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Maternal - Fetal Tıp ve Perinatoloji Derneği Türkiye
23-06-1998

Comparative Complications of Amniocentesis, Chorionic Villus Sampling and Cordocentesis

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28-29.04.2017 İzmir

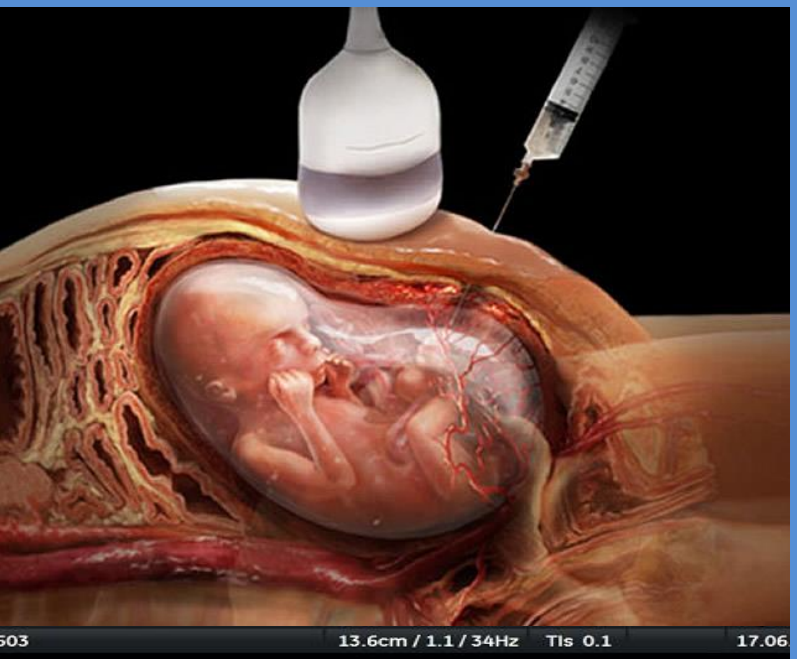
Miscarriage rate -without any invasive procedure

	N	US (weeks)	Miscarriage (Weeks)	Miscarrage Rate (%)
Wilson et al.	918	12	<20	2.3
Gilmore et al	806	12	<28	2.1
Liu et al	1068	12	<28	1.5
Tabor et al	2304	16	<28	0.7

The indications for amniocentesis and CVS:

Maternal age ≥ 35 years	57.7%
Previous child with chromosome abnormality	3.4%
Parent carrier of chromosome abnormality	1.1%
Chromosome abnormality in the family	5.0%
Mental retardation in a previous child or in the family	2.0%
Increased risk of monogenic disease	3.3%
Increased risk of open fetal malformation i.E. Neural tube defect or abdominal wall defect	2.1%
Increased risk of chromosomal abnormality following a triple test,	6.1%
Ultrasound scan (2nd tri)	3.0%
Combined first-trimester risk assessment	3.8%
Malformation on ultrasound (1st tri)	3.9%
Miscellaneous	8.5%

Amniocentesis



- At or beyond 15 + 0 completed weeks of gestation
- 20 – 22-G needle
- Transabdominally under continuous ultrasound guidance
- Avoidance of the placenta is preferable, especially in Rhesus-negative women
- To minimize contamination with maternal cells, the first 2mL of fluid should be discarded

Technique

20 – 22-G needle transabdominally under continuous ultrasound guidance

- comparing 20-G and 22-G intrauterine bleeding rates were similar (4/100 *vs* 8/100)
- A retrospective study (*n* = 793) reported similar fetal loss rates with 20-G (1.57%), 21-G (1.47%) and 22-G (1.61%) needles

Timing

- Early (< 14 + 0 weeks) *vs* midtrimester (> 15 + 0 weeks) amniocentesis
  - higher rate of total fetal losses (7.6% *vs* 5.9%),
  - fetal talipes (1.3% *vs* 0.1%) and
  - post-procedure amniotic fluid leakage (3.5% *vs* 1.7%)

Study	Gestational age at amniocentesis, weeks	Rate of amniotic fluid leakage, %	Rate of talipes in the infants, %
Tabor et al., 1986 [8]	16	1.7	0.8
Smidt-Jensen et al., 1992 [30]	15	2.8	0.5
CEMAT, 1998 [19]	15	2.4	0.2
Philip et al., 2004 [29]	14	9.7	0.9
CEMAT, 1998 [19]	12	4.6	1.3
Sundberg, 1997 [28]	12	4.4	1.7

Fetal Diagn Ther 2010;27:1–7

Laboratory aspects

- Failure of amniocyte culture is reported after 0.1% of procedures.
- Blood-stained amniotic fluid and late gestational age at amniocentesis increase the risk of culture failure
- Amniotic cell mosaicism is seen in 0.25% of procedures
- A retrospective study of amniocentesis after 28 gestational weeks reported a 9.7% culture failure rate

Complications

- **Fetal Loss**
  - Procedure-related risk of miscarriage for amniocentesis is 0.11% (95% CI, −0.04 to 0.26%)
  - A review from Denmark of 147 987 invasive procedures, published in 2016,
    - miscarriage of 0.56% within 28 days
    - a risk of stillbirth of 0.09% within 42 days after amniocentesis

