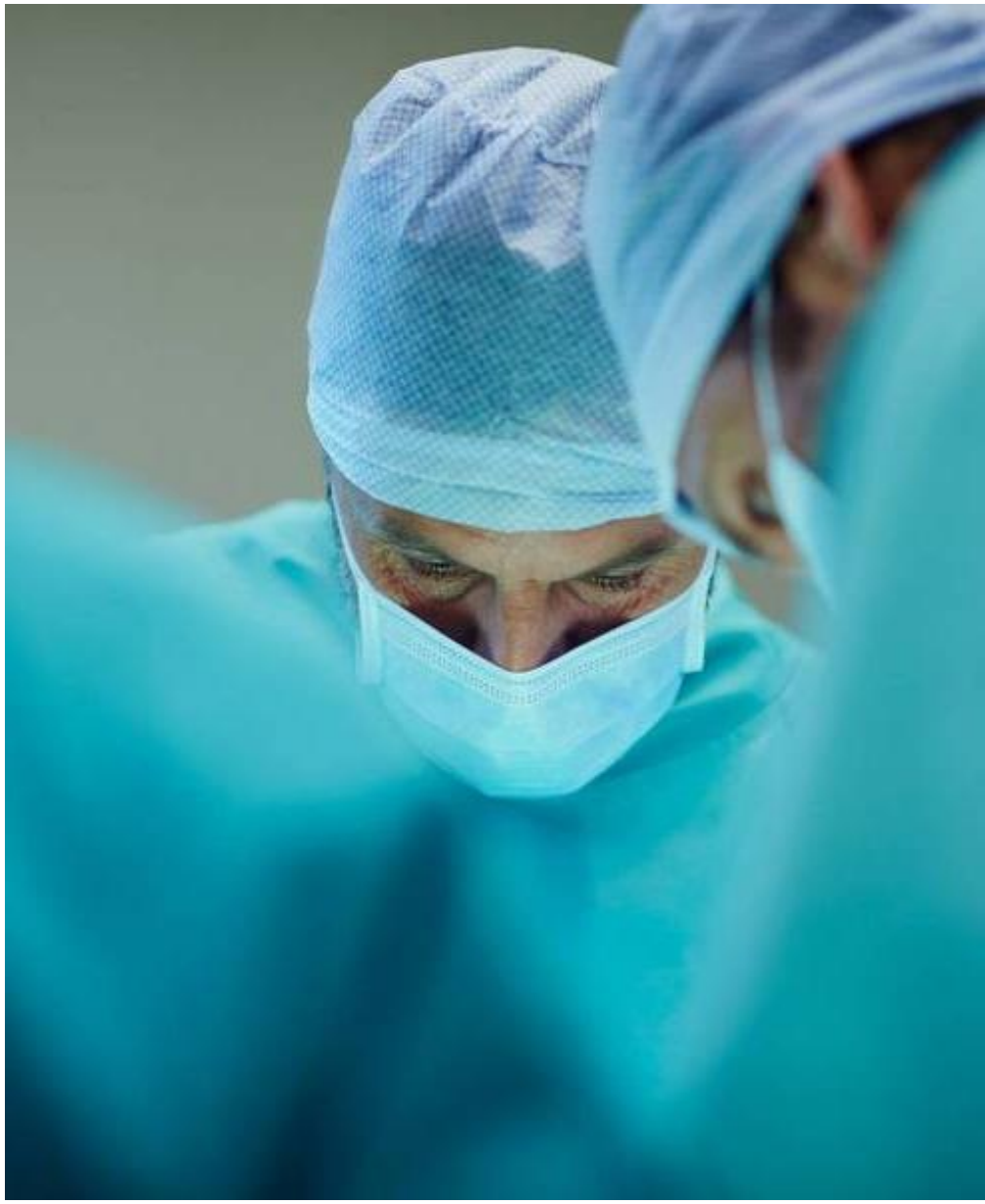
Post-operative anaemia in adults

AGENDA

- STUDY TEAM
- BACKGROUND
- IMP ADMINISTRATION
- SAFETY REPORTING



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STUDY TEAM

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TRIAL ORGANIZATION

FUNDER

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TRIALS UNIT

NOTTINGHAM CLINICAL TRIALS UNIT

MEET THE TEAM

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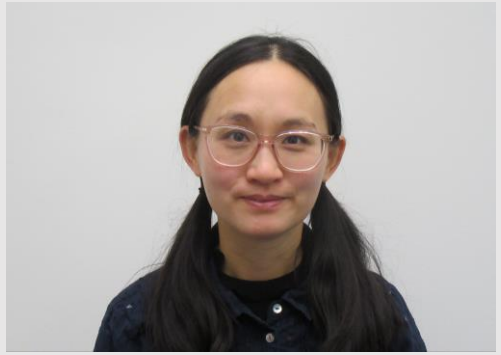

