# Treacher Collins syndrome: Genectis and OSAS

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Primary objectives:1. To analyze the exact pathogenic mutations in the TCOF1 gene in TCS 2. To determine the severity, prevalence, natural course within the cohort TCS patients and potential metabolic and physical effects of OSAS in TCSSecondary...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Skin and subcutaneous tissue disorders congenital |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON33933

**Source**
ToetsingOnline

**Brief title**
Treacher Collins Syndrome

### Condition

- Skin and subcutaneous tissue disorders congenital
- Upper respiratory tract disorders (excl infections)

**Synonym**
Obstructive Sleep Apnea Syndrome (OSAS) Treacher Collins Syndrome

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Genetics, OSAS, Sleep Apnea, Treacher Collins

## Outcome measures

### Primary outcome

1. Newly found yet undiscoverd mutations in the TCOF1 gene

2. OSAS parameters will be defined in this TCS population and the natural

course, severity, prevalence and potential metabolic and physical effects of

OSAS in this population will be determined.

### Secondary outcome

1. length, weight and bloodpressure will be determined in the TCS population

# Study description

### Background summary

Treacher Collins syndrome (TCS) is a rare congenital craniofacial disfigurement. Its deformities can range from a slight defect of the cilia to severe defects such as micrognatia and zygomaticotemporomaxillary dysostosis. As well as mandibular hypoplasia and the underdevelopment of the auricles, the downslant of the eyelids, coloboma of the eyelids and hypoplasia of the zygomatic bone and lateral orbital wall are common features of this condition. The disease always occurs bilaterally and affects males and females equally. TCS patients are characterized by a normal intelligence level.
Genetics
TCS is an autosomal dominant disorder of craniofacial development with an incidence of 1 in 50,000 live births. In more than 60% of cases there is no previous family history and the condition is thought to arise as the result of a de novo mutation. Loss-of-function mutations in the TCOF1 gene have been demonstrated to underlie TCS. Although most cases of TCS can be diagnosed clinically, the variable expression observed in this condition, together with the high rate of new mutations may present the clinician with diagnostic difficulties. Up to now mutation analysis of the TCOF1 gene has resulted in the identification of over 120 different mutations that are spread throughout the gene.
Recently, molecular analysis has been used to facilitate both prenatal and

postnatal diagnosis in families with a history of TCS. In a subset of these families, TCS was diagnosed in the proband, but the status of the parents could not be established unequivocally on the basis of clinical examination alone. In these families, molecular analysis determined that one parent carried the mutation, resulting in a 50% recurrence risk in future patients. So diagnosing TCS genetically is becoming more important both prenatally and postnatally.
OSAS
Children and adults diagnosed with TCS are at risk for obstructive sleep apnea syndrome (OSAS). OSAS is defined as a disorder of breathing during sleep, characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupt normal ventilation. Clinical symptoms of OSAS are snoring, difficulty in breathing and apnea during sleep, but these symptoms are often not recognized by patients, parents or physicians. Only the newborns with TCS and overt obstructive breathing are recognized as such. Routine screening for OSAS has never been part of the treatment plan for these patients. Leaving OSAS untreated may result in major physical and functional impairment due to the disturbed sleep patterns, for instance failure to thrive, recurrent infections, feeding difficulties, disturbed cognitive functions, attention deficits, delay of development, cor pulmonale, hypertension, pulmonary hypertension, coronary artery disease, cerebrovascular disease and sudden death. OSAS in non-syndromal patients is associated with a high BMI, however there is a clinical impression that patients with TCS have a low BMI, probably due to the extra effort necessary for respiration during the night and/or metabolic changes. Studies have demonstrated that non-syndromal patients diagnosed with OSAS have increased circulating levels of multiple biomarkers of both systemic and local inflammation such as interleukin 6, tumor necrosis factor α (TNFα) and C-reactive protein (CRP). Thereby OSAS in non-syndromal patients often coexists with the metabolic syndrome. However, effective treatment of OSAS is associated with a fall in cholesterol levels.Treatment options for OSAS vary from wearing an orthognatic device during the night, giving oxygen, nocturnal non-invasive ventilation, adenotonsillectomy, tracheostomy or surgical advancement of the maxilla.

**Study objective**

Primary objectives:
1. To analyze the exact pathogenic mutations in the TCOF1 gene in TCS
2. To determine the severity, prevalence, natural course within the cohort TCS patients and potential metabolic and physical effects of OSAS in TCS

Secondary objective:
1. To design a treatment protocol for TCS with respect to screening for OSAS

**Study design**

This is a observational prospective, descriptive study. All patients diagnosed

with TCS that have been/are under treatment in the Erasmus MC or Erasmus MC - Sophia Children*s Hospital will be included.
This study contains one cohort.

**Study burden and risks**

Investigation:
1 polysomnography in 1 night at home + venapuncture at the outpatient clinic + 3 questionnaires
Time schedule:
1 night at home + 10 minutes for visiting the outpatient clinic + 10 minutes for filling out the questionnaires

The polysomnography has nog risks or complications, it is a non-invasive investigation. Venapuncture will is not likely to have great risks. In total 5 tubes will be collected.

In conclusion: The risks are nihil for both parts of the investigation
Genetic outcome will not have any consequences for the severiity, prognose and treatment of the patient. Whenever OSAS is detected there will be an appropiate (mostly non-invasive) multidiscipline treatment available.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

## Inclusion criteria

- Treacher Collins Syndrome diagnosis
- Treated in the Erasmus MC, University Medical Center craniofacial center
- Informed consent
- Dutch-speakers who are able to answer the questions in the questionnaires

## Exclusion criteria

- Patients who are not able to speak and understand Dutch

# Study design

## Design

**Study type:** Observational invasive

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Basic science |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-09-2009 |
| Enrollment: | 43 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 03-03-2009 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 |
|---|---|
| CCMO | NL23068.078.08 |