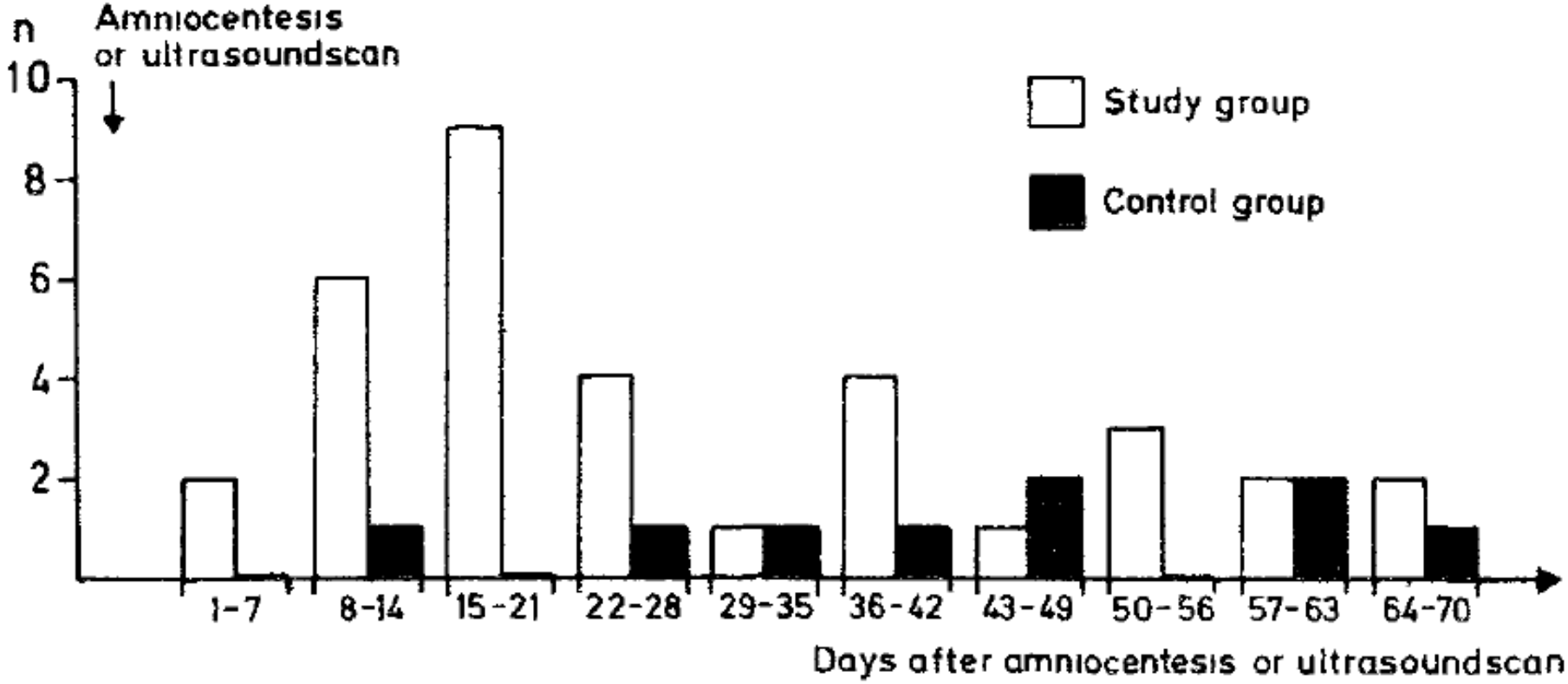
Randomised trial of AC vs no procedure

- 4606 women aged 25-34 yrs
- No risk factor for spontaneous abortion

	Study group A/S N: 2302	Control group No proc. N: 2304
Fetal Loss Rate (%)	1.7	0.7

Procedure related loss rate 1.0% (95% CI 0.3-1.5%)

Tabor et al 1986



Tabor et al 1986

Table 3 Incidence–rate difference meta-analysis to derive aggregate summary statistics for estimated procedure-related loss before 24 weeks' gestation in women undergoing amniocentesis

	Amniocentesis group		*Control group*			
Reference	*Total* (n)	*Miscarriage rate* (n (% (95% CI)))	*Total* (n)	*Miscarriage rate* (n (% (95% CI)))	*Procedure-related loss* (% (95% CI))	P
Muller, 2002[23]	3472	31 (0.89 (0.61–1.27))	47 004	197 (0.42 (0.36–0.48))	0.47 (0.24 to 0.71)	0.0003
Eddleman, 2006[25]	3096	31 (1.00 (0.68–1.42))	31 907	300 (0.94 (0.84–1.05))	0.06 (−0.30 to 0.42)	0.6976
Kong, 2006[26]	3468	39 (1.12 (0.80–1.53))	1125	13 (1.16 (0.62–1.97))	−0.03 (−0.75 to 0.68)	0.8727
Towner, 2007[28]	15 005	69 (0.46 (0.36–0.58))	17 045	90 (0.53 (0.42–0.65))	−0.07 (−0.22 to 0.09)	0.4258
Odibo, 2008[29]	11 695	113 (0.97 (0.80–1.16))	39 594	335 (0.85 (0.76–0.94))	0.12 (−0.07 to 0.31)	0.2348
Pitukkijronnakorn, 2011[33]	2990	11 (0.37 (0.18–0.66))	1495	3 (0.20 (0.04–0.59))	0.17 (−0.18 to 0.51)	0.4099
Corrado, 2012[34]	2990	30 (1.00 (0.68–1.43))	487	4 (0.82 (0.22–2.09))	0.18 (−0.77 to 1.13)	0.4720
Pooled analysis (random effects)	42 716	324 (0.81 (0.58–1.08))	138 657	942 (0.67 (0.46–0.91))	0.11 (−0.04 to 0.26)	0.1435
Cochran's Q (*P*)		46.43 (< 0.0001)		117.15 (< 0.0001)	9.97 (0.1259)	
I^2 statistic (% (95% CI))		87.1 (74.5–92.0)		94.9 (92.3–96.3)	39.8 (0.0–73.4)	
Bias (*P*)		2.9443 (0.3653)		0.2387 (0.9441)	0.6228 (0.6661)	

Only the first author is listed for each study.

Ultrasound Obstet Gynecol 2015; 45: 16–26.

Complications

- *Amniotic fluid leakage*
  - Its occurrence is reported to vary between 1 and 2%
  - Leakage rate increases with decreasing gestational age
  - Spontaneous sealing of the membranes is commonly observed

Complications

- *Chorioamnionitis*
  - The risk of chorioamnionitis and uterine infection after genetic amniocentesis is low (< 0.1%)
- *Needle injury*
  - The occurrence of needle injury to the fetus is extremely rare
- *Maternal complications*
  - Severe maternal complications related to amniocentesis, including sepsis or even death, have been reported in a very small number of cases

Complications

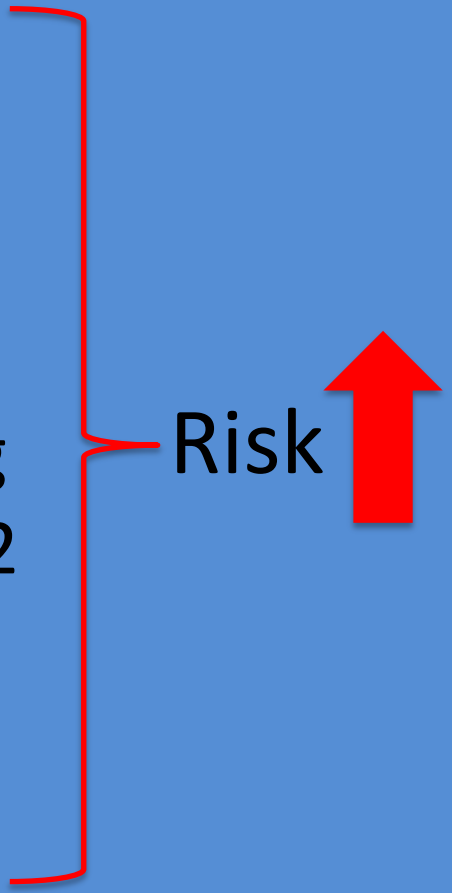
- *Risk factors for complications*
  - Lower fetal loss rates have been documented if more than 100 procedures are performed per annum
  - A higher number of attempts (three or more punctures) increases the risk of fetal loss. If more than two punctures are necessary, it has been suggested to delay the procedure by 24 hours

