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# ASSISTED REPRODUCTION AND PREGNANCY OUTCOMES



# Case

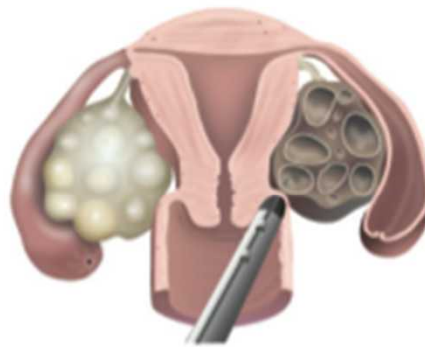


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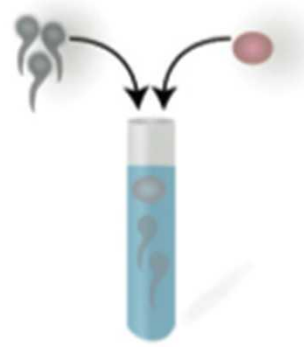




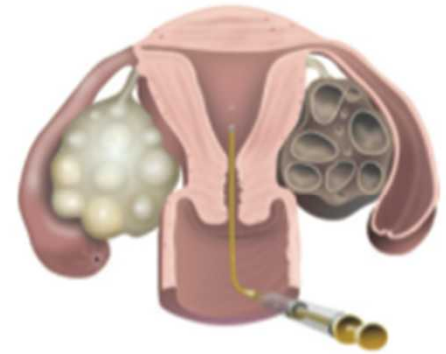
Step 1



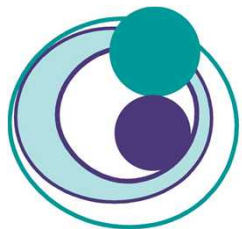
Step 2



Step 3



Step 4



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# More than one.....



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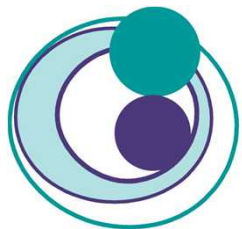
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# Singletons.....

- Many individual factors
- Difficult to isolate as most are inter-related
- Subdivide into type of ART



# General Evolving Trends



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# Preterm Birth

- <32 weeks RR 2.3
- <37 weeks RR 1.84-2.3
- Contribution of spontaneous PTB is unknown

## Risk Factors

- Primiparity
- Smoking
- BMI
- Vanishing twin
  - *Sasanova et al. Hum Reprod 2011*

# Low Birth Weight

## Relative Risks (RR)

- <2500g RR 1.40-2.20
- <1500g RR 2.7-3.78
- SGA <10<sup>th</sup> centile RR 1.98

## Risk Factors

- Smoking
  - BMI
  - Maternal age
  - Duration of infertility
- *Sasanova et al. Hum Reprod 2011*



# Fresh vs Frozen

- Higher birth weight
- Reduced risk
  - SGA
  - Preterm Birth

- *Henningsen et al. Fert Steril 2011*

# Birth Defects

- Mixed results
  - Confounders
    - BMI
    - IVF/ICSI > IVF
- No association
  - *Davies et al NEJM 2012*
- Genital organ malformation  
HR 2.32
  - *Basso O and Olsen DD. Hum Reprod 2003*
- Septal heart defects aOR 2.1
- Oesophageal atresia aOR 4.5
- Anorectal atresia aOR 3.7
  - *Reefhuis et al. Hum Reprod 2009*

# Placental Associated Disorders

~~Low Birth Weight~~ ★

~~Preeclampsia~~ ★

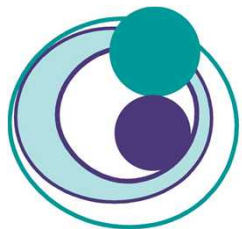
Abnormal Implantation

★ Placenta Accreta ★

★ Antepartum Haemorrhage ★

★ Post-Partum Haemorrhage ★

Post-Partum ~~Depression~~



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# Imprinting Disorders

- Beckwith-Widemann
- Russell-Silver
- Prader-Willi
- Angelman
- McCune Albright
- Actual risk is low
  - < 1 in 5000
- Exact biological etiology is uncertain

