



Risk of adverse obstetric outcome after early pregnancy complications

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FIRST TRIMESTER COMPLICATIONS

- First trimester events and complications are common
- Distressing for the patient
- Fear for outcome → miscarriage?

- Clinician:
 - Confirm fetal viability
 - To reassure and to support the couple

FIRST TRIMESTER COMPLICATIONS

Are these women, who had a first trimester complication, at risk of obstetric and perinatal complications in the subsequent or ongoing pregnancy?

LITERATURE REVIEW

1st trimester events

Miscarriage

Recurrent miscarriage

Termination of pregnancy

1st trimester complications

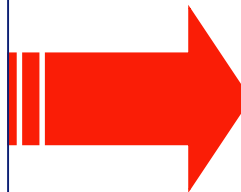
Threatened miscarriage

Intrauterine hematoma

CRL- discrepancy

Vanishing twin

Hyperemesis gravidarum



Placental related disorders

Preeclampsia

Placental abruption

SGA $p < 10^{\text{th}}$ and $p < 5^{\text{th}}$

Obstetric outcome

PPROM

Preterm delivery < 37 weeks

Preterm delivery < 34 weeks

Perinatal Outcome

Congenital malformation

5 min Apgar Score < 7

Fetal and neonatal death

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LITERATURE REVIEW

- Pubmed 1980-2009
- Using combinations of MeSH terms for each specific association
- Using 'umbrella' approach (pregnancy outcome, etiology, risk factors)
- Reference lists were searched by hand

- Excluded: non-English, without a control group or with an inappropriate control group, poorly defined obstetric and perinatal outcome

- Number of appropriate studies found: 57
- Mostly retrospective population-based, cohort and case-control studies

LITERATURE REVIEW

Predicting adverse obstetric outcome after early pregnancy events and complications: a review

Human Reproduction Update, Vol.15, No.4 pp. 409–421, 2009

R.H.F. van Oppenraaij¹, E. Jauniaux², O.B. Christiansen³,
J.A. Horcajadas⁴, R.G. Farquharson⁵ and N. Exalto^{1,6}, on behalf
of the ESHRE Special Interest Group for Early Pregnancy (SIGEP)

- Odds Ratio (OR) and Standard Error (SE) were used for analysis
- Meta-analyse: Random effects model
- MIX 1.7^{1,2}



1 Bax et al., 2006; 2 Bax et al., 2008

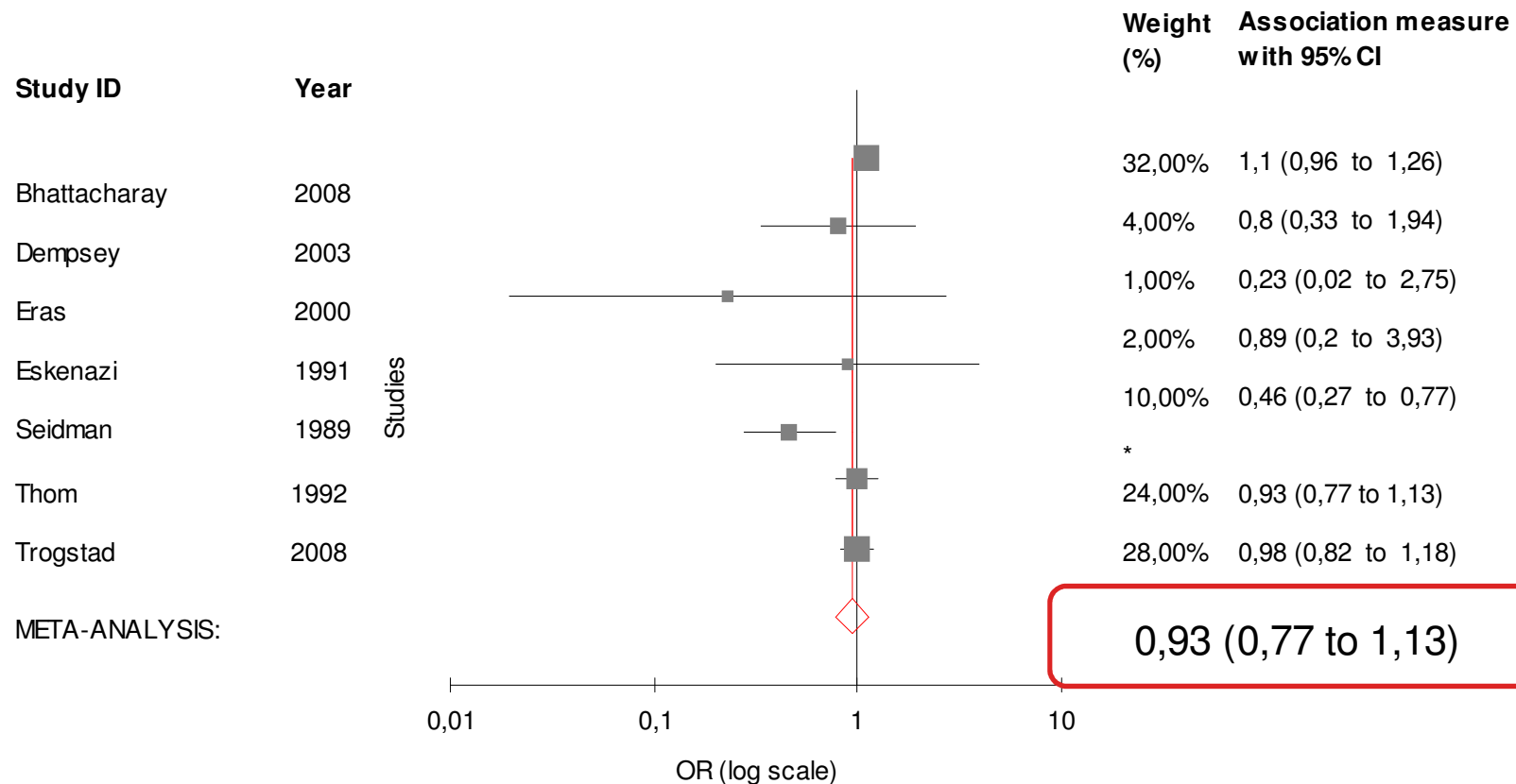
PREVIOUS MISCARRIAGE(S)

Risk of adverse obstetric outcome in the subsequent pregnancy

- At least controlled for: parity and age
- Single miscarriage - 20 studies
- Two or more miscarriages - 14 studies
- Three or more miscarriages - 5 studies



