

# Comparison of two methods of administering a short-acting sedative drug during hip and knee replacement surgery under spinal anesthesia

<b>Submission date</b> 18/03/2026	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 19/03/2026	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 19/03/2026	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Public, Scientific, Principal investigator

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## Additional identifiers

## Study information

Scientific Title

A randomized controlled trial comparing intermittent bolus administration versus target-controlled infusion of remimazolam for moderate sedation in adult patients undergoing hip or knee arthroplasty under spinal anesthesia

## **Study objectives**

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

1. approved 02/08/2023, Ethics Committee of the Hospital of Traumatology and Orthopaedics (Duntes iela 22, Riga, LV - 1005, Latvia; +371 (0)67 399 266; izg@tos.lv), ref: 41/2023/1
2. approved 26/04/2024, Ethics Committee of the Hospital of Traumatology and Orthopaedics (Duntes iela 22, Riga, LV - 1005, Latvia; +371 (0)67 399 266; izg@tos.lv), ref: 29/2024/1

### **Primary study design**

Interventional

### **Allocation**

Randomized controlled trial

### **Masking**

Open (masking not used)

### **Control**

Active

### **Assignment**

Parallel

### **Purpose**

Treatment

### **Study type(s)**

### **Health condition(s) or problem(s) studied**

Sedation management in adult patients undergoing hip or knee arthroplasty under spinal anesthesia

### **Interventions**

Participants are randomly assigned in a 1:1:1 ratio using computer-generated block randomisation to one of three intervention arms: intermittent bolus administration of remimazolam, target-controlled infusion using the Masui pharmacokinetic model, or target-controlled infusion using the Zhou pharmacokinetic model.

All participants receive standard intraoperative monitoring, including electrocardiography, non-invasive blood pressure, and pulse oximetry. Supplemental oxygen is administered via nasal cannula. Moderate sedation is targeted, defined as a Modified Observer's Assessment of Alertness/Sedation score of 2 to 3, with sedation level assessed at 5-minute intervals.

In the bolus group, remimazolam is administered as an initial intravenous bolus of 0.04 mg per kilogram over 2 minutes. Additional boluses of 0.04 mg per kilogram are administered as needed to maintain the target sedation level.

In the target-controlled infusion groups, remimazolam is administered using an infusion pump guided by pharmacokinetic models implemented in a clinical decision-support application. Initial effect-site concentration targets are set between 0.2 and 0.4 micrograms per millilitre, with adjustments made in increments of 0.05 to 0.10 micrograms per millilitre based on the sedation level. If oversedation occurs, the infusion is reduced or temporarily discontinued.

All interventions are continued throughout the surgical procedure under spinal anesthesia.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Remimazolam

### **Primary outcome(s)**

1. Sedation quality (time in target sedation range) measured using Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale assessed at 5-minute intervals; proportion of measurements with score 2–3 expressed as percentage at initiation of sedation to end of the surgical procedure
2. Sedation variability (time outside target range) measured using MOAA/S scale assessed at 5-minute intervals; proportion of measurements with score <2 (oversedation) and >3 (undersedation), expressed as percentages at initiation of sedation to end of the surgical procedure

### **Key secondary outcome(s)**

1. Sedative drug utilisation measured using total remimazolam dose normalised to body weight and duration (milligrams per kilogram per hour) at initiation of sedation to end of the surgical procedure
2. Haemodynamic stability – hypotension measured using incidence of systolic blood pressure <90 mmHg or mean arterial pressure <60 mmHg (binary per patient) at during intraoperative period
3. Haemodynamic stability – bradycardia measured using Incidence of heart rate < 50 beats per minute (binary per patient) at During intraoperative period
4. Respiratory safety – hypoxia measured using incidence of peripheral oxygen saturation < 94% (binary per patient) at during intraoperative period

5. Pharmacodynamic response (effect-site concentration–response relationship) measured using logistic regression modelling of probability of achieving MOAA/S 2–3 as a function of effect-site concentration (micrograms per millilitre) at during intraoperative period

**Completion date**

05/12/2024

## Eligibility

**Key inclusion criteria**

1. Adult patients aged 18 years or older
2. Scheduled for elective hip or knee arthroplasty
3. Planned to undergo surgery under spinal anesthesia
4. American Society of Anesthesiologists physical status class I–III
5. Able to provide written informed consent

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

90 years

**Sex**

All

**Total final enrolment**

42

**Key exclusion criteria**

1. Hepatic impairment (alanine aminotransferase or aspartate aminotransferase  $>100$  IU L<sup>-1</sup> or aspartate aminotransferase to alanine aminotransferase ratio  $\geq 2:1$ )
2. Known hypersensitivity or allergy to benzodiazepines
3. Chronic or daily use of benzodiazepines
4. Cognitive impairment precluding reliable assessment of sedation level or informed consent
5. Contraindications to spinal anesthesia
6. Contraindications to procedural sedation

**Date of first enrolment**

01/09/2023

**Date of final enrolment**

05/12/2024

## Locations

## Countries of recruitment

Latvia

## Sponsor information

### Organisation

Riga Stradiņš University

### ROR

<https://ror.org/03nadks56>

## Funder(s)

### Funder type

### Funder Name

Investigator initiated and funded

## Results and Publications

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not expected to be made available