Complications

- A bloody or discolored (i.e. brownish) specimen may reflect current intraamniotic bleeding and is consistently reported to herald a higher risk of post-procedural fetal loss.
- Expert opinion suggests that an operator's competence should be reviewed when loss rates exceed 4/100 consecutive amniocenteses

Risk factors

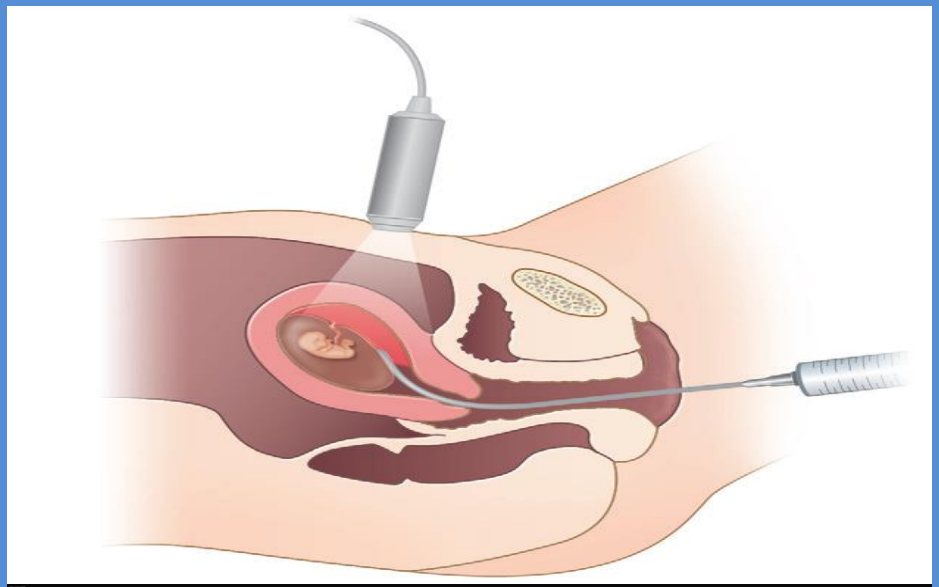
- Uterine fibroids
- Mullerian malformations
- Chorioamniotic separation
- Retrochorionic hematoma
- Previous or current maternal bleeding
- Maternal body mass index > 40 kg/m2
- Multiparity (>3 births)
- Manifest vaginal infection
- History of three or more miscarriages

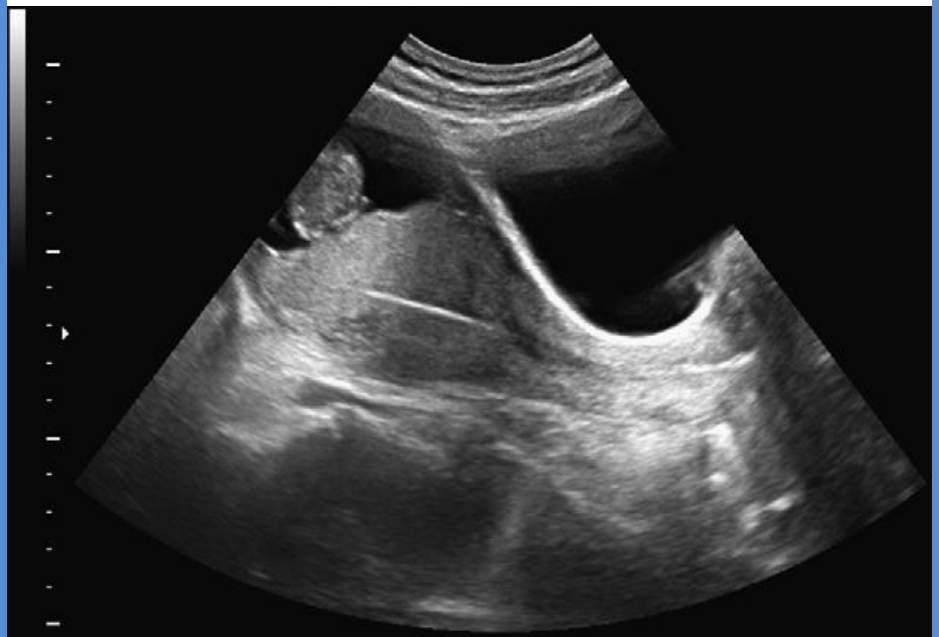


Chorionic Villus Sampling (CVS)

- Performed after 10 + 0 gestational weeks
- Transabdominally or transcervically
- Under continuous ultrasound guidance
- A single needle of 17 – 20 G or a two-needle set of outer 17/19 G and inner 19/20 G may be used
- A minimum amount of 5 mg villi in each sample is required to achieve a valid result

Chorionic Villus Sampling (CVS)