SINGLE PREVIOUS MISCARRIAGE & PREECLAMPSIA



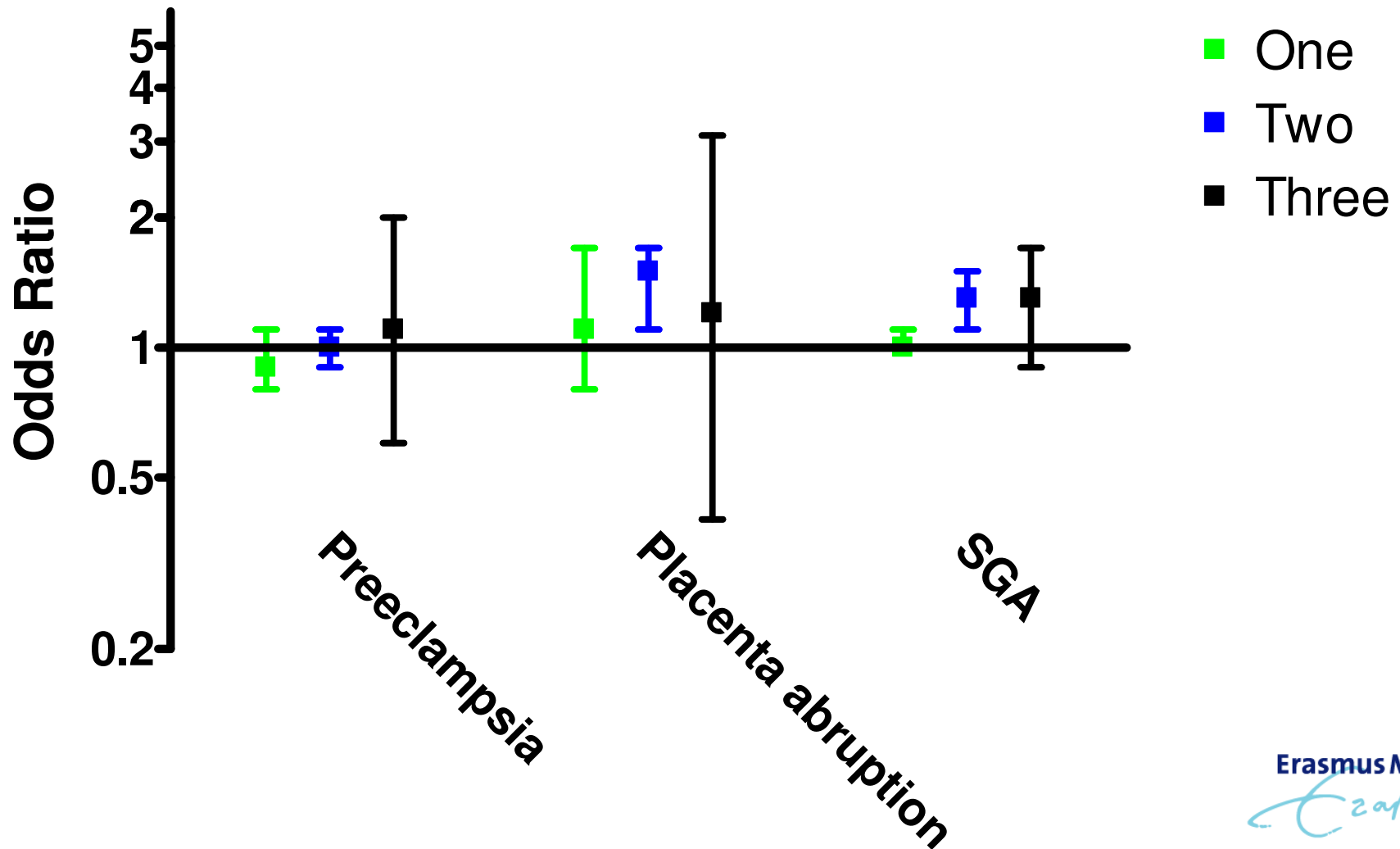
Studies controlled for: age, BMI, parity and smoking

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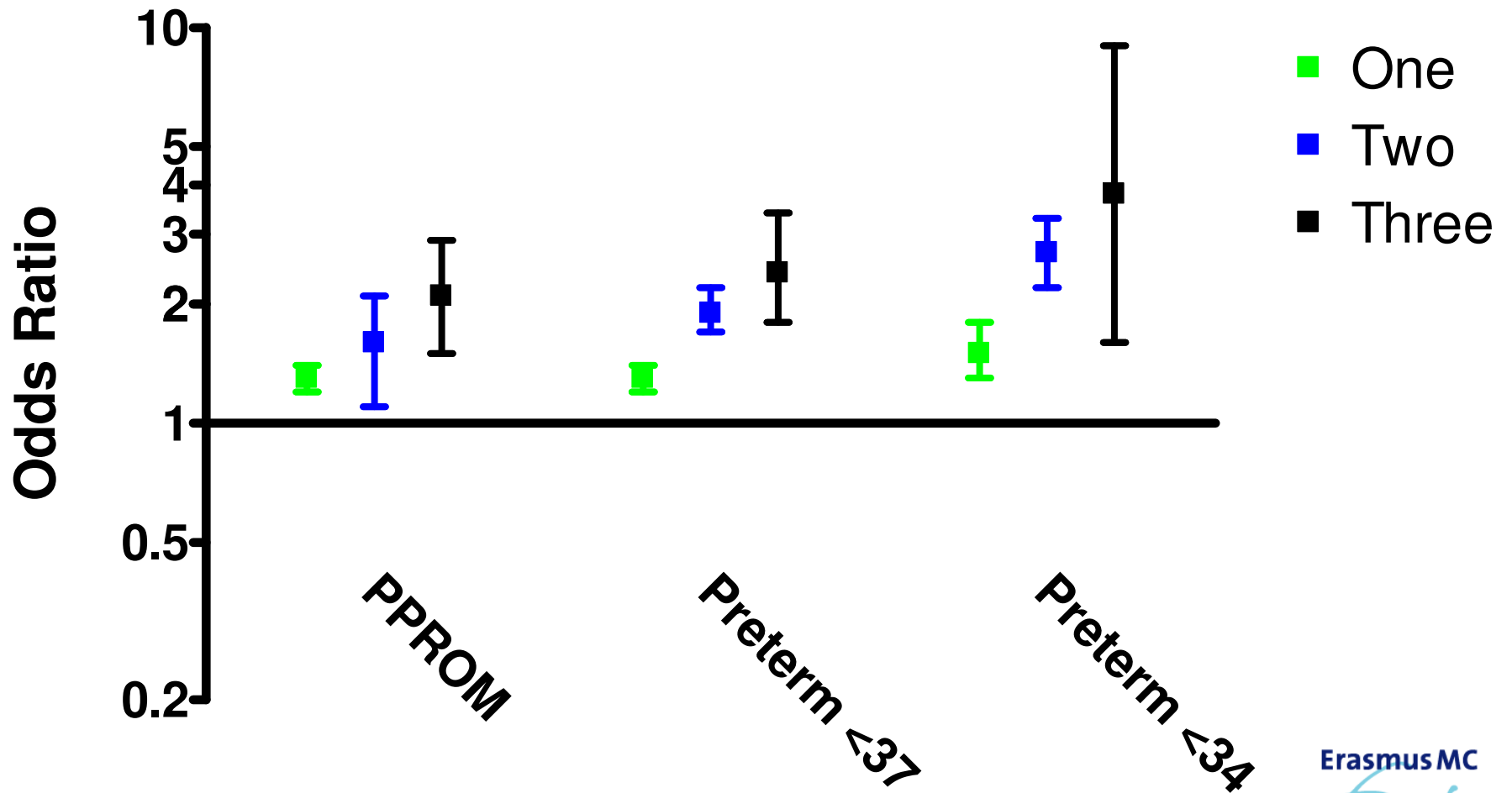