## Guidelines for the Management of Vasa Previa

This guideline has been prepared by the Diagnostic Imaging Committee and the Maternal Fetal Medicine Committee and approved by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

### Abstract

**Objectives:** To describe the etiology of vasa previa and the risk factors and associated condition, to identify the various clinical presentations of vasa previa, to describe the ultrasound tools used in its diagnosis, and to describe the management of vasa previa.

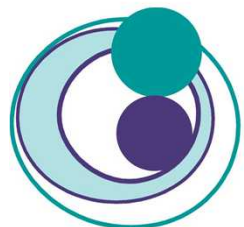


**The Royal  
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New Zealand  
College of  
Obstetricians and  
Gynaecologists**

College Statement  
**C-Obs 47**  
1st Endorsed: July 2012  
Current: July 2012  
Review: July 2015

**C-Obs 47**

**Vasa Praevia**



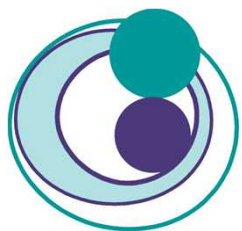
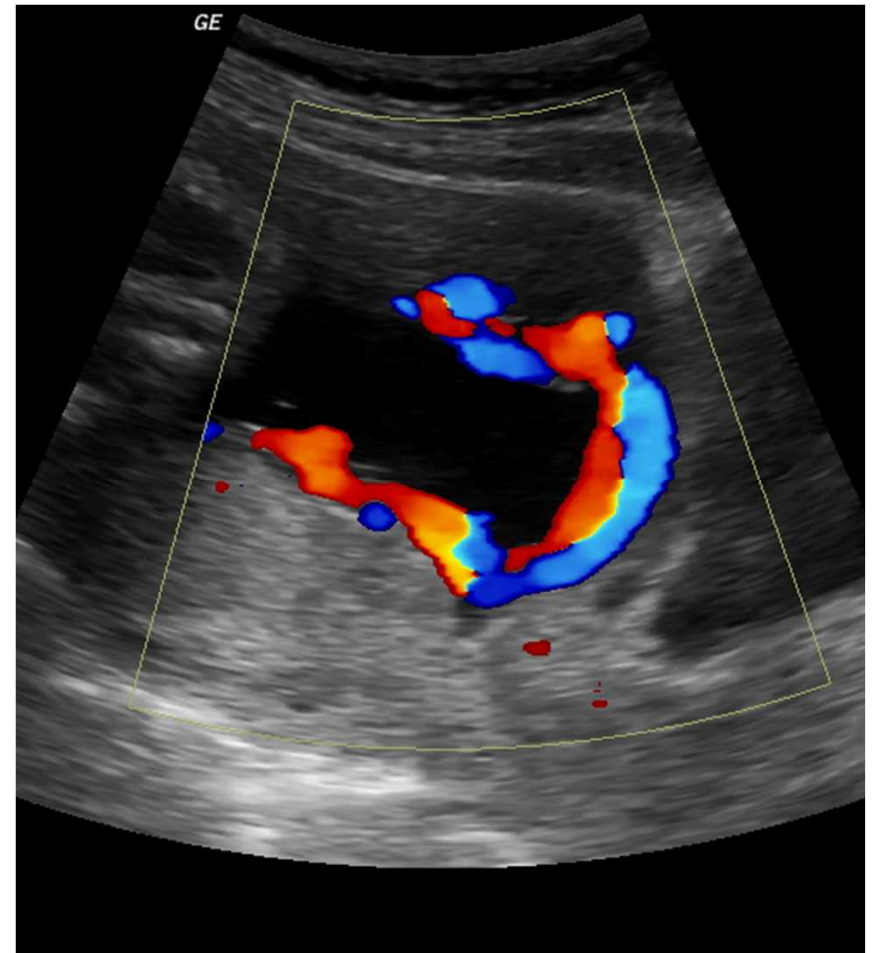
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- Background rate 1:2200
- IVF Rate 1:202
  