YUHUANG XI
Trial Coordinator

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BACKGROUND

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BACKGROUND

- POST-OPERATIVE ANAEMIA IS COMMON IN OLDER PATIENTS.
- ASSOCIATED WITH INCREASED MORTALITY, LONGER LENGTH OF STAY AND POORER QUALITY-OF-LIFE.
- ANNUALLY ~60,000 HIP FRACTURE AND ~19,000 EMERGENCY LAPAROTOMY PATIENTS DEVELOP ANAEMIA POST-SURGERY.
- THIS REPRESENTS 62% OF ALL LAPAROTOMY PATIENTS AND 87% OF ALL HIP FRACTURE PATIENTS.
- BY 2033, IN ENGLAND, 87,000 ADULTS PER YEAR ARE EXPECTED TO HAVE POST OPERATIVE ANAEMIA FROM HIP FRACTURE SURGERY.

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BACKGROUND

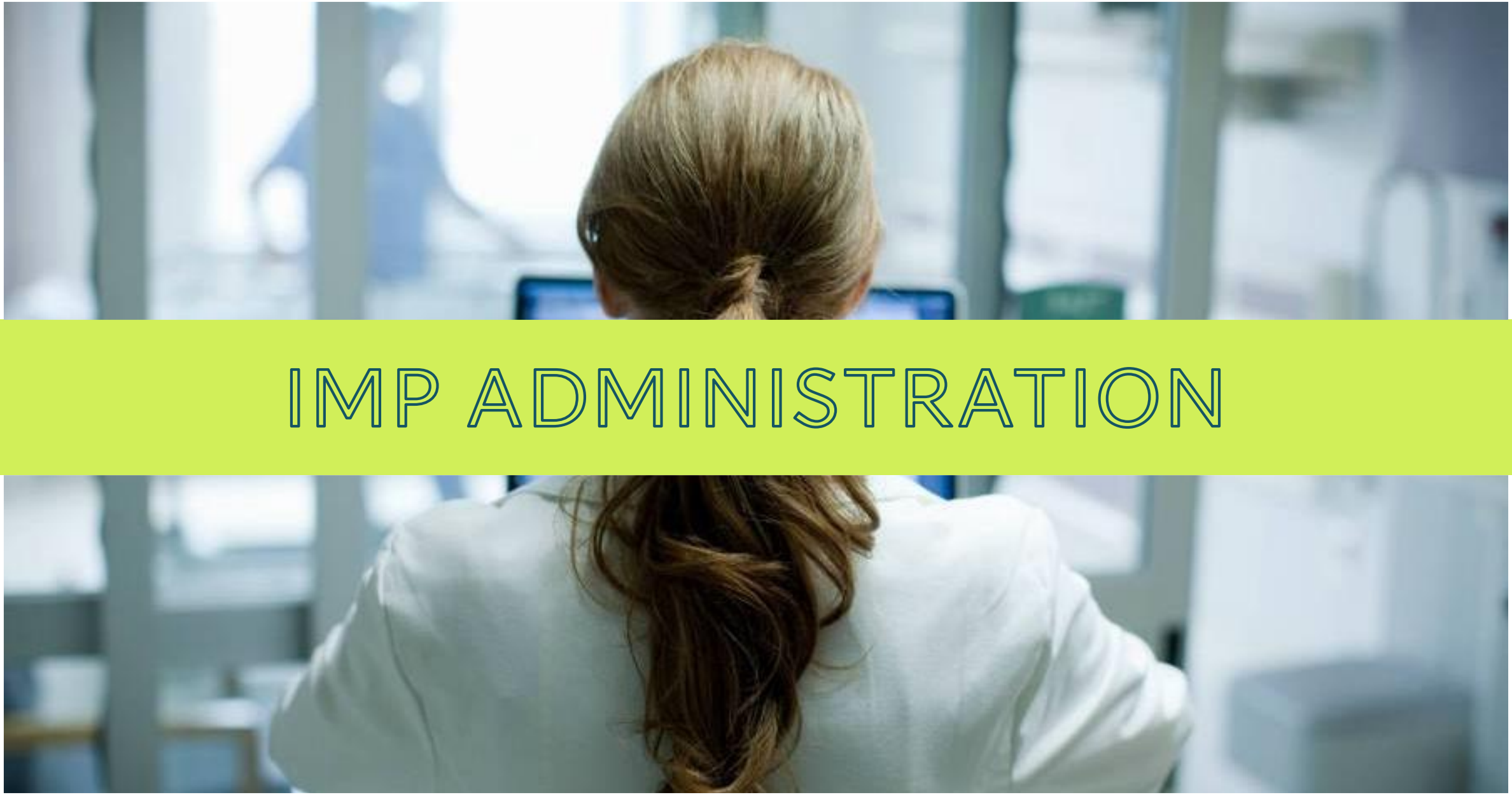
CURRENTLY, THE BEST TREATMENT FOR POST-OPERATIVE ANAEMIA IS UNCLEAR

BROADLY, 3 TREATMENTS:

1. MOST HOSPITALS USUAL CARE (NICE, 2015)
2. SOME HOSPITALS USUAL CARE + IV IRON
3. FEWER HOSPITALS USUAL CARE + IV IRON + ESA

Lack of high-quality clinical evidence for treatments in post-operative anaemia

We don't know what the best option is for these patients



IMP ADMINISTRATION

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3 TREATMENT GROUPS

USUAL CARE	‘Wait and watch’ to determine if anaemia resolves itself. Transfusion for severe anaemia as per NICE 2015 guidelines.
USUAL CARE + IV IRON	As above, plus a *single dose* of IV iron.
USUAL CARE + IV IRON + ESA	As above, plus a *single dose* of subcutaneous darbepoetin.

Patients are randomly allocated to one of three groups

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PHARMACY

- IMP not supplied to sites by POP-I.
- Sites to use local stock:
  - IV Iron (Ferric derisomaltose 100mg/ml as per dosing table)
  - ESA (Darbepoetin alfa 150mcg).
- Open label trial and no additional trial specific labelling/accountability needed.
- Sites should maintain local accountability and dispensing records as per routine practice.

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IMP ADMINISTRATION

WHEN?

As soon *as feasible*, within the 1-10 period post-surgery.

WHO?

Staff listed on the delegation log. Shorter training package available for staff who undertake only this activity in the POP-I trial.

WHAT DOSE?

The ESA is a one-time dose of 150mcg of darbepoetin alfa, administered subcutaneously.

The IV Iron is a one-time dose, determined using a simplified dosing table. Patients should be prescribed **this dose of iron up to 20mg iron per kg bodyweight**.