PREVIOUS MISCARRIAGE(S) & PLACENTAL DISORDERS



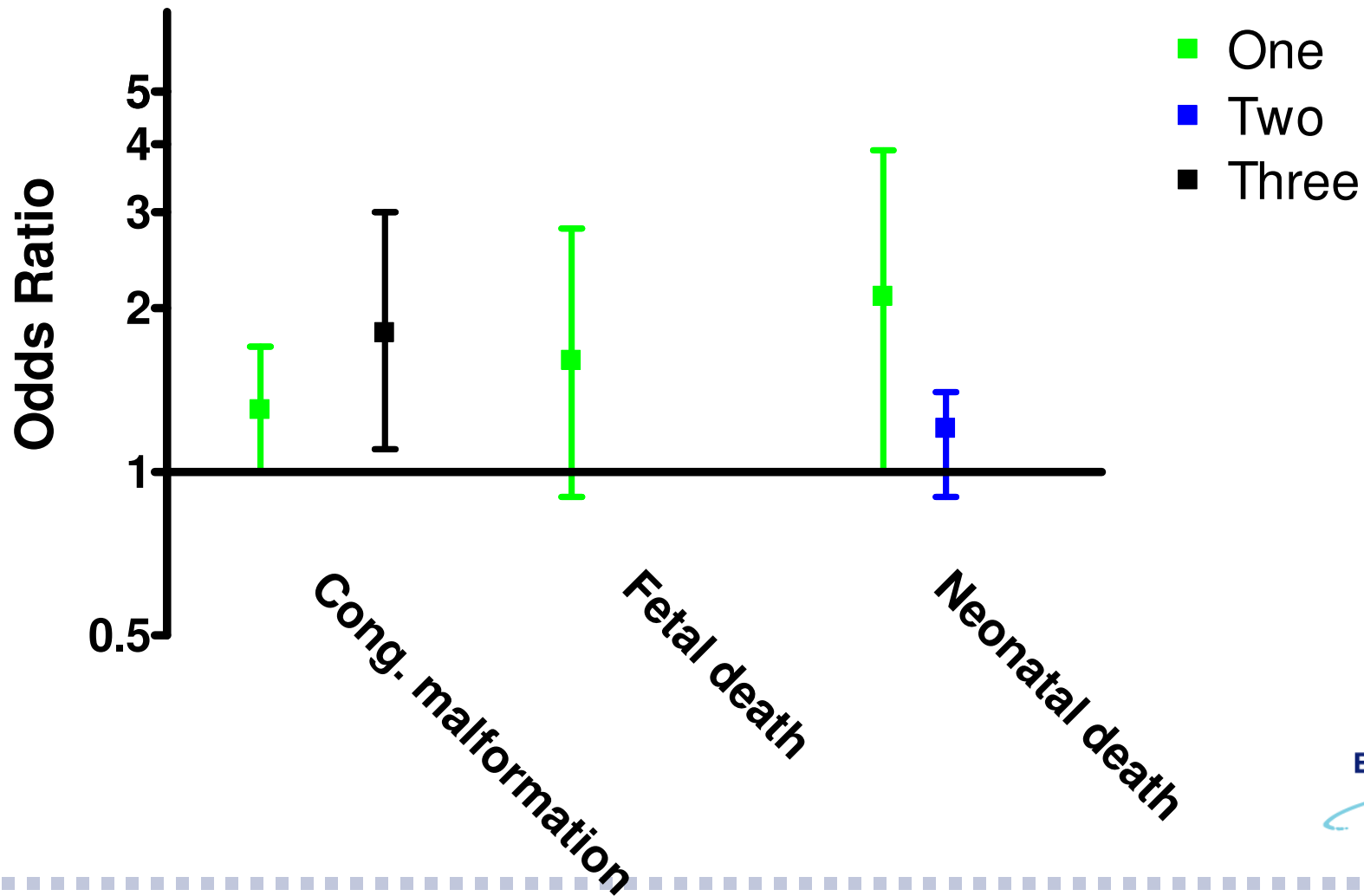


PREVIOUS MISCARRIAGE(S) & OBSTETRIC OUTCOME





PREVIOUS MISCARRIAGE(S) & PERINATAL OUTCOME



MISCARRIAGE(S) & ADVERSE OUTCOME: ETIOLOGY



- Short interpregnancy interval
 - Inadequate time to recover results in depletion of maternal nutrients¹
 - Previous term delivery → increased risk of preterm delivery²
 - Stratification of interpregnancy interval after miscarriage: no association³
- Treatment modality
 - MIST-trial: no difference in infection and live birth rate^{4,5}
 - No good studies on treatment modality and specific adverse obstetric outcome

1 Winkvist, 1992; 2 Conde-Agudelo, 2006; 3 Buchmayer, 2004; 4 Smith, 2009; 5 Trinder, 2006

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MISCARRIAGE(S) & ADVERSE OUTCOME: ETIOLOGY



- Shared risk factors for recurrent miscarriage and obstetric complications
 - Thrombophilia disorders
 - Maternal immunological or hormonal abnormalities
 - Chromosomal abnormalities
 - Infection
 - Incompetent cervix
 - Uterine abnormalities
- Only one study made a differentiation in underlying causes¹
 - Too small to permit correct analysis