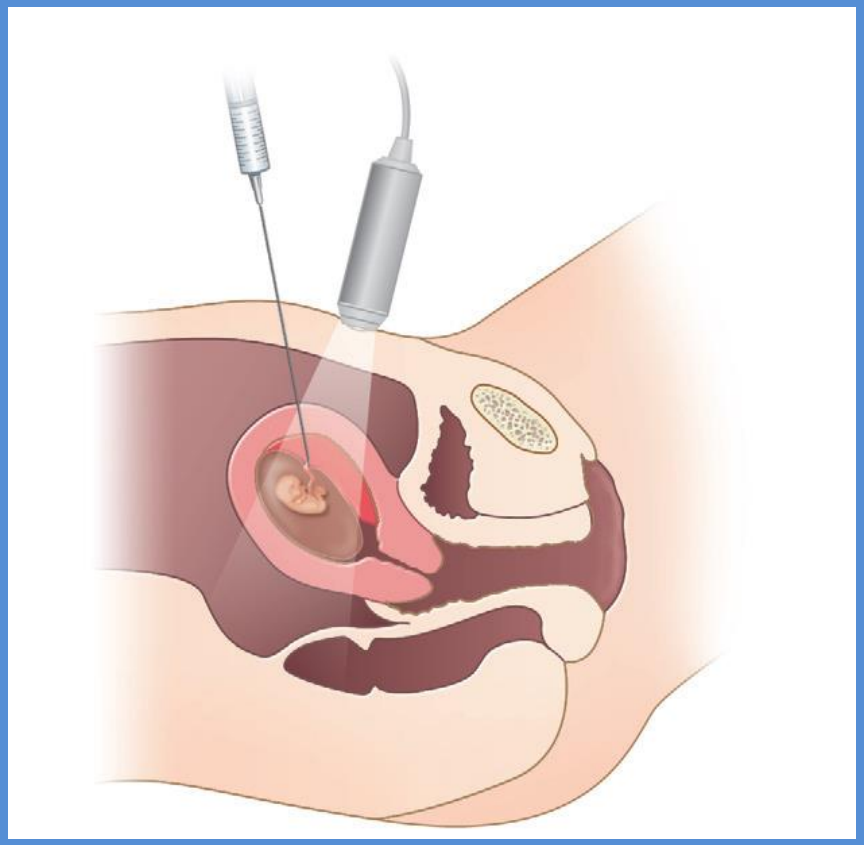




***Transcervical approach*.**

- Biopsy forceps are inserted transvaginally through the cervical canal to the trophoblastic area, or a catheter with plastic or metal stylet under syringe aspiration may be used
- The amount of villi obtained in the sample must be checked visually.
- A minimum amount of 5 mg villi in each sample is required to achieve a valid result.
- Sampling failure is reported to occur in 2.5–4.8% of procedures

Chorionic Villus Sampling (CVS)



Timing

- CVS should not be performed before 10 + 0 completed weeks of gestation, due to the higher risk of fetal loss and complications before this time.
- Reports from the early 1990s highlighted an increased incidence of limb reduction/oromandibular hypoplasia in fetuses which underwent CVS earlier than 10 weeks of gestation
- The limbs and mandible seem to be more susceptible to vascular disruption before 10 weeks

Chorionic Villus Sampling (CVS)

Laboratory aspects

- Failure of the cytotrophoblastic culture < 0.5% of procedures
- Placental cell mosaicism is seen in 1% of procedures.
- In these cases, genetic counseling is recommended and amniocentesis may be indicated to differentiate true fetal mosaicism from confined placental mosaicism

Complications

Fetal loss

- Between 0.2% and 2%
- This risk appears to be lower in experienced centers and to decrease with increasing experience, ranging between 1/150 and 1/500
- The fetal loss rate after transcervical CVS was reported to be 2.5%

Table 4 Incidence–rate difference meta-analysis to derive aggregate summary statistics for estimated procedure-related loss before 24 weeks' gestation in women undergoing chorionic villus sampling (CVS)

	CVS group		*Control group*			
Reference	*Total* (n)	*Miscarriage rate* (n *(% (95% CI)))*	*Total* (n)	*Miscarriage rate* (n *(% (95% CI)))*	*Procedure-related loss (% (95% CI))*	P
Lau, 2005[38]	1355	25 (1.85 (1.20–2.71))	1125	13 (1.16 (0.62–1.97))	0.69 (–0.29 to 1.67)	0.2276
Odibo, 2008[39]	5148	138 (2.68 (2.26–3.16))	4803	161 (3.35 (2.86–3.90))	–0.67 (–1.35 to 0.01)	0.0653
Akolekar, 2011[40]	2396	44 (1.84 (1.34–2.46))	31 460	360 (1.14 (1.03–1.27))	0.69 (0.24 to 1.15)	0.0042
Pooled analysis (random effects)	8899	207 (2.18 (1.61–2.82))	37 388	534 (1.79 (0.61–3.58))	0.22 (–0.71 to 1.16)	0.6385
Cochran's Q (*P*)		6.69 (0.0352)		99.47 (< 0.0001)	10.21 (0.0061)	
I^2 statistic (% (95% CI)		70.1 (0.0–89.1)		98.0 (96.9–98.6)	80.4 (0.0–91.9)	
Bias (*P*)		–5.08 (0.2873)		7.06 (0.6332)	—	

Only the first author is listed for each study.

Ultrasound Obstet Gynecol 2015; 45: 16–26.

Complications

- A meta-analysis of four randomized trials showed that, compared with second-trimester amniocentesis, **transcervical CVS** carries a significantly higher risk of
  - total pregnancy loss (RR, 1.40 (95% CI, 1.09–1.81)) and
  - spontaneous miscarriage (RR, 1.50 (95% CI, 1.07–2.11))

Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database Syst Rev 2003; 3: CD003252

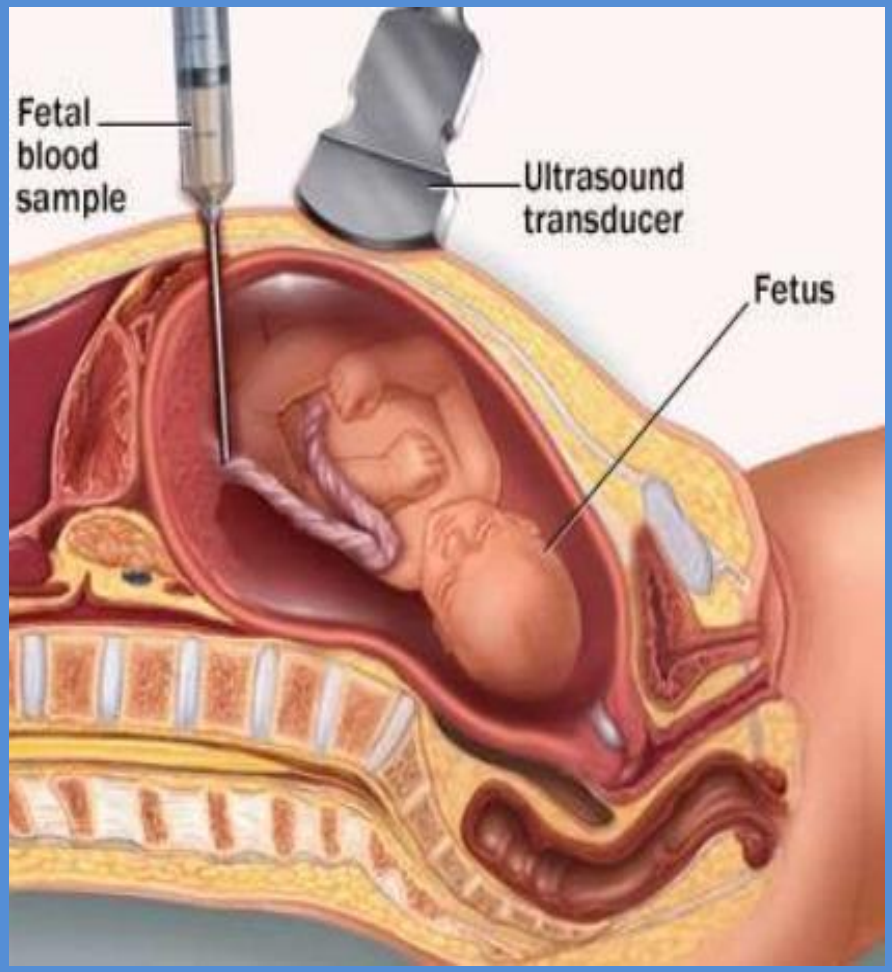
Complications

- ***Vaginal bleeding***
  - Vaginal bleeding is reported to occur in 10% of cases. more frequent after the transcervical (up to 30% of cases).
- ***Uncommon complications***
  - The risk of amniotic fluid leakage following CVS is exceedingly rare, occurring after < 0.5% of procedures
  - The risk of chorioamnionitis and uterine infection after CVS is extremely small (1–2/3000).

