

# The Perioperative ADministration of Dexamethasone and Infection trial

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We plan to conduct a large, pragmatic, multicentre, randomised non-inferiority trial to determine whether the use of intraoperative dexamethasone, a widely used antiemetic in perioperative medicine, is associated with an unacceptable increased risk...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Will not start
<b>Health condition type</b>	Bacterial infectious disorders
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON47052

### Source

ToetsingOnline

### Brief title

The PADDI trial

### Condition

- Bacterial infectious disorders

### Synonym

surgical site infections, wound infections

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Alfred Health

**Source(s) of monetary or material Support:** Vergoeding per patient geïnccludeerd in het UMC Utrecht. De studie als geheel is gefinancierd door de NHMRC (overheidssubsidie Australie)

## Intervention

**Keyword:** dexamethasone, infection, surgery

## Outcome measures

### Primary outcome

Surgical Site Infection at 30 days

### Secondary outcome

PONV OUTCOMES

1. Nausea (0-24 hours)- Nausea as measured on a numerical rating scale (NRS) in the first 24 hours following surgery

2. Vomiting (0-24 hours)- Vomiting (occurrence and number of events) within first 24hours following surgery

PAIN OUTCOMES

3. Highest pain score (NRS) at rest and on movement in the first 24 hours

4. Chronic Post-Surgical Pain (at 6 months)- defined as pain over the surgical site, for at least three months after surgery, that cannot be explained by other causes, such as disease recurrence or a pre-existing pain syndrome.

OTHER OUTCOMES

5. Hospital stay: from the start (date, time) of surgery until actual hospital discharge.

6. Quality of recovery: QoR-15 score on days 1, and 30
7. C-reactive protein (CRP) concentration- Days 1 and 2 postop.
8. Proportion of patients requiring insulin
9. Hypoglycaemia rates
10. Hyperglycaemic rates
11. Other infections (i.e. non-SSI) at 30 days - see \*Infections Diagnostic Definitions\*
12. Sepsis- see \*Infections Diagnostic Definitions\*
13. Wound Dehiscence- partial or total disruption of any or all layers of the operative wound.
14. The relationship between diabetic status, glycaemic parameters (preoperative blood glucose, glycated haemoglobin (HbA1c)) and infective outcomes

## Study description

### Background summary

Dexamethasone is a synthetic glucocorticoid with potent anti-inflammatory and metabolic effects. It is frequently administered in the perioperative period, most commonly for prophylaxis and treatment of postoperative nausea and vomiting (PONV). The growing concern about the routine administration of dexamethasone in the perioperative period is due to a lack of safety data in relation to infection risk, particularly in vulnerable populations such as patients with diabetes and children. Proposed mechanisms of infective risk include a) the potential for immunosuppression, b) the theoretical impairment of wound healing and c) induced hyperglycaemia. Any or all of these may contribute to an increased risk of perioperative infection.

### Study objective

We plan to conduct a large, pragmatic, multicentre, randomised non-inferiority

trial to determine whether the use of intraoperative dexamethasone, a widely used antiemetic in perioperative medicine, is associated with an unacceptable increased risk (2%) of postoperative infection in 8880 adult surgical patients. There is biological plausibility that dexamethasone may alter our defined primary and secondary outcomes (see below). The trial has been endorsed by the Australian and New Zealand College of Anaesthetists (ANZCA) Clinical Trials Network and the Australian Society for Infectious Diseases Clinical Research Network, representing the first collaboration between these two organizations

## **Study design**

International, multicentre, prospective, randomised, double blind, placebo-control, parallel assessment, stratified, non-inferiority safety and effectiveness study.

## **Intervention**

Patients will be randomised to receive dexamethasone 8 mg or saline placebo, administered intravenously within 5 minutes after induction of anaesthesia.

## **Study burden and risks**

The intervention in this trial is a common prophylactic intervention to prevent postoperative nausea and vomiting following general anaesthesia. In daily clinical practice, whether or not this intervention is used depends on the attending anaesthetist, and varies between anaesthetists. The risks of participation in this trial is therefore not different from that of other patients undergoing a surgical procedure.

The burden for the participants consists of 4 blood samples (most of these are taken regardless within the context of routine care), and the completion of a number of short questionnaires: once before the operation, and on 2 occasions in the 6 months following the operation.

## **Contacts**

### **Public**

Alfred Health

Commercial Road 55

Melbourne 3004

AU

### **Scientific**

Alfred Health

Commercial Road 55  
Melbourne 3004  
AU

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

- \* Adult patients \*18 years of age
- \* American Society of Anesthesiologists (ASA) physical status 1-4
- \* Elective or Expedited non-cardiac surgery of at least 2 hours duration under general anaesthesia ( $\pm$  regional block)
- \* At least two hours\* duration
- \* Requiring a hospital stay of at least one postoperative night
- \* A surgical skin incision > 5 cm in length or multiple incisions with a total incision length of 5 cm.

### Exclusion criteria

- \* Poorly controlled type 1 diabetes (HbA1c > 9.0%)
- \* Endovascular procedure with a small (< 5 cm length) skin incision
- \* Ophthalmic surgery
- \* Planned dexamethasone (or other corticosteroid) therapy ( e.g. history of intractable PONV, maxillofacial surgery, intracranial neurosurgery)
- \* Recent (< 2 weeks since end of treatment) infective episode requiring treatment with antibiotics
- \* Chronic antibiotic therapy (e.g. for bronchiectasis, cystic fibrosis etc)
- \* When surgery is indicated for an infective process (e.g. infected joint prosthesis)
- \* A history of allergy or adverse reaction to glucocorticoids

- \* Planned postoperative intubation or ventilation
- \* Concurrent immunosuppressive therapies
- \* Current or recent (within preceding 1 month) systemic use of glucocorticoids
- \* Surgical procedures within the preceding 2 months
- \* Known immunosuppressed state
- \* Known moderate or severe liver disease (Hepatitis A, B, C, with cirrhotic liver states, primary biliary cirrhosis, sclerosing cholangitis - any of these with portal hypertension and/or variceal bleeding)
- \* Dialysis-dependent renal failure
- \* When the index surgical procedure is expected to require a further surgical procedure within the subsequent 30 days.
- \* Metastatic cancer

## Study design

### Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

### Recruitment

NL	
Recruitment status:	Will not start
Enrollment:	125
Type:	Anticipated

### Medical products/devices used

Product type:	Medicine
Brand name:	dexamethasone
Generic name:	dexamethasone
Registration:	Yes - NL outside intended use

## Ethics review

Approved WMO

Date: 26-07-2018

Application type: First submission

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date: 05-12-2018

Application type: Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register	ID
Other	ACTRN12614001226695
EudraCT	EUCTR2016-003431-37-NL
CCMO	NL58984.041.17