PREVIOUS TERMINATION(S) OF PREGNANCY

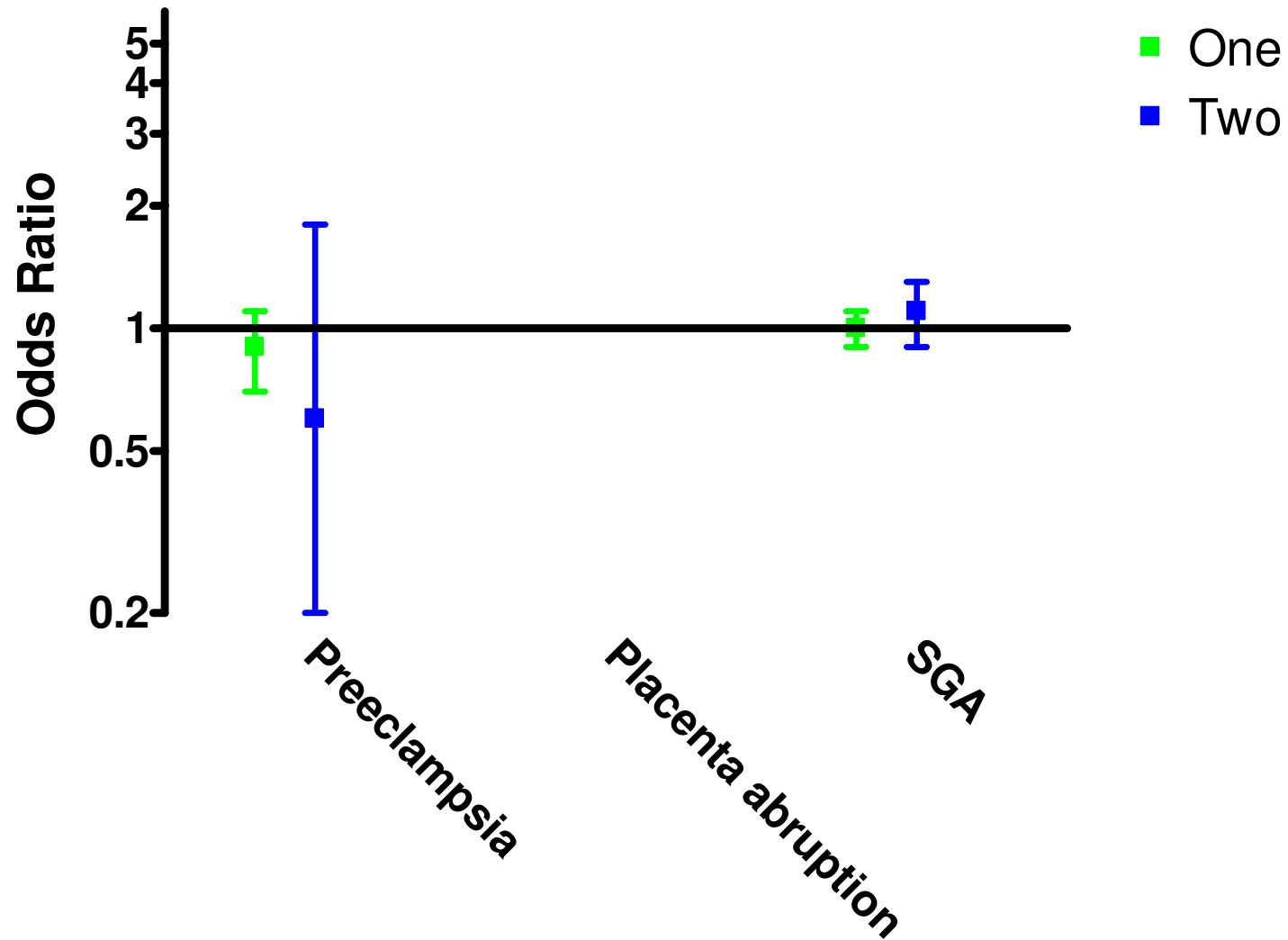
Risk of adverse obstetric outcome in the
subsequent pregnancy

At least controlled for: parity, age, ethnicity, socio-economics, BMI and smoking