- LR 7.75



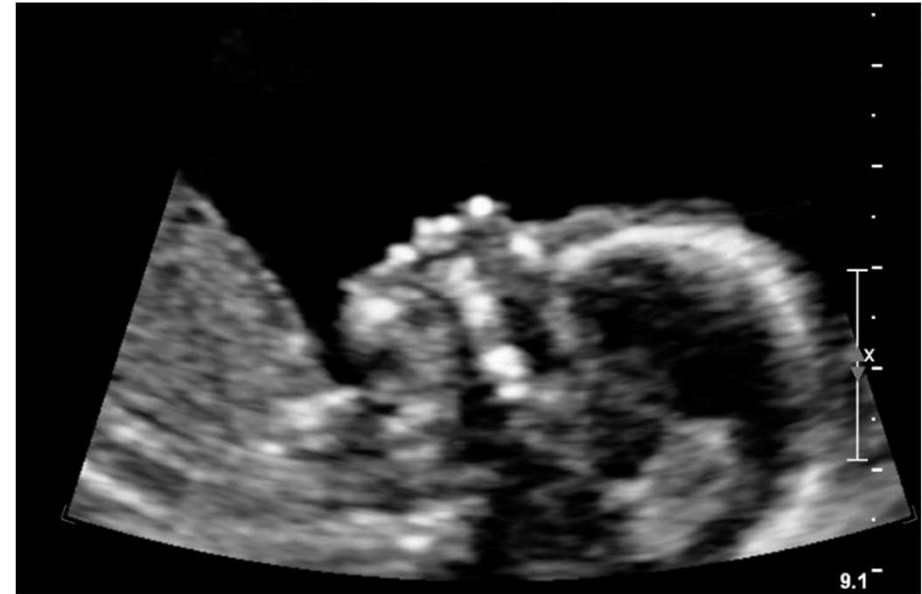
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# Overall Approach


- Obstetric Surveillance
  - PTB
  - LBW
  - PET
- USS Screening
  - Abnormal Implantation
  - Congenital Anomalies
  - Vasa Previa



# Guidelines



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British Fertility Society

Scientific Impact Paper No. 8  
May 2012

## In Vitro Fertilisation: Perinatal Risks and Early Childhood Outcomes

## SOGC CLINICAL PRACTICE GUIDELINES

No. 302, January 2014 (Replaces No. 173, February 2006)

### Pregnancy Outcomes After Assisted Human Reproduction

This clinical practice guideline has been prepared by the Genetics Committee, reviewed by the Reproductive Endocrinology and Infertility Committee and the Family Physicians Advisory Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Disclosure statements have been received from all contributors.

**Key Words:** Assisted human reproduction, assisted reproductive technology, pregnancy outcomes, multiple gestation, imprinting, congenital anomalies, imprinting disorders.

#### Abstract

**Objective:** To review the effect of assisted human reproduction (AHR) on perinatal outcomes, to identify areas requiring further research with regard to birth outcomes and AHR, and to provide guidelines to optimize obstetrical management and counselling of prospective Canadian parents.

**Outcomes:** This document compares perinatal outcomes of different types of AHR pregnancies with each other and with those of spontaneously conceived pregnancies. Clinicians will be better informed about the adverse outcomes that have been documented in association with AHR, including obstetrical complications, adverse perinatal outcomes, multiple gestations, structural congenital abnormalities, chromosomal abnormalities, and imprinting disorders.

