# Appendix 1

**Oct 2014**

IRIS
IUGR Risk Selection Study

# Protocol

## Introduction and accountability

The IRIS (**I**UGR **Ri**sk **S**election) study is a nationwide clinical trial, funded by ZonMw, to assess the (cost-)effectiveness of routinely performed ultrasonography in the third trimester among low risk pregnant women receiving midwife-led care on perinatal mortality and severe perinatal morbidity. Regarding the performance of biometry ultrasound measurements in midwife-led care quality criteria have been predefined. For additional information, please visit irisstudie.nl.

It is essential for the IRIS study that the care providers both in midwife-led care as well as in obstetrician-led care follow the exact same protocol. Only if assessments and management are performed in a uniform matter, the study can adequately investigate whether routine ultrasound is effective and cost-effective in improving perinatal outcomes. Therefore, we kindly ask all health care providers, who monitor women participating in the IRIS study, to follow this multidisciplinary protocol.

This protocol is based on up-to-date national guidelines of the two involved professional organisations: Royal Dutch Association of Midwives (KNOV)[1] and Dutch Society of Obstetrics and Gynaecology (NVOG)[2]. Wherever these guidelines provide insufficient guidance, the protocol was supplemented by results from a Delphi study which was particularly conducted for the IRIS study. In this Delphi study both midwives (working in primary, secondary or tertiary care, or as sonographer) and obstetricians have participated.

You can deviate from the protocol on the basis of the respective clinical situation.
For questions or comments, please contact the IRIS research team via e-mail Irisstudie@vumc.nl or call us at 020-4441746.

**References:**

[1] Opsporing Foetale Groeivertraging [Detection of Fetal Growth Restriction], April 2013 http://www.knov.nl/uploads/knov.nl/knov_downloads/403/file/KNOVstandaard_Opsporing_Foetale_Groeivertraging_april_2013.pdf

[2] Foetale groeibeperking versie 2.1 [Fetal growth restriction version 2.1] http://nvog-documenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=828

# Recommendations Midwife-led Care: Control strategy

Regarding the following recommendations we assume that there is no indication for hypertensive disorder (yet) as well as no sign of reduced fetal movements. The gestational age is at least 26 weeks and 0 days.

| | |
|---|---|
| • Monitor fetal growth using standardized fundal height (SFH) measurement from 26 weeks' gestation onwards, with a minimum interval of 2 weeks. | **K** |
| • Report the SFH measurement results in centimetres in the personal file of the pregnant woman. | **I** |
| • Only perform a biometry scan if you are worried about fetal growth based on previous fundal height measurements in combination with your clinical assessment. | **I** |
| • If a biometry ultrasound scan is indicated: | |
| 1. The ultrasounds should be carried out by a (midwife) sonographer who passed the quality control assessment of the IRIS study. | **I** |
| 2. Plot the abdominal growth (AC) measurement on the fetal growth reference curve by Verburg. | **I** |
| 3. Measure the amount of amniotic fluid in the single deepest vertical pocket. | **I** |
| • Refer to obstetrician-led care if: | |
| 1. the AC measurement is <P10 according to the reference curve by Verburg **OR** | **I** |
| 2. sequential AC measurements show slow growth on the reference curve by Verburg – this is a decrease of at least 20 percentiles *(e.g. from P70 to P50 with a minimum interval of 2 weeks)* **OR** | **I** **D** |
| 3. the single deepest vertical pocket is <2 cm. | **S** |

**D** Delphi-study: multidisciplinary consensus based

**I** Based on predefined IRIS study criteria (protocol)

**K** KNOV-guideline Detection of Fetal Growth Restriction, April 2013

**S** Decided by scientific Steering Committee IRIS study

# Recommendations Midwife-led Care: Intervention strategy

Regarding the following recommendations we assume that there is no indication of hypertensive disorder (yet) as well as no sign of reduced fetal movements. The gestational age is at least 26 weeks 0 days.

| | |
|---|---|
| • Monitor fetal growth using standardized fundal height (SFH) measurement from 26 weeks' gestation onwards, with a minimum interval of 2 weeks. | **K** |
| • Report the SFH measurement results in centimetres in the personal file of the pregnant woman. | **I** |
| • Plan the first biometry ultrasound between 28 and 30 weeks' gestation. | **I** |
| • Plan the second biometry ultrasound scan between 34 and 36 weeks' gestation.<br>- It is recommended that this second ultrasound scan is conducted by the same sonographer who carried out the first scan. | **I**<br>**D** |
| • The ultrasounds should be carried out by a (midwife) sonographer who passed the quality assessment of the IRIS study. | **I** |
| • Plot the abdominal growth (AC) measurement on the reference curve by Verburg. | **I** |
| • Measure the amount of amniotic fluid in the single deepest vertical pocket. | **I** |
| • Refer to obstetrician-led care if:<br>1. the AC measurement is <P10 according to the reference curve by Verburg **OR** | **I** |
| 2. sequential AC measurements show slow growth on the reference curve by Verburg<br>– this is a decrease of at least 20 percentiles *(e.g. from P70 to P50 with a minimum interval of 2 weeks)* **OR** | **I**<br>**D** |
| 3. the single deepest vertical pocket is <2 cm. | **S** |