This is because at doses exceeding this mg/kg, the SmPC states that the dose should be given across two administrations, 7 days apart, which is not feasible in this trial.

Hb (g/L)	Patients body weight <50 kg	Patients body weight 50 kg to<70 kg	Patients with body weight ≥70 kg
100 - 110	500 mg	1,000 mg	1,500 mg
<100	500 mg	1,500 mg	2,000 mg

RECORDING DATA?

Once administered, please inform the local team at site so they complete 'Treatment Allocation' in REDCap database.

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IMP ADMINISTRATION

Dosing table for IV Iron within the POP-I trial

	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)
Hb 100-110 (g/L)	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
Hb<100 (g/L)	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
Weight (kg)	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39

	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)
Hb 100-110 (g/L)	500	500	500	500	500	500	500	500	500	500	1000	1000	1000	1000	1000
Hb<100 (g/L)	500	500	500	500	500	500	500	500	500	500	1000	1020	1040	1060	1080
Weight (kg)	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54

	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)
Hb 100-110 (g/L)	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
Hb<100 (g/L)	1100	1120	1140	1160	1180	1200	1220	1240	1260	1280	1300	1320	1340	1360	1380
Weight (kg)	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69

	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)
Hb 100-110 (g/L)	1400	1420	1440	1460	1480	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500
Hb<100 (g/L)	1400	1420	1440	1460	1480	1500	1520	1540	1560	1580	1600	1620	1640	1660	1680
Weight (kg)	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84

	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)	Dose (mg)
Hb 100-110 (g/L)	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500	1500
Hb<100 (g/L)	1700	1720	1740	1760	1780	1800	1820	1840	1860	1880	1900	1920	1940	1960	1980
Weight (kg)	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99

For patient's whose weight is ≥100kg, administer 1500mg (Hb 100g-110g/L) or 2000mg (Hb<100g/L)

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SAFETY REPORTING

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ADVERSE EVENTS REPORTED AT DISCHARGE