- Single TOP - 18 studies
- Two or more TOP - 17 studies

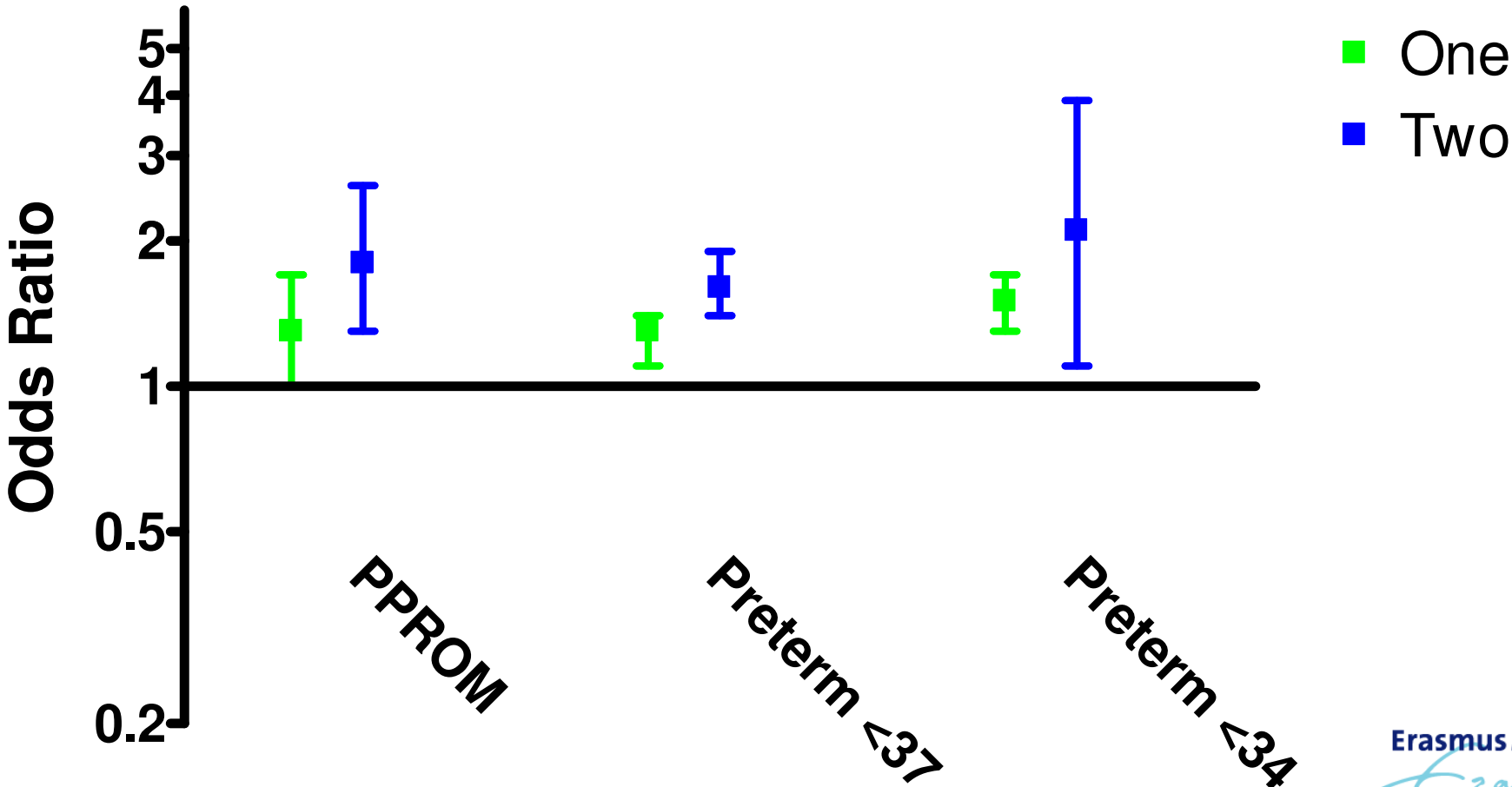


PREVIOUS TOP & PLACENTAL DISORDERS



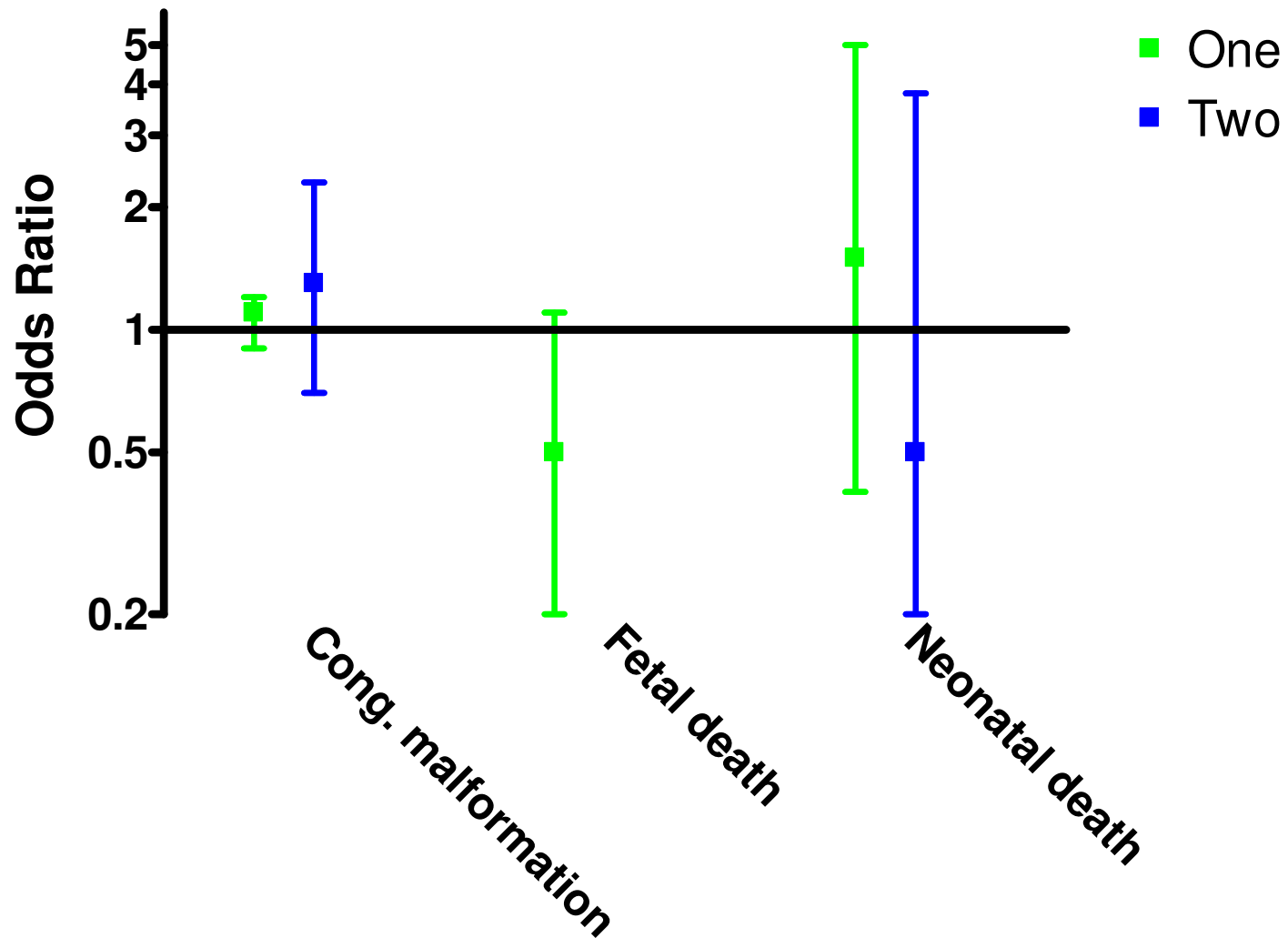


PREVIOUS TOP & OBSTETRIC OUTCOME





PREVIOUS TOP & PERINATAL OUTCOME





TOP & ADVERSE OUTCOME: ETIOLOGY

- Short or long interpregnancy interval
 - Stratification of interpregnancy interval after TOP¹: no association
- Treatment modality
 - No good studies
- Timing of TOP
 - No good studies
- Complicated TOP
 - cervical damage, infection, tissue retention, adhesions

1 Zhou, 2003;



THREATENED MISCARRIAGE

- Incidence 14-20%^{1,2}
- ~50% miscarriage¹⁻³ → confirmation of viability → 2-14% miscarriage³⁻⁵