**Evidence:** Published literature was retrieved through searches of MEDLINE and the Cochrane Library from January 2000 to December 2012 using appropriate controlled vocabulary and key words (assisted reproduction, assisted reproductive technology, ovulation induction, intracytoplasmic sperm injection, embryo transfer, and in vitro fertilization). Results were not restricted to systematic reviews, randomized controlled trials, controlled clinical trials, and observational studies; studies of all designs published in English from January 2000 to December 2012 were reviewed, and additional publications were identified from the bibliographies of these articles. Searches were updated on a regular basis and incorporated in the guideline in August 2013. Only (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

**Values:** The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

#### Summary Statements

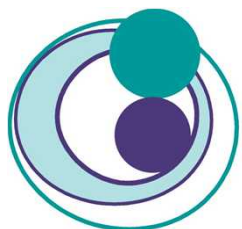
1. There is increasing evidence that infertility or subfertility is an independent risk factor for obstetrical complications and adverse perinatal outcomes, even without the addition of assisted human reproduction (1-2).
2. The relative risk for an imprinting phenotype such as Silver-Russell syndrome, Beckwith-Wiedemann syndrome, or Angelman syndrome is increased in the assisted reproduction population, but the actual risk for one of these phenotypes to occur in an assisted

J Obstet Gynaecol Can 2014;36(1):64-83

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these guidelines. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the SOGC.



# Advanced Maternal Age



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## OBSTETRICS

# Pregnancy outcome at extremely advanced maternal age

Yariv Yogev, MD; Nir Melamed, MD; Ron Bardin, MD; Kinneret Tenenbaum-Gavish, MD; Gadi Ben-Shitrit, MD; Avi Ben-Haroush, MD

**OBJECTIVE:** The purpose of this study was to evaluate pregnancy outcome in women at extremely advanced maternal age ( $\geq 45$  years).

**STUDY DESIGN:** We compared the condition of women aged  $\geq 45$  years ( $n = 177$ ) in a 10:1 ratio (20-29, 30-39, and 40-44 years.). Sub-group analysis compared the condition of women aged 45-49 years with those women aged  $\geq 50$  years.

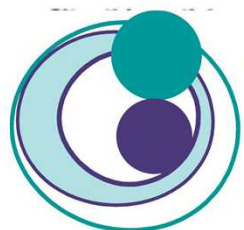
**RESULTS:** The rates of gestational diabetes mellitus and hypertensive complications were higher for the study group, compared with the whole group (17.0% vs 5.6% and 19.7% vs 4.5%, respectively;  $P < .001$ ), as was the rate of preterm delivery at  $< 37$  and  $< 34$  weeks of gestation (odds ratio [OR], 2.1; 95% confidence interval [CI], 1.2–3.6

and OR, 3.5; 95% CI, 1.4–9.0, respectively). The rates of cesarean delivery (OR, 31.8; 95% CI, 18.0–56.1), placenta previa, postpartum hemorrhage, and adverse neonatal outcome were significantly higher among the study group. The risk for gestational diabetes mellitus, pre-eclampsia toxemia, preterm delivery, and neonatal intensive care unit admission was increased for women aged  $\geq 50$  years.

**CONCLUSION:** Pregnancy at extreme advanced maternal age is associated with increased maternal and fetal risk.

**Key words:** advanced maternal age, complication, neonatal, pregnancy

Yogev Y, Melamed N, Tenenbaum-Gavish K, et al. Pregnancy outcome at extremely advanced maternal age. Am J Obstet Gynecol