Complications

- There have been some reports associating CVS with development of preeclampsia later in pregnancy, possibly due to placental damage, but these findings have not been consistent across studies and a meta-analysis failed to show an association.
- Similarly, a case–control study did not detect an association between CVS and impaired fetal growth;

Fetal Blood Sampling (FBS, Cordocentesis)



- Transabdominally after 18 + 0 weeks, using a 20 – 22-G needle under ultrasound guidance.
- If the placenta is anterior, a puncture of the cord at the level of placental insertion is suggested;
- if the placenta is posterior, a free loop of the cord or the intra-abdominal portion of the umbilical vein is sampled

Indications

Suspected Fetal Anemia
Red blood cell alloimmunization
Infections
Parvovirus
TORCH*
Chronic fetomaternal hemorrhage
Management of Neonatal AIT
Routine at 32–34 wk
Miscellaneous
Fetal thyroid disease
Fetal arrhythmia resistant to maternal therapy
Suspected congenital immunodeficiency

*Toxoplasmosis, other [congenital syphilis and viruses], rubella, cytomegalovirus, and herpes simplex virus.

Complications

- **Fetal Loss**
  - The risk of fetal loss after FBS is between 1% and 2%
  - Factors associated with increased risk of fetal loss after FBS include fetal anomalies, IUGR and gestational age < 24 weeks.

Fetal Loss Rate Associated With Cordocentesis At Midgestation

	Cordocentesis group	*Control group*	*Statistical significance*
Fetal loss (No.)	33 (3.2%)	18 (1.8%)	$P < .05$*
Spontaneous abortion at <28 wk (No.)	18 (1.8%)	7 (0.7%)	$P < .05$*
Dead fetus in utero at >28 wk (No.)	15 (1.5%)	11 (1.1%)	$P > .05$*
Live birth (No.)	987 (96.8%)	999 (97.9%)	$P > .05$*
Preterm delivery (No.)	141 (13.8%)	128 (12.0%)	$P > .05$*
Term delivery at >37 wk (No.)	846 (82.9%)	871 (85.2%)	$P > .05$*
Gestational age at delivery (wk, mean ± SD)	38.1 ± 2.3	37.9 ± 2.8	$P > .05$†
Birth weight (g, mean ± SD)	2,926 ± 519	2,951 ± 628	$P > .05$†
Intrauterine growth restriction (birth weight <10th percentile) (No.)	89 (8.7%)	95 (9.3%)	$P > .05$*
Major complications			
Premature rupture of membranes (No.)	38 (3.7%)	38 (3.7%)	$P > .05$*
Chorioamnionitis (No.)	9 (0.9%)	5 (0.5%)	$P > .05$*
Abruptio placentae (No.)	4 (0.4%)	6 (0.6%)	$P > .05$*
Pregnancy-induced hypertension (No.)	53 (5.2%)	48 (4.7%)	$P > .05$*
Cesarean delivery (No.)	206 (20.2%)	188 (18.4%)	$P > .05$*

*By McNemar test (from 2040 pregnancies).
†By paired *t* test (from 2040 pregnancies).