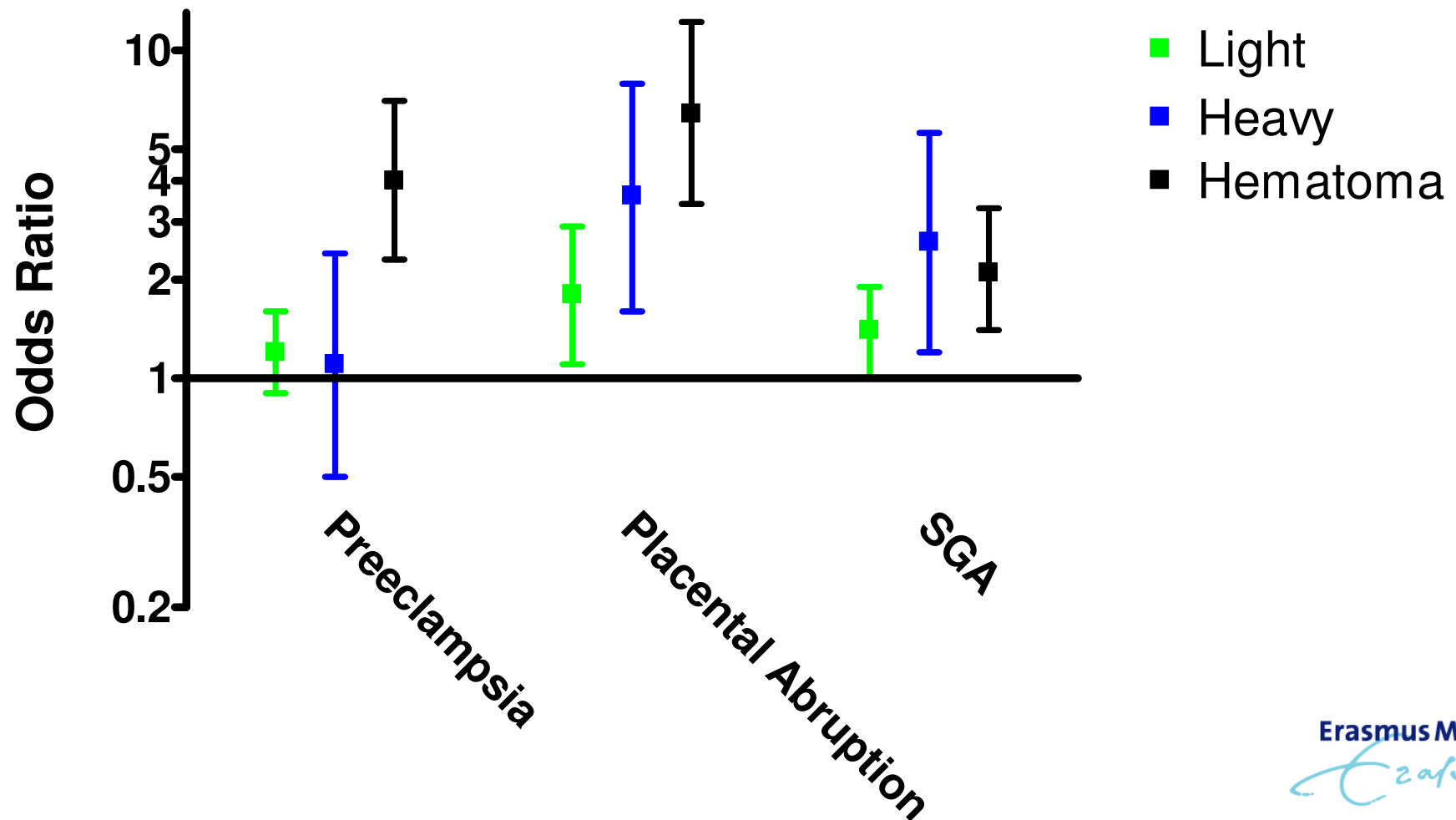
Risk of adverse obstetric outcome in the ongoing pregnancy

- At least controlled for age and parity in studies of blood loss
- (Light) blood loss - 9 studies
- Heavy blood loss - 3 studies
- Intrauterine hematoma - 4 studies

