# The effect of total knee replacement surgery on immune functioning in elderly

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON53227

**Source**
ToetsingOnline

**Brief title**
Immu-KNEE-ty

### Condition

- Other condition

**Synonym**
aging, Immunosenescence

**Health condition**

immunosenescentie

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Wageningen Universiteit
**Source(s) of monetary or material Support:** NWO-TTW,Nutricia

## Intervention

**Keyword:** Elderly, Immune functioning, Knee arthroplasty, Monocytes

## Outcome measures

### Primary outcome

The main study parameter is the change from baseline in monocyte-derived TNFa production at 1 week after surgery. TNFa production will be measured after ex vivo stimulation of whole blood with inflammatory stimuli and normalized for monocyte count.

### Secondary outcome

Secondary study parameters are:

- Change from baseline in monocyte-derived cytokine production at 1 day, 1 week, ± 2 weeks and ± 6 weeks post-surgery.

- Change from baseline in additional parameters of immune functioning at 1 day, 1 week, ± 2 weeks and ± 6 weeks post-surgery. These additional parameters of immune functioning are:

• Composition of immune cell populations (monocytes, lymphocytes, neutrophils, eosinophils, basophils)

• Systemic inflammation

• Phagocytic function of monocytes

• Monocyte HLA-DR expression

- Synovial inflammation.

- Other study parameters: sex, age, BMI, ASA classification, Kellgren-Lawrence classification, Patient Reported Outcome Measures (PROMs), functional outcomes, amount and period of use of analgesic therapies and presence of cold and flu-like symptoms.

# Study description

### Background summary

The world population is progressively aging. As humans age, their immune system becomes weaker through a process called immunosenescence. This age-related decline in immune functioning results in an increased susceptibility to infections. Vulnerability to infections is particularly prevalent in elderly with chronic diseases or elderly that experienced an incident, such as a fall-related trauma or surgery. Most likely, this is due to immunosuppression resulting from such an immune challenge. Currently, there are no standard interventions used to improve immune functioning in these immune-suppressed elderly. However, before the potential of such interventions can be explored, postoperative immune suppression in elderly first needs to be demonstrated.

### Study objective

The primary objective of this study is to determine changes in monocyte-derived TNFa production after total knee replacement surgery in elderly. As secondary objective, additional parameters of immune functioning will be assessed. In addition, the course of immune functioning following total knee replacement surgery will be investigated.

### Study design

Prospective ex vivo study in which immune functioning of elderly will be assessed at multiple timepoints before and after total knee replacement surgery (i.e., ± 6 weeks before, and 1 day, 1 week, ± 2 weeks, and ± 6 weeks after surgery). Each patient will serve as his/her own control. Immune functioning will be measured in monocytes for which blood samples will be used. Changes in monocyte responsiveness are considered indicative for changes in immune functioning.

### Study burden and risks

Burden and potential risks for the patient are estimated to be minor. During

the study, 5 blood samples of 20 mL will be collected over a period of ± 12 weeks, resulting in a total blood draw of 100 mL. Blood sampling will be combined with regular care visits, with the exception of one occasion where blood sampling will be performed at home by the Trombosedienst. Patients could experience mild pain by the venipuncture, which occasionally leads to lightheadedness, fainting and hematoma. During surgery a sample of synovial fluid (± 2 mL) will be taken from surgical waste. Before and after surgery patients will report their pain medication intake and the presence of cold- and flu-like symptoms in a diary. Patients do not directly benefit from the study but receive a financial compensation of ¤50,-.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Elderly (65 years and older)

## Inclusion criteria

- Planned for primary total knee replacement surgery

- Aged 65 years or over
- Diagnosed with osteoarthritis
- ASA Physical Status Classification of II or III
- Willing to donate a blood sample at 5 different timepoints
- Able to give written informed consent

### Exclusion criteria

- Daily use of high doses NSAIDs within the 14 days before inclusion: Defined as higher than maintenance dose in the *farmacotherapeutisch kompas*. For example: acetylsalicylic acid > 4 g /day; diclofenac > 75 mg/day; naproxen > 500 mg/day; ibuprofen> 1600 mg/day; celecoxib > 200 mg/day - Use of systemic corticosteroids - Use of antibiotics within the 14 days before inclusion - Current diagnosis of cancer - Diagnosed with a primary immunodeficiency disorder (e.g., Severe Combined Immunodeficiency (SCID), Common Variable Immune Deficiency (CVID), X-linked agammaglobulinemia, selective immunoglobulin A deficiency, chronic granulomatous disease) - Vaccination (e.g., immunization against COVID-19, influenza, pneumonia, and travel-related infections) within the 14 days before inclusion and during the study period - Current participation in other scientific research

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

### Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 12-03-2024 |
| Enrollment: | 14 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 29-06-2023 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 08-05-2024 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 |
|---|---|
| ClinicalTrials.gov | NCT05920148 |
| CCMO | NL84069.091.23 |