**D** Delphi study: multidisciplinary consensus based

**I** Based on predefined IRIS study (protocol)

**K** KNOV-guideline Detection Fetal Growth Restriction, April 2013[1]

**S** Decided by scientific Steering Committee IRIS study

# Protocol (obstetrician-led care version)

## Introduction and accountability

The IRIS (IUGR Risk Selection) study is a nationwide clinical trial, funded by ZonMw, to assess the (cost-)effectiveness of routine third trimester ultrasonography on perinatal mortality and severe perinatal morbidity among low risk pregnant women receiving midwife-led care. Regarding the performance of biometry ultrasound measurements in midwife-led care quality criteria have been predefined. For additional information, please visit irisstudie.nl.

It is essential for the IRIS study that the care providers both in ~~the~~ midwife-led care as well as in obstetrician-led care follow the exact same protocol. Only if assessments and management are performed in a uniform manner, the IRIS study can adequately investigate whether routine ultrasound is effective and cost-effective in improving perinatal outcomes. Therefore, we kindly ask all health care providers, who monitor women participating in the IRIS study, to follow this multidisciplinary protocol.

This protocol is based on up-to-date national guidelines of the two involved professional organisations: Royal Dutch Association of Midwives KNOV[1] and Dutch Society of Obstetrics and Gynaecology (NVOG)[2]. In line with the NVOG, the IRIS study group recommends that obstetrician-led care providers will follow the IRIS study protocol for clinical management for all participants in the IRIS study, even if the AC and the estimated fetal weight screening fall within the normal range. This means that all measurements as described in the '*Recommendations after referral from midwife-led care: additional screening or diagnosis in obstetrician-led care*', will be conducted in any case. If a suspicion of IUGR has been confirmed during these measurements, the '*Recommendations after transfer to obstetrician-led care*' will be followed. That is, the second part of the IRIS study protocol.

The recommendations of this protocol are in line with standard, usual antenatal care. The IRIS study group assumes that obstetric management in this protocol is also applied among participants of the IRIS study who have been referred to obstetrician-led care for some other reason, but who may be subject of a suspicion of fetal growth restriction at a later time.

For questions or comments, please contact the IRIS research team via e-mail (Irisstudie@vumc.nl ) or call us at 020-4441746.

*Note*: Midwife-led care providers screen for fetal growth restriction using standardized fundal height (SFH) measurement while taking the total clinical picture into account. In case this leads to concerns about fetal growth restriction, an ultrasound will be conducted. The abdominal growth (AC) plotted on the reference curve by Verburg will be used as main indicator. Based on these findings, a referral for screening or diagnosis to obstetrician-led care centre can be indicated.

**References:**

[1] Opsporing Foetale Groeivertraging, april 2013 [Detection of Fetal Growth Restriction] http://www.knov.nl/uploads/knov.nl/knov_downloads/403/file/Standaard%20Foetale%20groeivertraging.pdf

[2] Foetale groeibeperking versie 2.1 [Fetal growth restriction version 2.1] http://nvogdocumenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=828

Note referral to perinatological centre Version 1.0, 19-09-2007 Consensus based NVOG: Verwijzing naar een perinatologisch centrum: www.**nvog**-documenten.nl/richtlijn/doc/download.php?id=764

# Recommendations after referral from midwife-led care: additional screening and/or diagnosis in obstetrician-led care

The following recommendations apply to pregnant women who participate in the IRIS study and have been referred for additional screening and diagnosis to obstetrician-led care due to the suspicion of fetal growth restriction. We assume that the referred women do not have a hypertensive disorder and that no reduced fetal movements have been reported. The gestational age is at least 26 weeks and 0 days.