1 Everett 1997; 2 Weiss et al., 2004; 3 Wijesiriwardana et al., 2006; 4 Johns et al., 2006; 5 Schauburger et al., 2005

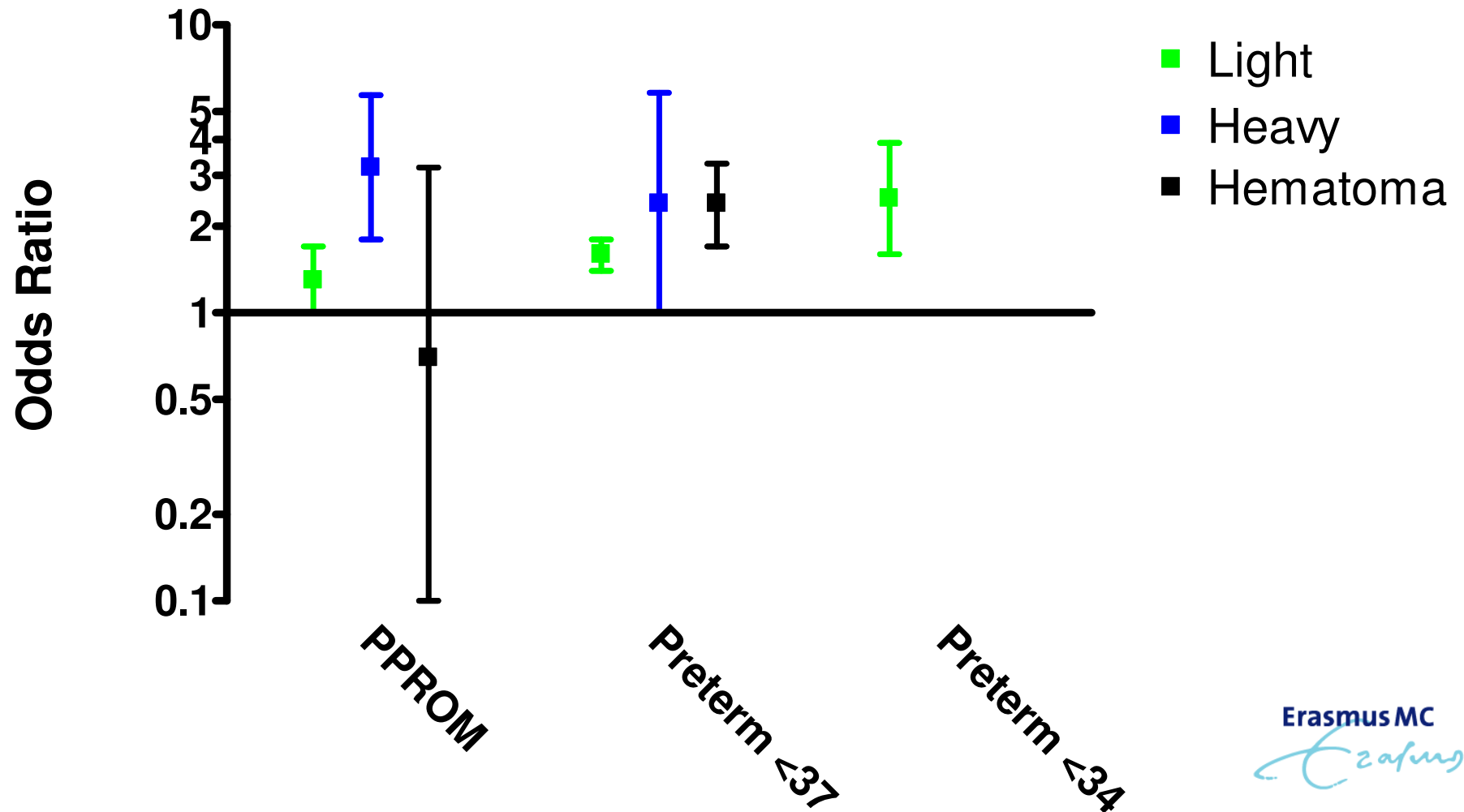


THREATENED MISCARRIAGE & PLACENTAL DISORDERS



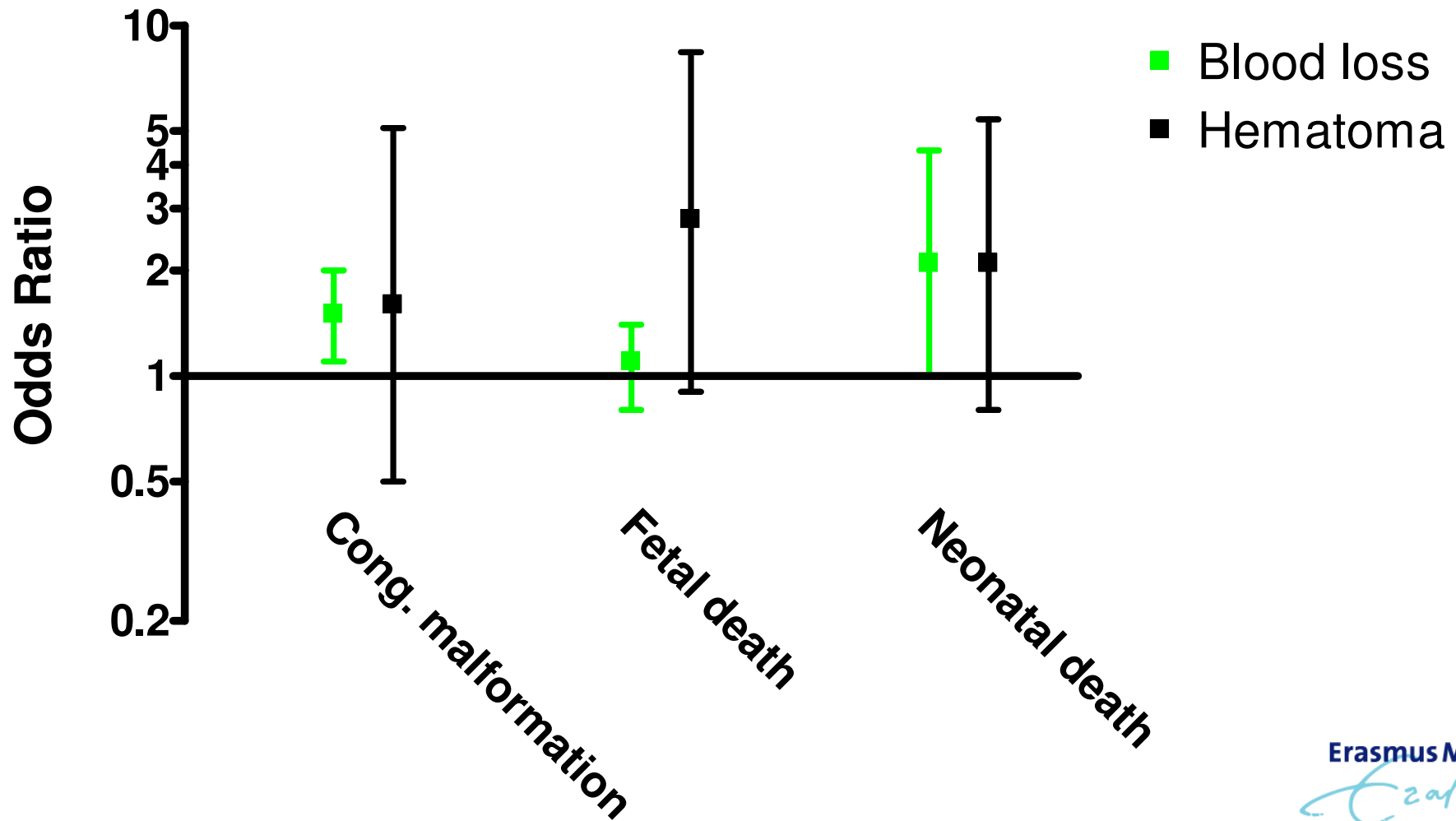


THREATENED MISCARRIAGE & OBSTETRIC OUTCOME





THREATENED MISCARRIAGE & PERINATAL OUTCOME



THREATENED MISCARRIAGE & ADVERSE OUTCOME: ETIOLOGY



- Could be the result of an impaired placentation
 - At risk for adverse obstetric outcome
 - Congenital malformation
- Could cause disruption of the chorionic-amniotic plane^{1,2,3}
 - Rupture of membrane
 - Chronic inflammatory reaction → stimulate contractions
 - Nidus for infection
- Could lead to placental insufficiency secondary to scarring⁴
 - SGA, preeclampsia and placental abruption

1 Johns and Jauniaux 2006; 2 Weiss, 2003; 3 Wijesiriwardana, 2006; 4 Williams, 1991



CRL DISCREPANCY

- If measured Crown-Rump Length (CRL) is smaller than expected (2-6 days)
- Associated with higher risk of miscarriage¹
- Associated with aneuploidy²⁻⁶

1 Reljic 2001; 2 Kuhn et al., 1995; 3 Schermer et al., 1997; 4 Bahado-Sing et al., 1997; 5 Falcon et al., 2005; 6 Goldstein et al., 1996;



CRL DISCREPANCY & OUTCOME

Obstetric outcome	CRL discrepancy	N
Preeclampsia	no data	0
Placental abruption	no data	0
PPROM	no data	0
Preterm delivery <37 weeks	1.0 (0.7-1.5)	1
Very preterm delivery <34 weeks	2.0 (1.1-4.0)	1
Perinatal outcome		
Intrauterine growth restriction <5 th	2.8 (1.9-4.3)	1
Small for gestational age <10 th	1.1 (1.0-1.2)	1
Congenital malformation	no data	0
Low 5-minute Apgar score	no data	0
Intrauterine fetal death	no data	0
Perinatal death	0.8 (0.2-3.3)	1

Data are reported as Odds Ratio (OR) with 95% Confidence Interval

CRL discrepancy: Dating issue or very early growth restriction?