Am J Obstet Gynecol 2001;184:719-23

Summary -Amniocentesis

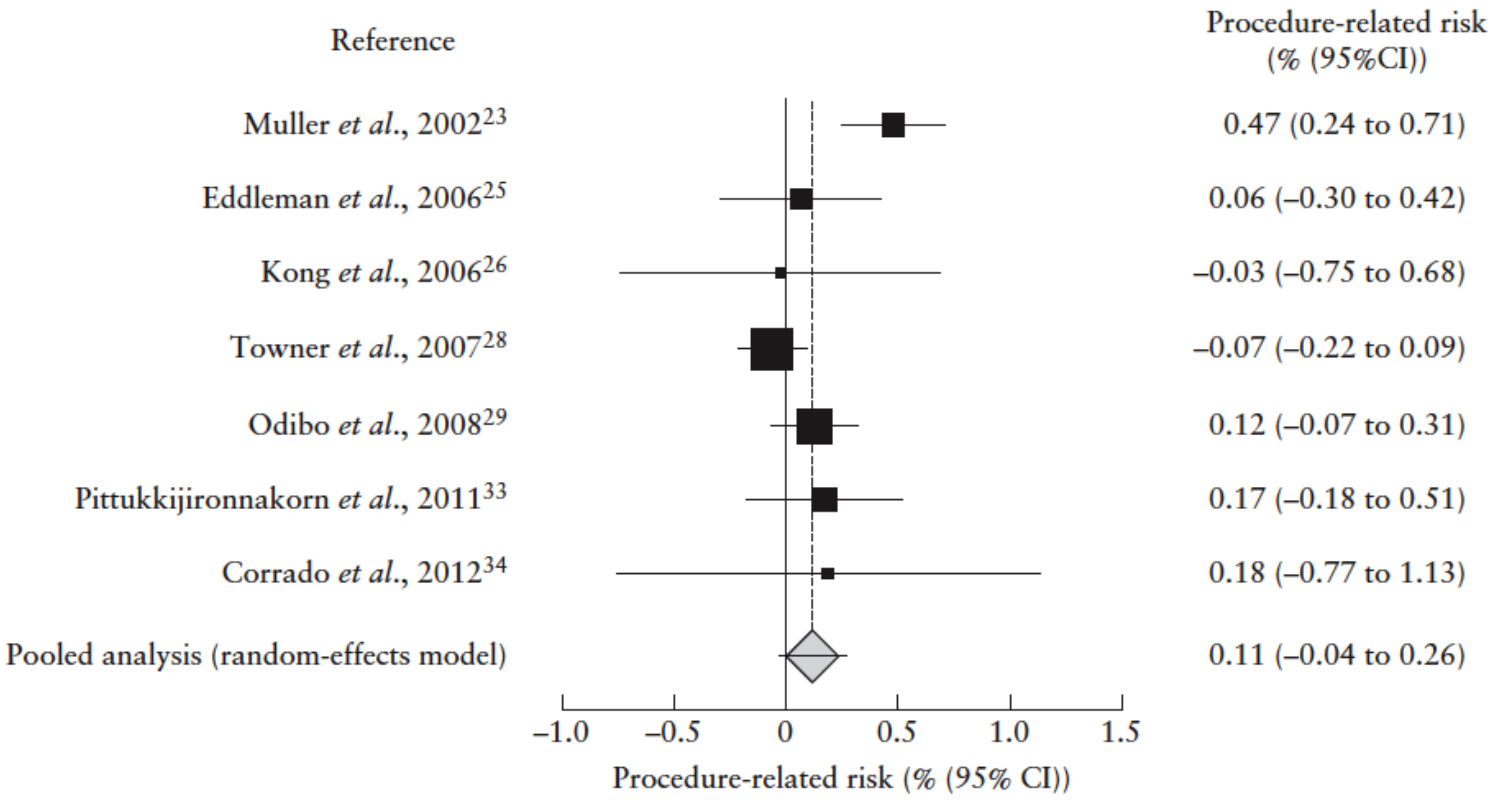


Figure 3 Forest plot showing estimated procedure-related risk of miscarriage before 24 weeks' gestation with 95% CIs derived from each of the controlled studies and weighted pooled summary estimate using a random-effects model and incidence–rate difference meta-analysis in women who underwent amniocentesis.

Summary -CVS

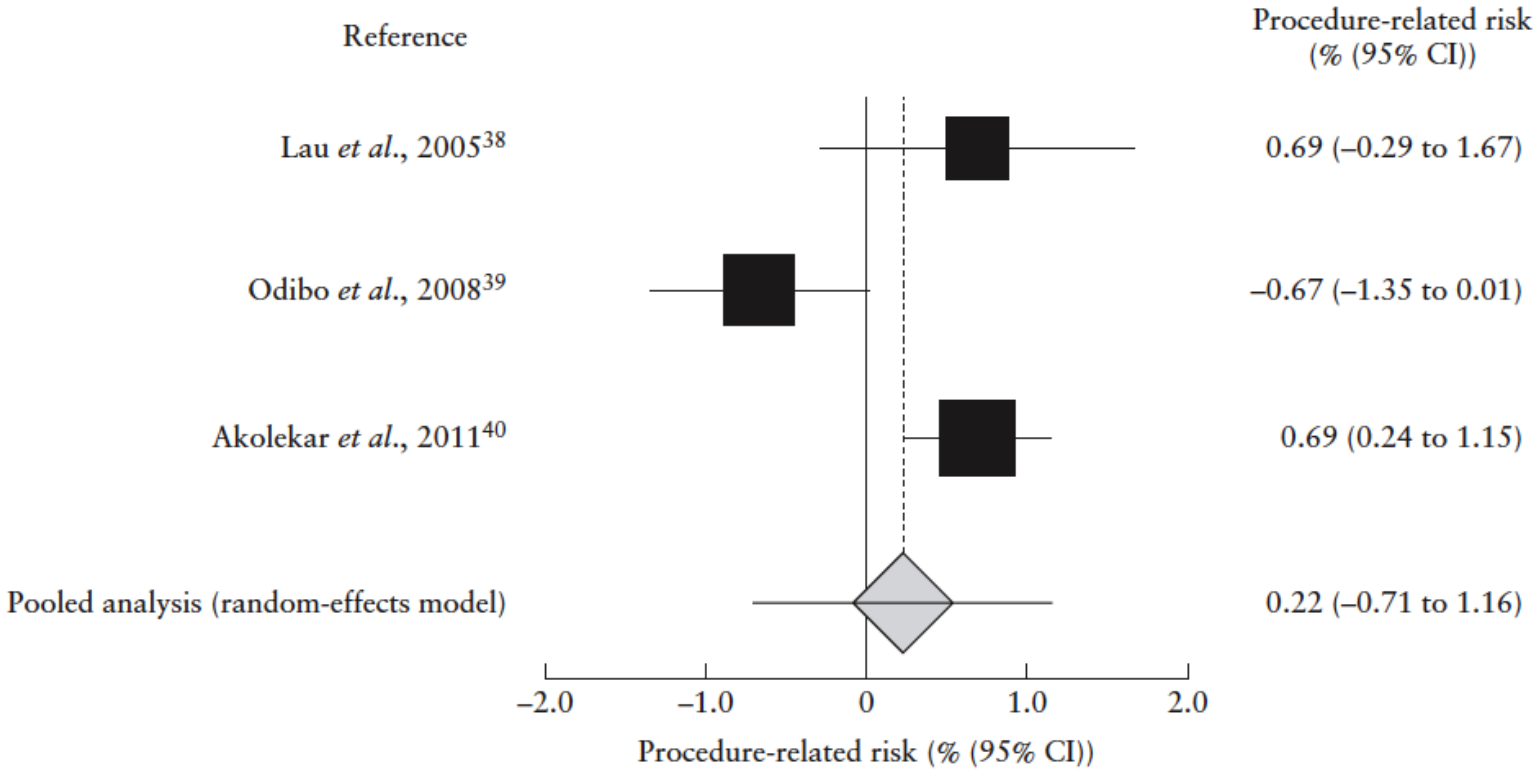
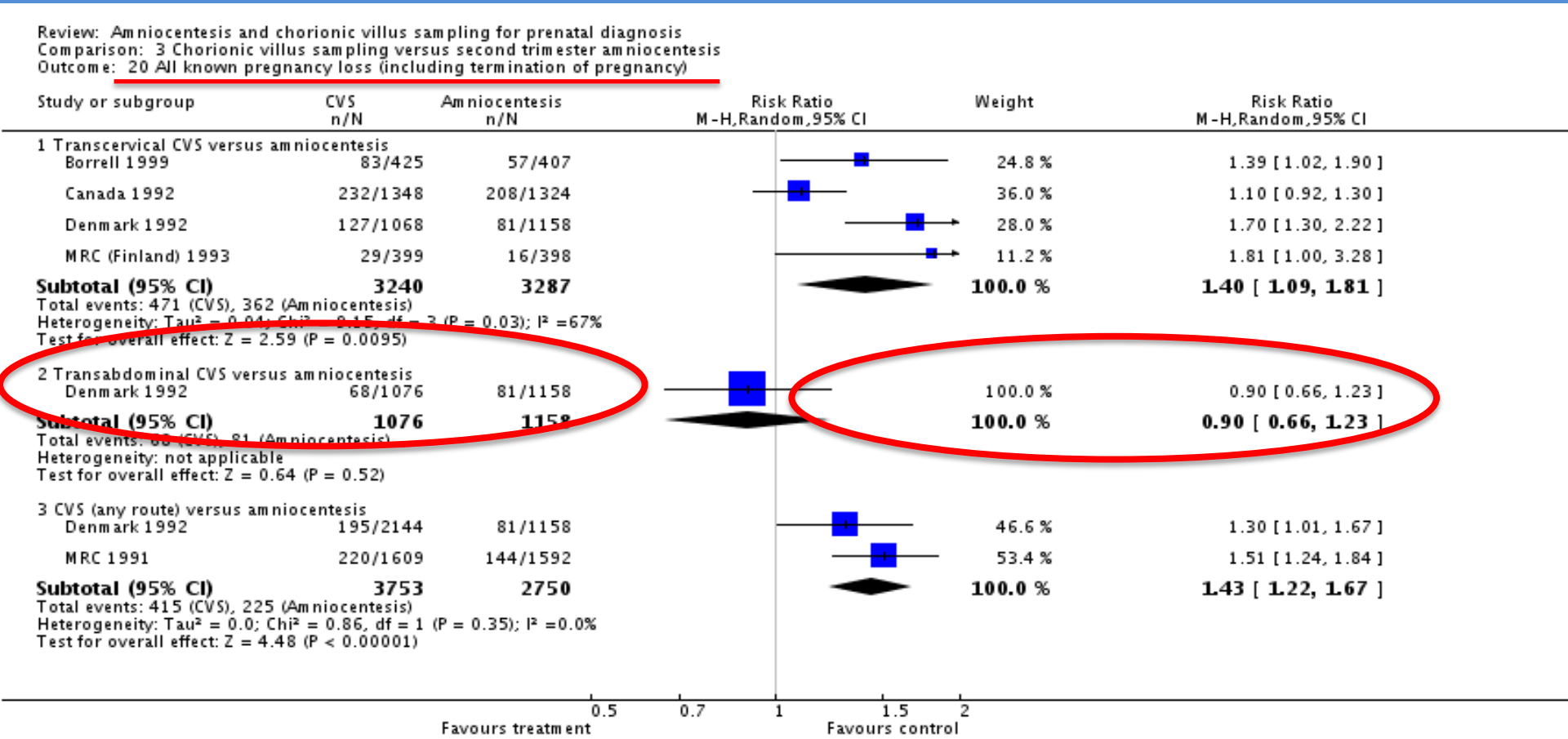


