

# Comparison of false positive rates in prenatal combined screening and cell free DNA screening for trisomy 21

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<b>Registration date</b> 03/08/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/10/2022	<b>Condition category</b> Genetic Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Down's syndrome, also called also called trisomy 21, is a genetic condition that causes learning disability and characteristic physical features. Screening during pregnancy can determine the likelihood of a baby being born with Down's syndrome. The gold standard screening test is called the combined test because it combines an ultrasound scan with a blood test. The mother's age and the information from these two tests is used to work out the risk of the baby having Down's syndrome. However, recent research suggests that the test can be improved by adding another test called cell-free fetal DNA screening. Cell-free fetal DNA is DNA from the baby that is found circulating freely in the mother's blood stream. This additional test could improve screening by reducing the false-positive rate (the number of babies incorrectly diagnosed as having Down's syndrome). The aim of this study is to compare the false-positive rates of combined screening and cell-free DNA screening for Down's syndrome.

### Who can participate?

Women with single pregnancies coming for Down's syndrome screening at 11-13 weeks of pregnancy

### What does this study involve?

Participants undergo an ultrasound scan at 11-13 weeks of pregnancy. If fetal defects are found screening is not appropriate and invasive testing is performed. If no anomalies are found then participants are randomly allocated to undergo either cell-free DNA screening or combined screening. Both tests involve blood samples being taken. If there is a positive result invasive testing is offered. The numbers of false-positive cases in the two groups are compared.

### What are the possible benefits and risks of participating?

There are no risks as all the tests are already considered to be standard procedures

### Where is the study run from?

University of Tuebingen (Germany)

When is the study starting and how long is it expected to run for?

July 2016 to October 2017

Who is funding the study?

Cenata GmbH (Germany)

Who is the main contact?

Prof. Karl Oliver Kagan

## Contact information

### Type(s)

Scientific

### Contact name

Prof Karl Oliver Kagan

### Contact details

University of Tuebingen

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## Additional identifiers

### Protocol serial number

2015 - 1

## Study information

### Scientific Title

Comparison of false positive rates in prenatal combined screening and cell free DNA screening for trisomy 21

### Acronym

ReFaPo study

### Study objectives

After a detailed ultrasound examination at 11 - 13 weeks with a normal result, cell-free DNA can reduce the false positive rate compared to combined screening based on maternal age, fetal nuchal translucency, PAPP-A and free beta-hCG.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

University of Tuebingen medical faculty ethics committee, 06/10/2015, ref: 572/2015BO1

**Study design**

Single-center randomised controlled trial

**Primary study design**

Interventional

**Study type(s)**

Screening

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

Prenatal screening for trisomy 21

**Interventions**

Following the normal ultrasound examination, randomization is performed into cell-free DNA screening or combined screening (maternal age, fetal NT, PAPP-A and free beta hCG).

In the cell free DNA (cfDNA) screening group, the risk for trisomy 21 will be calculated based on cell free DNA. For this analysis, blood will be taken and sent to CENATA GmbH who does the analysis. In general the analysis takes 3-5 days. The result will be a risk score. The case is considered to be screen positive if the risk is 1:100 or higher.

In the combined screening group, blood is taken for the analysis of PAPP-A and free beta hCG. The analysis will also done by a commercially driven laboratory. The risk will be calculated by the software of the Fetal Medicine Foundation UK. A risk for trisomy 21 of 1:100 or more is considered to be screen positive. In case of a screen positive result, invasive testing is offered. If the patient opts against invasive testing, we wait until the end of the pregnancy. Screen positive euploid cases are considered to be false positive cases.

All methods (screening by cfDNA, combined screening and invasive testing) are standard procedures in fetal medicine.

**Intervention Type**

Other

**Primary outcome(s)**

Number and proportion of false positive cases in each arm. False positive cases are defined as euploid cases with a risk for trisomy 21 > 1:100. The karyotype will either be obtained by invasive testing somedays after the screening test or after birth.

**Key secondary outcome(s)**

1. Number of cases that cannot be randomized (due to fetal defects, increased NT, multiple gestations). This data will become available at 11-13 weeks' gestation.
2. Time interval between randomization and return of the blood results
3. Number of cases without results in each study arm. This data will be become available latest 2 weeks after the blood sample is taken.
4. Number of women who opt for invasive testing. This data will generally be available within the consecutive 4 weeks after the screening test but theoretically the invasive test can be carried out through the pregnancy.
5. Acceptance of each screening test. The patient will be contacted by us to assess the acceptance level of each of the screening tests. This will be done 4 weeks after the screening test and after birth.

**Completion date**

01/10/2017

**Eligibility****Key inclusion criteria**

1. Patients coming for prenatal screening for trisomy at 11-13 weeks' gestation
2. Singleton pregnancies
3. Normal ultrasound examination without increased nuchal translucency thickness >3.5mm and without fetal defects. If NT is increased or there are fetal defects, screening is not appropriate and invasive testing is performed
4. Informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

Female

**Total final enrolment**

1376

**Key exclusion criteria**

1. Increased nuchal translucency thickness
2. Fetal defects
3. Multiple gestations

**Date of first enrolment**

01/08/2016

**Date of final enrolment**

01/03/2017

**Locations****Countries of recruitment**

Germany

**Study participating centre**

**University of Tuebingen**  
Department of Obstetrics and Gynaecology  
Germany  
72076

## Sponsor information

### Organisation

University of Tuebingen (Germany)

### ROR

<https://ror.org/03a1kwz48>

## Funder(s)

### Funder type

Industry

### Funder Name

Cenata GmbH (Germany)

## Results and Publications

### Individual participant data (IPD) sharing plan

Not provided at time of registration

### IPD sharing plan summary

Other

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/01/2019	05/08/2019	Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	in German version 1.0		10/10/2022	No	No