Midwife-led caregivers may suspect fetal growth restriction based on systematic measurements of standardized fundal height (SFH) combined with the total clinical picture. If there are concerns about fetal growth, a scan is performed. The measurement of the abdominal circumference (AC) plotted on the reference curve by Verburg is used as main indicator. Based on these findings, a referral for screening or diagnosis to obstetrician-led care is indicated. In line with the guidelines of the Dutch Society of Obstetrics and Gynaecology (NVOG),[2] please perform all measurements described below, even if AC and the estimated fetal weight (EFW) fall within the normal range. Back referral to midwife-led care due to the following findings can be considered.

| | |
|---|---|
| • Assess fetal growth based on AC plotted on the reference curve by Verburg. Stay alert for asymmetric growth based on AC, FL, BPD, HC ratios. | **S** |
| • Stay alert for signs and symptoms of hypertensive disorders and reduced fetal movements. | **N** |
| • Measure the pulsatility index (PI) of the umbilical artery<br>- if the umbilical artery Doppler is ≥P95, it is recommended to also measure the middle cerebral artery Doppler. This is an indication for a change in management (e.g. providing obstetrician-led care, more frequent check-ups) | **N+D**<br>**D** |
| • Assess the amount of amniotic fluid by measuring the single deepest vertical pocket<br>- if the deepest pocket is <2 cm, there is an indication for adjusting the management (e.g. providing obstetrician-led care, more frequent check-ups) | **I**<br>**S** |
| • Regardless of the gestational age, in case of suspected IUGR, cardiotocography (CTG) monitoring is not indicated as long as there is no decrease in fetal movements, no hypertensive disorder has been diagnosed, and no abnormal Doppler measurements have been observed. | **N+D** |
| • For a correct interpretation of fetal growth patterns we recommend 2 sequential biometry ultrasounds, with a minimum interval of 2 weeks | **D** |

**D** Delphi study: multidisciplinary consensus based

**I** Based on predefined IRIS study (protocol)

**N** NVOG committee guideline fetal growth restriction version 2.1 and 'Statement tertiary high perinatological centre referral.' Version 1.0 19-09-2007 Consensus based NVOG.

**S** Decided by scientific Steering Committee IRIS study

# Recommendations after referral to obstetrician-led care

The following recommendations apply to pregnant women who participate in the IRIS study and who were referred to obstetrician-led care due to a confirmed suspicion of IUGR by obstetrician-led care. In this group of women, back referral to midwife-led care is, in principal, not indicated. These recommendations are in line with usual obstetrician-led care.

- Offer pregnant women a screening for infectious diseases if:
  - **either** the AC ≤P2,3 — **S**
  - **or** there are specific risk factors (based on medical history or ultrasound results). Gestational age is not a determining factor to be considered. — **D**

  Perform serology tests on Cytomegalic virus infection (CMV) and Toxoplasma Gondii. — **DD**

  Check the results of the first trimester blood test with regard to syphilis. — **D**

- Offer the pregnant woman a **fetal anomaly scan** (FAS) if no SAS or advanced ultrasound examination was conducted during this pregnancy — **D**
  - offer this by means of an advanced sonography if the AC is ≤P2,3 — **S**

- Provide the possibility of **invasive diagnostics** if the AC is ≤P2,3 — **D**
  - consider individual risk factors and gestational age: be more cautious as the gestational age progresses. Make sure to involve the possible added value of the diagnosis in determining the further obstetric management and in supporting and preparing parents on the birth of a child with a chromosomal disorder. — **D**

- Continue management of a pregnancy with AC <P5 in obstetrician-led care, even if no abnormalities are found in additional tests. — **D**

- As long as there are no other complications: Repeat the biometric ultrasound every 2 weeks and use the AC measurement for assessing fetal growth. Stay alert for asymmetric growth based on AC, FL, BPD, HC ratios. — **D**

- Also asses the amount of amniotic fluid at least every 2 weeks by measuring the deepest vertical pocket during the biometric ultrasounds. Also measure the PI of umbilical artery. — **D**
  - if the PI of the a. umbilicalis is ≥P95 or if the diastolic flow is absent, there is an indication to reconsider obstetric management (*e.g. assessment of middle cerebral artery Doppler, more frequent checks, starting fetal cardiotocography exams)* — **D**

- A pregnancy with a reasonable chance of (or need to) delivery at 32 weeks and/or an estimated birth weight <-1250 g, should be monitored in a tertiary high care perinatological centre. **N+S**

    - Consult a tertiary high care perinatologist about considering to administer magnesium sulphate (MgSO4) for fetal neuroprotection in case of (suspected) IUGR at a gestational age <32 weeks. **D**

**D** Delphi study: multidisciplinary consensus based

**N** NVOG committee guideline fetal growth restriction version 2.1 and 'Statement tertiary high perinatological centre referral.' Version 1.0 19-09-2007 Consensus based NVOG.

**S** Decided by scientific Steering Committee IRIS study