ADVERSE EVENTS (KNOWN SIDE EFFECTS)

(REPORTED UNTIL DAY 7 OR DISCHARGE, WHICHEVER COMES FIRST)

Immune system disorders

* Hypersensitivity * Anaphylactoid/ Anaphylactic shock

* must provide value

Nervous system disorders

* Headache * Paraesthesia * Dysgeusia * Blurred vision
* Loss of consciousness * Dizziness * Fatigue
* Dysphonia * Seizure * Tremor * Altered mental status (delirium)
* Convulsions

* must provide value

Cardiac disorders

* Tachycardia * Arrhythmia * Kounis Syndrome

* must provide value

Vascular disorders

* Hypotension * Hypertension * Thrombosis

* must provide value

Respiratory, thoracic and mediastinal disorders

* Chest pain *Dyspnoea * Bronchospasm

* must provide value

Gastrointestinal disorders

* Nausea * Abdominal pain * Vomiting * Dyspepsia

* Constipation * Diarrhoea

* must provide value

Skin and subcutaneous tissue disorder

* Rash * Pruritus * Urticaria * Flushing * Sweating

* Dermatitis * Angioedema * SJS/TEN * Multiform

* Blistering * Skin exfoliation

* Distant skin discolouration *Erythema

* must provide value

Metabolism and Nutritional disorders :

* Hypophosphataemia

* must provide value

Musculoskeletal and connective tissue disorders

* Back pain * Myalgia * Arthralgia * Muscle spasms

* must provide value

General disorders and administration site conditions

* Injection site reactions * Pyrexia * Chills/ shivering

* Infection* Local phlebitis reaction * Oedema

*Malaise * Influenza-like illness * injection site pain

* injection site bruising * injection site haemorrhage

* must provide value

Investigations:

* Hepatic enzyme increased

* must provide value

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PLEASE REPORT ANY ADVERSE EVENTS TO THE LOCAL TEAM AT SITE

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SERIOUS ADVERSE EVENTS

As the interventions are widely available within the NHS, adverse events (including known side effects) from these treatments will be collected as complications at discharge, day 30 and day 120.

The following **will be considered SAEs for any event that meet these criteria** and should be reported:

1. **Death**
2. **A life-threatening adverse event**
3. **Inpatient hospitalisation or prolongation of existing hospitalisation**
4. **A disability / incapacity**
5. **A congenital anomaly in the offspring of a participant**

Please report any suspected SAE's to the local team at site for escalation.

SAE's will be reported from the point of randomisation until discharge from hospital or 7 days post-randomisation, whichever is sooner.

SAE REPORTING

- Once you are aware of an SAE you must report this to NCTU immediately (within 24 hours)
- To report an SAE, email the SAE Form provided in your site file to: **nctu-sae@nottingham.ac.uk**

PROTOCOL DEVIATIONS

The following will be identified as a deviation of the Protocol:

- × Received allocated treatment more than 10 days after surgery
- × Received wrong allocated treatment

If unsure, just ask!

Please report any possible protocol deviations to the local team at site so that we can discuss the best way to account for them.

Email address: POP-I@nottingham.ac.uk

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THANK YOU FOR YOUR TIME

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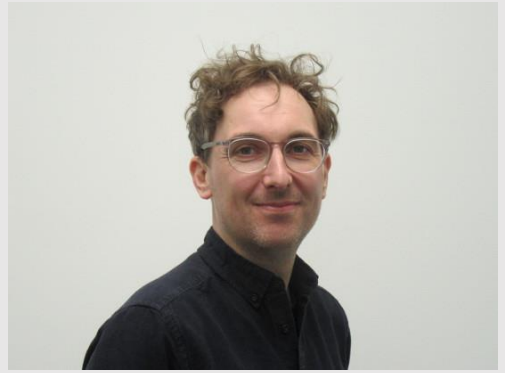
Senior Trial Manager



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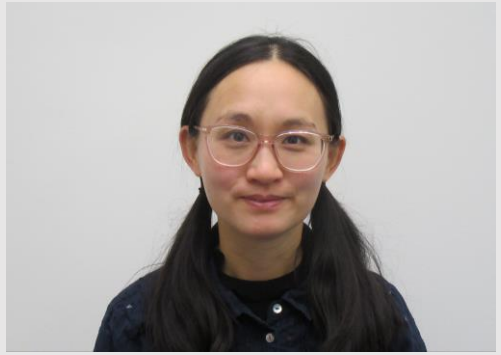

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