Figure 4 Forest plot showing estimated procedure-related risk of miscarriage before 24 weeks' gestation with 95% CIs derived from each of the controlled studies and weighted pooled summary estimate using a random-effects model and incidence–rate difference meta-analysis in women who underwent chorionic villus sampling.

Amniocentesis and chorionic villus sampling for prenatal diagnosis



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21 JUL 2003 DOI: 10.1002/14651858.CD003252
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003252/full#CD003252-fig-00320

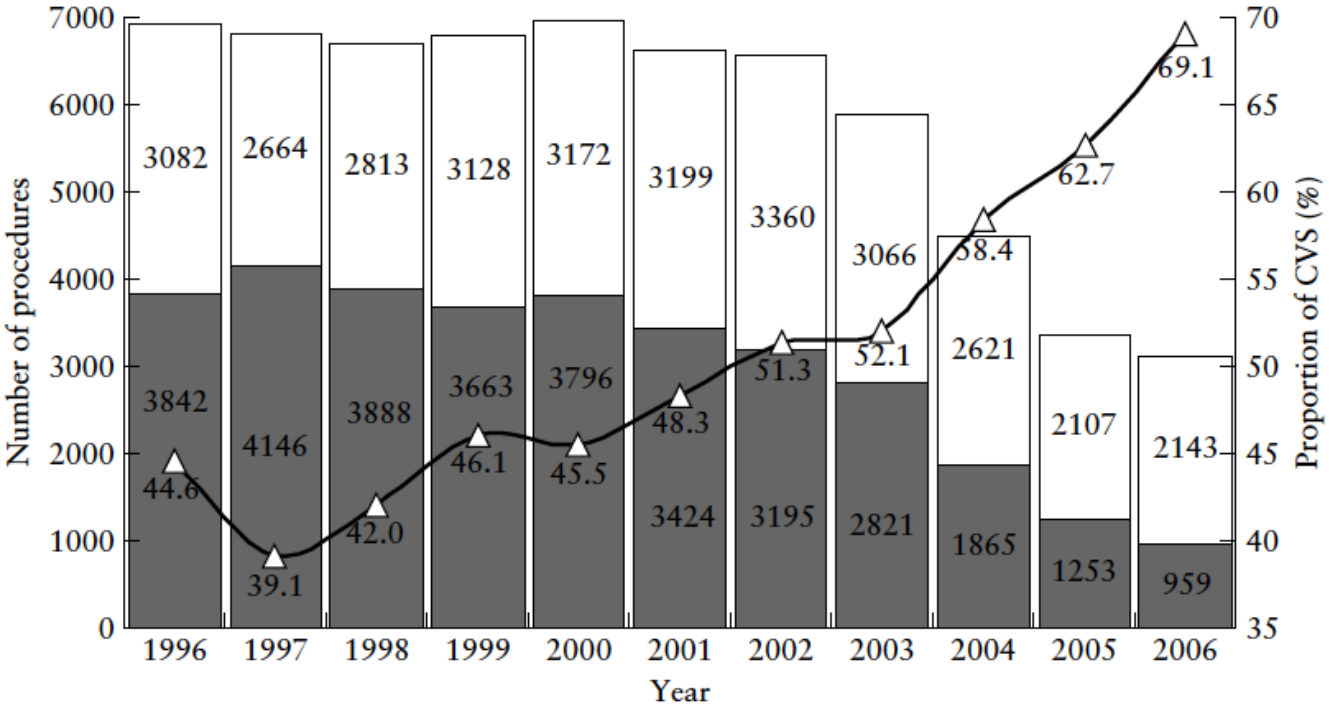

Figure 1 Number of amniocenteses (■) and chorionic villus samplings (CVS; □) performed in singleton pregnancies yearly from 1996 to 2006 in Denmark, and the proportion of CVS as a percentage of all invasive tests (△).

Tabor et al., Ultrasound Obstet Gynecol 2009; 34: 19–24

Table 1 Distribution of gestational age at the time of amniocentesis and transabdominal chorionic villus sampling in Denmark in the period 1996–2006

Time period	*Amniocentesis*					*Chorionic villus sampling*			
	< 15 weeks	*15–16 weeks*	*17–18 weeks*	*> 18 weeks*	*Total*	*< 9 weeks*	*9–10 weeks*	*≥ 11 weeks*	*Total*
1996–1998	3277 (27.6)	6110 (51.4)	1846 (15.5)	643 (5.4)	11 876	43 (0.5)	4355 (50.9)	4161 (48.6)	8559
1999–2001	2890 (26.6)	5739 (52.7)	1586 (14.6)	668 (6.1)	10 883	32 (0.3)	4107 (43.3)	5360 (56.4)	9499
2002–2004	799 (10.1)	5248 (66.6)	1201 (15.2)	633 (8.0)	7881	87 (1.0)	3293 (36.4)	5667 (62.6)	9047
2005–2006	141 (6.4)	1385 (62.6)	322 (14.6)	364 (16.5)	2212	33 (0.8)	519 (12.2)	3698 (87.0)	4250
Overall	7107 (21.6)	18 482 (56.3)	4955 (15.1)	2308 (7.0)	32 852	195 (0.6)	12 274 (39.1)	18 886 (60.2)	31 355

Data are given as *n* (% of the total for the time period).