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TABLE 2

## Delivery outcome for the study and comparison groups

Variable	Overall (n = 5487)	Group 1: 20-29 y (n = 1770)	Group 2: 30-39 y (n = 1770)	Group 3: 40-44 y (n = 1770)	Group 4: ≥45 y (n = 177)	P value
Gestational age, wk <sup>a</sup>	38.8 ± 2.2	39.2 ± 2.0	38.9 ± 2.2	38.5 ± 2.4 <sup>b</sup>	37.6 ± 2.5	< .001 (4≠3≠2,1)
<37, n (%)	541 (10.3)	130 (7.7)	152 (9.1)	221 (12.8)	38 (21.5)	< .001
<34, n (%)	149 (2.8)	27 (1.6)	49 (2.9)	62 (3.6)	11 (6.2)	< .001
<32, n (%)	76 (1.4)	15 (0.9)	23 (1.4)	34 (2.0)	4 (2.3)	.04
Spontaneous preterm delivery (<37 wk), n (%)	255 (47)	75 (58)	82 (54)	92 (42)	6 (15)	.01
Delivery mode, n (%)						
Normal vaginal delivery	3655 (66.6)	1384 (78.2)	1275 (72.0)	965 (54.5)	31 (17.5)	< .001
Instrumental delivery <sup>b</sup>	255 (4.6)	113 (6.4)	87 (4.9)	49 (2.8)	6 (3.4)	< .001
Cesarean delivery	1587 (28.9)	277 (15.7)	412 (23.3)	759 (42.9)	139 (78.5)	< .001
Elective cesarean delivery	551 (37.5)	55 (21.6)	131 (35.5)	293 (41.5)	72 (51.8)	< .001
Indication for cesarean delivery, n (%)						
Breech	265 (16.7)	55 (19.9)	79 (19.2)	101 (13.3)	30 (21.6)	.006
Multifetal gestation	75 (4.7)	13 (4.7)	28 (6.8)	26 (3.4)	8 (5.8)	.07
Dystocia	56 (3.5)	23 (8.3)	11 (2.7)	16 (2.1)	6 (4.3)	< .001
Nonreassuring fetal heart rate	79 (5.0)	14 (5.1)	13 (3.2)	40 (5.3)	12 (8.6)	.04
Placenta previa	35 (2.2)	2 (0.7)	10 (2.4)	20 (2.6)	3 (2.2)	.3
Previous cesarean delivery	461 (29.0)	43 (15.5)	127 (30.8)	268 (35.3)	23 (16.5)	< .001
Macrosomia	114 (7.2)	29 (10.5)	28 (6.8)	49 (6.5)	8 (7.0)	.13
Maternal request	NA	NA	NA	NA	20 (14.4)	
Preeclampsia	38 (2.4)	3 (1.1)	12 (2.9)	17 (2.2)	6 (4.3)	.18
Other	444 (28.0)	95 (34.3)	104 (25.2)	222 (29.2)	23 (16.5)	.001
Placenta previa	49 (0.9)	3 (0.2)	11 (0.6)	25 (1.4)	10 (5.6)	< .001
Placental abruption	37 (0.7)	6 (0.3)	12 (0.7)	17 (1.0)	2 (1.1)	.13
3rd-4th degree vaginal tears	26 (0.7)	9 (0.6)	15 (1.1)	2 (0.2)	0	.054
Postpartum hemorrhage	76 (1.4)	18 (1.0)	21 (1.2)	30 (1.7)	7 (4.0)	.007
Blood transfusions	24 (0.4)	3 (0.2)	5 (0.3)	14 (0.8)	2 (1.1)	.012
Postpartum fever	183 (3.3)	83 (4.7)	43 (2.4)	27 (1.5)	22 (12.5)	< .001
Prolonged hospitalization <sup>c</sup>	111 (2.0)	23 (1.3)	36 (2.0)	40 (2.3)	12 (7.2)	< .001
Intensive care unit admission	53 (0.96)	17 (1.0)	14 (0.8)	19 (1.1)	3 (1.7)	.1

NA, not applicable.

<sup>a</sup> Data are presented as mean ± SD; <sup>b</sup> Vacuum extraction or forceps delivery; <sup>c</sup> Hospitalization for more than 4 or 7 days after vaginal or cesarean delivery, respectively.

