INeS Follow-up;Medically assisted reproduction techniques: do they influence the offspring*s growth, health and neurodevelopment?
Follow-up of a randomized controlled trial

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The INeS Follow-up study will study the effect of type of MAR on offspring*s health. More specifically, which features of assisted conception (IVF-MNC, IVF-SET and IUI-COH) or natural conception affect child*s general health, growth, body...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON43505

Source
ToetsingOnline

Brief title
INeS Follow-up

Condition

- Other condition

Synonym
Cardiometabolic health, neurodevelopmental health

Health condition

cardiovasculaire gezondheid, metabolde gezondheid, groei, neurodevelopment

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: winstreserve

Intervention

Keyword: cardiometabolic disease, Medically assisted reproduction techniques, neurodevelopment, Offspring

Outcome measures

Primary outcome

Blood pressure at age 4-6 years

Secondary outcome

* General health status (including physician visits, hospital admissions,

medication use)

* Growth trajectory

* Anthropometry (including height, weight, hip-, waist- and upper arm

circumference)

* Body composition (including lean body mass, fat mass, total body water)

* Cardiovascular health (including arterial stiffness)

* Metabolic health (including glucose and insulin levels, lipid profile,

inflammatory markers)

* Development and behavior

Study description

Background summary

Subfertility, defined as the inability to conceive a child after 12 months of unprotected intercourse, affects millions of couples worldwide. Since the birth of the first test-tube baby in 1978, millions of these couples have been aided to conceive a child with medically assisted reproduction (MAR), such as ovulation induction, ovarian stimulation, intrauterine insemination (IUI), in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI).

On the short term, Children conceived by MAR are more often born with low birth weight (<2,500g) or pre-term (<27 weeks* gestation). IVF pregnancies have been associated with a higher risk of complications and adverse perinatal outcomes. For example, the risk of major congenital malformations was slightly higher with ICSI versus general populations [7]. A difference of 200g in birth weight was found between two commonly used culture media for IVF treatment. A similar difference in birth weight is seen between smoking and non-smoking pregnancies. In a Dutch cohort study, offspring birth weight and gestational age were lower after hormone stimulation [10]. Also MAR singletons seem to have a longer length of stay during the birth-admission.

On the longer term, parameters as BMI, cancer risk, respiratory disorders, cognitive functioning and motor development seems to be similar in MAR and naturally conceived children. However, there are indications that IVF-conceived children have higher peripheral fat, higher growth velocity in early life, higher blood pressure and higher fasting glucose concentrations than naturally conceived children.

MAR techniques correspond on the fact that they impose a drastically different environment on the earliest development of the embryo from in vivo. The altered early environment common to all types of MAR conception may result in changes in organ growth, endocrine function, physiology and metabolism leaving the developing embryo at greater risk of poor perinatal outcome, and poorer health in later life.

To date, studies to assess the health risks of MAR-conceived children have remained inconsistent, especially regarding the long-term outcomes. Furthermore, MAR consists of a multifaceted approach, which may involve hormone stimulation (with different regimens), mechanical damage to the oocyte during retrieval, differential circumstances in embryo culture media, and duration of embryo culture, each of which may be contributors to offspring outcomes. On the other hand, previous studies have also been challenged by the fact that poor offspring outcomes may be the result of non-procedure-related factors, including parental health, factors underlying the subfertility, age, smoking, BMI, chromosomal disorders, pregnancy complications, or a combination of these.

By following up children born after parents with a uniform diagnosis of unexplained or mild male factor infertility were randomized to fertility treatment with IUI-COH, IVF-SET or IVF-MNC, the present study aims to disentangle the contribution of each of these aspects of MAR on outcomes in childhood.

Study objective

The INeS Follow-up study will study the effect of type of MAR on offspring*s health. More specifically, which features of assisted conception (IVF-MNC, IVF-SET and IUI-COH) or natural conception affect child*s general health, growth, body composition, cardiometabolic health, development and behavior.

Study design

Prospective long term follow-up cohort study of children born to participants in a multicenter RCT (INeS-study).

Study burden and risks

Participants will be contacted three times for measurements. Parents will be asked to fill out age apropriate questionnaires concerning demographics, growth trajectory, general health, development and behavior (CBCL and BRIEF) of their child. Filling out the questionnaires will take approximately one hour. During the second stage two members of the research staff will visit participants close to their homes in a mobile research vehicle. In this vehicle a set of non-invasive measures, such as anthropometry and blood pressure, will be obtained. This visit will take between one and one and a half hours. A specialized nurse will perform a blood-draw in a separate visit at the participant*s home. The blood-draw is optional and parents give explicit consent. This will be done in the morning after an overnight fast. This visit will approximately take 15 minutes. Children will be measured when they are between 4-6 years old.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

The study population comprises all children born to couples who participated in the INeS-study (registered as NL12782.018.07, METC 2007_064). The INeS-study consisted of couples seeking fertility treatment after at least 12 months of unprotected intercourse. Females were between 18 and 38 years of age and had an unfavorable prognosis for natural conception (less than 30% according to the Hunault model). Couples were diagnosed with an unexplained or mild subfertility. Couples were excluded in case of polycystic ovarian syndrome (PCOS)/anovulation, endometriosis, bilateral tubal pathology or endocrine disorders. 602 Couples were randomly allocated to three cycles of IVF-SET, six cycles of IVF-MNC or six cycles of IUI-COH. ;There were 354 children born in the INeS-study: 313 singletons, 19 twins and 1 triplet. These children were born during the 12 month follow-up period (n<=333) or somewhat thereafter (n<=9).

Exclusion criteria

There are no exclusion criteria.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-09-2016
Enrollment:	354
Type:	Actual

Ethics review

Approved WMO

Date:	31-05-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL56267.018.16