Tabor et al., Ultrasound Obstet Gynecol 2009; 34: 19–24

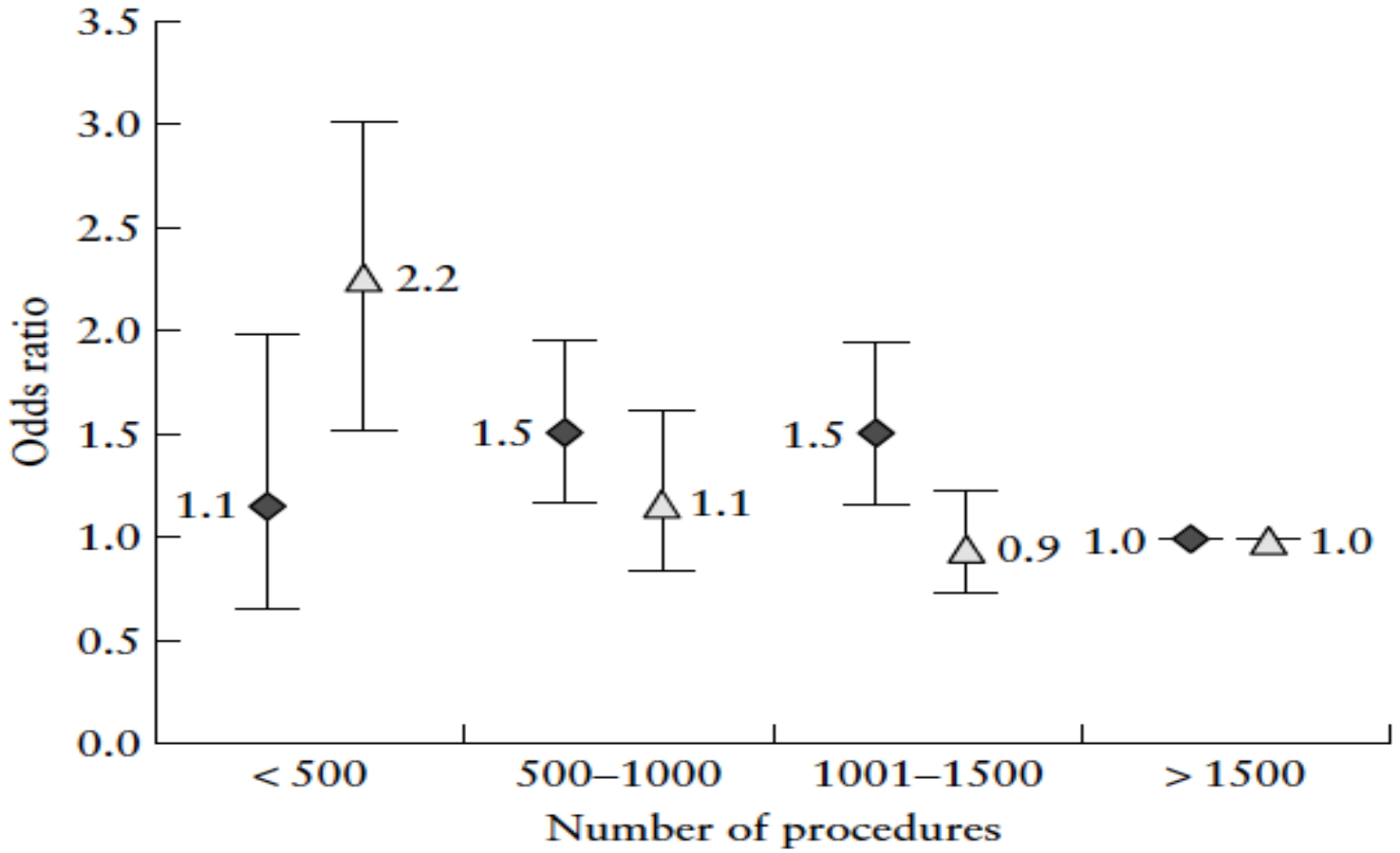

Figure 3 Postprocedural risk of fetal loss (odds ratio (OR) with 95% CI) after chorionic villus sampling (◆) and amniocentesis (△) according to number of procedures performed in the 11-year study period. Departments performing > 1500 procedures were used as a reference group, and their OR set at 1.

Tabor et al., Ultrasound Obstet Gynecol 2009; 34: 19–24

Long Term Follow-up for CVS and AC

Table 2—Long-term follow-up of the study population (CVS) and control (AC). Values are given as *n* (%) or mean (SD)

	CVS	AC
Infants eligible for long-term follow-up	1383	1427
Lost to follow-up	149	225
Total infants in follow-up*	1234 (89.2)	1202 (84.2)
Death in infancy	5	2
Complete assessment by questionnaire	1229	1200
Infant age at follow-up (years)	4.2 (1.8)	4.5 (1.6)
Admission to neonatal department†	185 (15.1)	191 (15.9)
Preterm delivery/SGA	74 (6.0)	75 (6.3)
Admission to paediatric department (>1st week)†	94 (7.7)	76 (6.3)
Consultation with medical specialist†	539 (43.9)	483 (40.3)
Respiratory problems	87 (7.1)	79 (6.6)
Malformation†	88 (7.2)	76 (6.3)
Evident function complication†	25 (2.0)	24 (2.0)
Doubtful function complication†	77 (6.3)	81 (6.8)
Physical growth <p10†	124 (10.1)	122 (10.1)

SGA, small for gestational age.
*Percentage of total number of study group.
†Percentage of completely assessed children.

Prenat Diagn 2002; 22: 598–604.

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Technique modifications for reducing the risks from amniocentesis or chorionic villus sampling (Review)

Mujezinovic F, Alfirevic Z

- For amniocentesis three interventions were evaluated - intramuscular progesterone, hexoprenaline and selecting high or low puncture sites for late 'blind' procedure - each intervention in a single small study. There was no conclusive evidence of benefit for any of them.
- The same applies for terbutaline tocolysis and use of continuous vacuum aspiration during CVS.

Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD008678