	<b>Maternal Age</b>			
	<b>20-29 years</b>	<b>30-39 years</b>	<b>40-44 years</b>	<b>Over 45 years</b>
<b>Gestational Diabetes</b>	1.4%	4.2%	10.2%	17%
<b>Gestational Hypertension</b>	2.0%	2.3%	3.2%	9.0%
<b>Pre-Eclampsia</b>	0.7%	1.5%	2.4%	10.7%
<b>Placental Abruption</b>	0.3%	0.7%	1.0%	1.1%
<b>Placenta Previa</b>	0.2%	0.6%	1.4%	5.6%
<b>Delivery &lt; 37 weeks</b>	7.7%	9.1%	12.8%	21.5%
<b>Caesarean Delivery</b>	15.7%	23.3%	42.9%	78.5%
<b>Birthweight &lt;10<sup>th</sup> centile</b>	10.7%	8.5%	9.8%	11.3%
<b>Admission to NICU</b>	6.3%	7.4%	8.6%	10.7%

Yogev Y, Melamed N, Tenenbaum-Gavish K, et al. Pregnancy outcome at extremely advanced maternal age. Am J Obstet Gynecol 2010;203:558.e1-7.



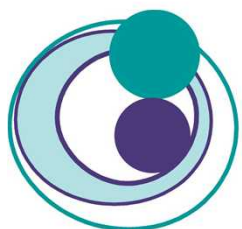
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Scientific Impact Paper No.34

February 2013

## **Induction of Labour at Term in Older Mothers**



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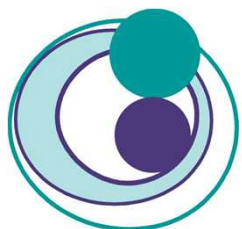
**Table 1. Rate and absolute risk of stillbirth and neonatal death by maternal age in the UK<sup>14</sup>**

Maternal age (years)	Stillbirths <sup>a</sup>		Neonatal deaths <sup>a</sup>	
	Rate (95% CI) <sup>b</sup>	Absolute risk (95% CI)	Rate (95% CI) <sup>c</sup>	Absolute risk (95% CI)
25–29	4.6 (4.3, 4.9)	1/ 217 (1/204, 1/233)	2.9 (2.7, 3.2)	1/345 (1/312, 1/370)
30–34	4.7 (4.4, 5.0)	1/213 (1/200, 1/227)	2.6 (2.4, 2.8)	1/385 (1/357, 1/417)
35–39	5.5 (5.1, 5.9)	1/182 (1/169, 1/196)	2.9 (2.6, 3.2)	1/345 (1/312, 1/385)
≥40	7.6 (6.6, 8.7)	1/132 (1/115, 1/152)	3.8 (3.1, 4.6)	1/263 (1/217, 1/323)

<sup>a</sup> Second and subsequent deaths from pregnancies with multiple losses are excluded

<sup>b</sup> Rates per 1000 maternities

<sup>c</sup> Rates per 1000 live births



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# AMA Protocol

- Pre-Conceptional Counselling
  - Outline risks of pregnancy
  - Folic Acid 0.8 mcg/d

# Antenatal Mx

- Booking scan
- Low-dose Aspirin
- Booking HbA1c, TFTs
- Aneuploidy
  - CFTS Screening
  - NIPT
  - Invasive
- 24-28 week polycose
- PET Screening
- Detailed Anatomy scan
- Consider ruling out vasa previa
- 24 week uterine artery Dopplers
- Serial Growth Scans
- From 37 weeks
  - Serial CTGs
- Delivery
  - By EDC
  - Consider El LSCS in some cases



# Additional References

- SOGC. Pregnancy outcomes after assisted human reproduction. *JOGC* 2014
- Hayashi et al. Adverse obstetric and perinatal outcomes of singleton pregnancies maybe related to maternal factors associated with infertility rather than the type of assisted reproductive technology procedure used. *Fert Steril* 2012 98(4):922-928
- RCOG. In Vitro Fertilisation: Perinatal Risks and Early Childhood Outcomes. Scientific Impact Paper No 8. 2012