Which is the most cost-efficient paradigm of early screening for fetal congenital abnormalities?

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This study is designed to identify the best performing screening strategy within the options currently available in the Dutch prenatal screening program by investigating whether postponement of the dating scan to 12-13 weeks and NIPT thereafter...

Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON48336

Source
ToetsingOnline

Brief title
First trimester screening

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
congenital anomalies, Congenital chromosomal anomalies

Research involving
Human

Sponsors and support

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

Intervention

Keyword: costs, irst trimester, NIPT

Outcome measures

Primary outcome

Identify in how many NIPT tests were unable to provide a conclusive result in study arm A versus B.

Inconclusive NIPT results/ no results are defined as of the following:

*NIPT cannot be performed because of spontaneous fetal loss diagnosed at ultrasound examination

*NIPT is correctly performed but gives an inconclusive result

*NIPT is not performed because of exclusion criteria identified at ultrasound examination

Secondary outcome

The secondary objectives are to:

* Identify the proportion of TOPs in strategies A and B

* Identify the timing of termination of pregnancy in fetuses with congenital abnormalities in group A versus group B; OR timing of definitive diagnosis of anomaly in case of test-positive ultrasound result

* Investigate whether a difference in dating of the pregnancy exists if the CRL is measured at 10 weeks or at 12-13 weeks gestation

* Investigate patient*s preferences for strategies A and B

* Identify the most cost-effective screening strategy

* Sensitivity and specificity of strategies A and B

Study description

Background summary

Prenatal screening was introduced in The Netherlands in 2007. The program included the Combined test, with ultrasound (US) measurement of nuchal translucency (NT), performed between 11-13+6 weeks as screening for trisomy 21, 18 and 13, and the structural anomaly scan (SEO) at 18-21 weeks for the detection of fetal structural anomalies. Since April 2017, non-invasive prenatal testing (NIPT) has replaced the CT as first tier first-trimester screening test. This is performed in a study setting (Trident 2 study) and is financed, partly by the woman herself (Euro 175) and partly subsidized by the government (the remaining Euro 500). As a consequence of offering NIPT to all pregnant women, the CT is hardly performed anymore. This implies that the nuchal translucency is no longer measured and information of fetal anatomy is only obtained at 20 weeks. Even in case of severe fetal anomalies, such as anencephaly, parents may only be informed at 20 weeks. The actual NIPT is performed from 10 weeks gestation and the protocol suggests that an ultrasound scan should be performed within one week of the NIPT for dating of the pregnancy, by crown-rump-length (CRL) measurement of the fetus. Exclusion criteria for NIPT are currently the presence of a fetal NT of * 3,5mm and/or the presence of fetal structural anomalies. In such cases a more detailed kind of genetic investigation (arrays CGH) is indicated, rather than NIPT, which targets especially the three common trisomies 21,18 and 13 and only rather large genetic aberrations. Unfortunately the chosen paradigm of first trimester screening, in the Netherlands is not designed for a proper application of the exclusion criteria, as the US scan prior to NIPT is performed too early (10 weeks), at a stage where both assessment of the NT thickness and exclusion of structural anomalies warranting a more informative type of genetic investigation, is not invariably possible. Moreover, performance of NIPT at such an early gestational age increases the number of failed tests, owing to a lower fetal fraction, which is dependent on gestational age. The prevalence of failed test for a NIPT performed at 10-11 weeks is expected to be about 2-3% and it decreases with increase in gestational age. When an inconclusive NIPT result is obtained there are a number of options: 1) the test can be repeated, or 2) the woman can choose for a CT, if still possible. In case the test fails again (chance 30%) the woman can decide to undergo further investigations (detailed scan or invasive procedure for karyotyping). The time required for the whole process in these cases is experienced as stressful and frustrating by both parents and caregivers. Another argument in favor of possibly postponing the moment NIPT is carried out is the fact that in about 1-2% of cases the pregnancy may demise between 10 weeks and 13 weeks.
The use of NIPT in all these cases (thickened NT, presence of structural anomalies, test failure due to low fetal fraction and fetal demise) results in unnecessary costs. This is relevant, given the high price of NIPT set at about

700-800 euro within the Trident 2 study.

Study objective

This study is designed to identify the best performing screening strategy within the options currently available in the Dutch prenatal screening program by investigating whether postponement of the dating scan to 12-13 weeks and NIPT thereafter could decrease the number of inconclusive NIPT results, reduce costs and allow for full application of the exclusion criteria for NIPT.

Study design

This is a multicenter randomized-controlled trial.

Intervention

Patients will be asked to participate into the study and, if consent is obtained, they will be allocated to one of two different care models:
A) US scan at 10 weeks followed by NIPT (care as usual)
B) US scan at 12-13 weeks, followed by NIPT.

Study burden and risks

Both the ultrasound examination and NIPT provide no risk to the pregnant woman or her child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Women with singleton pregnancies who choose for NIPT as first trimester screening test will be included in the study. In order to be included women need to give informed consent by signing a written informed-consent form.
Ultrasound practicing using Astraia software for data registration will be included.

Exclusion criteria

Women younger than 18 years and incapacitated persons will be excluded from the study.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-05-2019
Enrollment:	2235
Type:	Anticipated

Ethics review

Approved WMO Date:	21-05-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL67663.042.18