VANISHING TWIN PHENOMENON

Spontaneous reduction of a
multiple pregnancy

Incidence 10-30%¹⁻³

IVF-population

1 Dickey et al., 2002; 2 Landy and Keith 1998; 3 Pinborg et al., 2005

Picture: The Gloaming



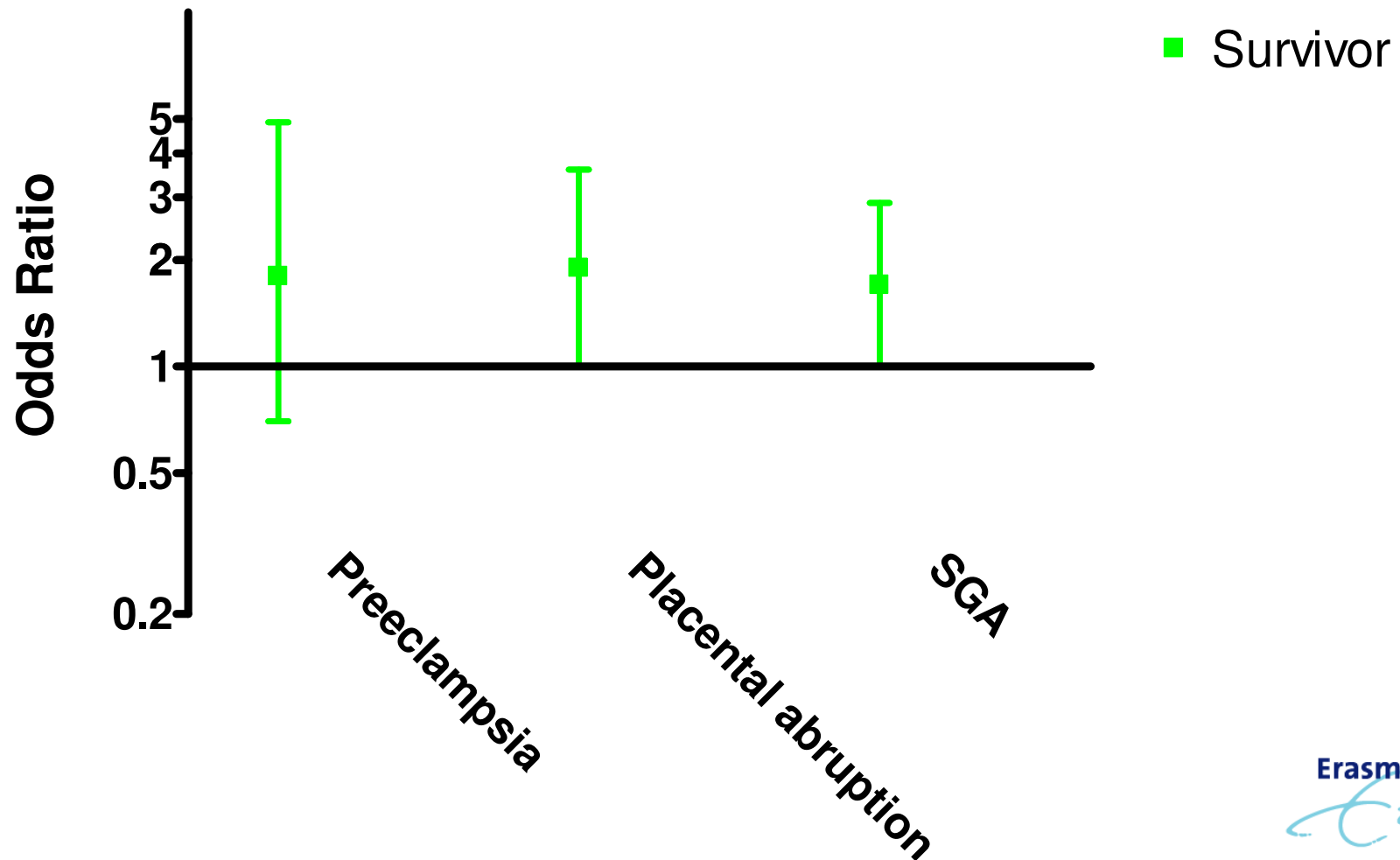
VANISHING TWIN PHENOMENON

Survivors of vanishing twin IVF pregnancies, which were spontaneously reduced from twin to singleton pregnancies, were compared with singleton IVF pregnancies

- Vanishing twin - 7 studies
- Only one study controlled for: age, ICSI vs. IVF and parity¹

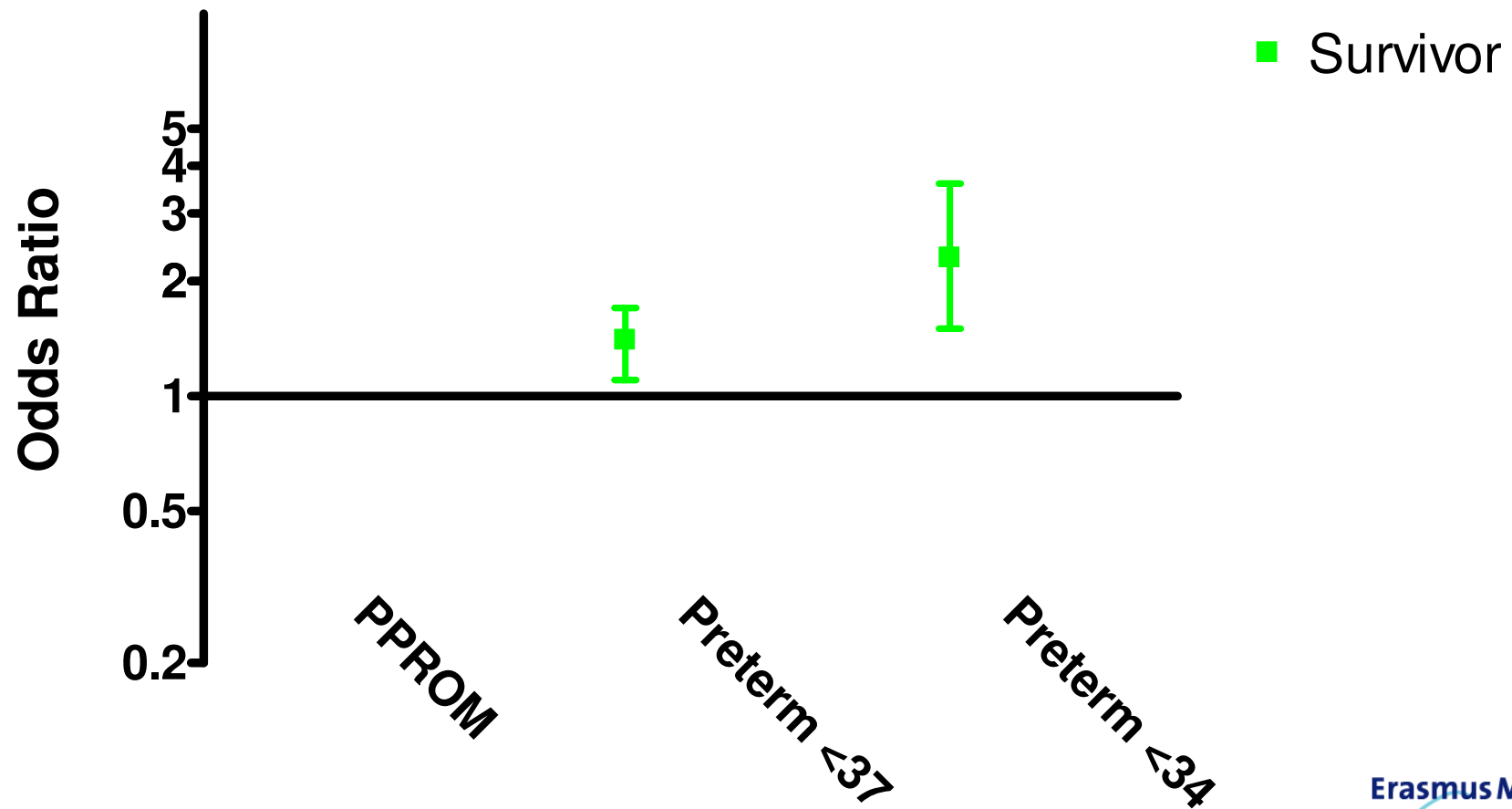


VANISHING TWIN & PLACENTAL DISORDERS



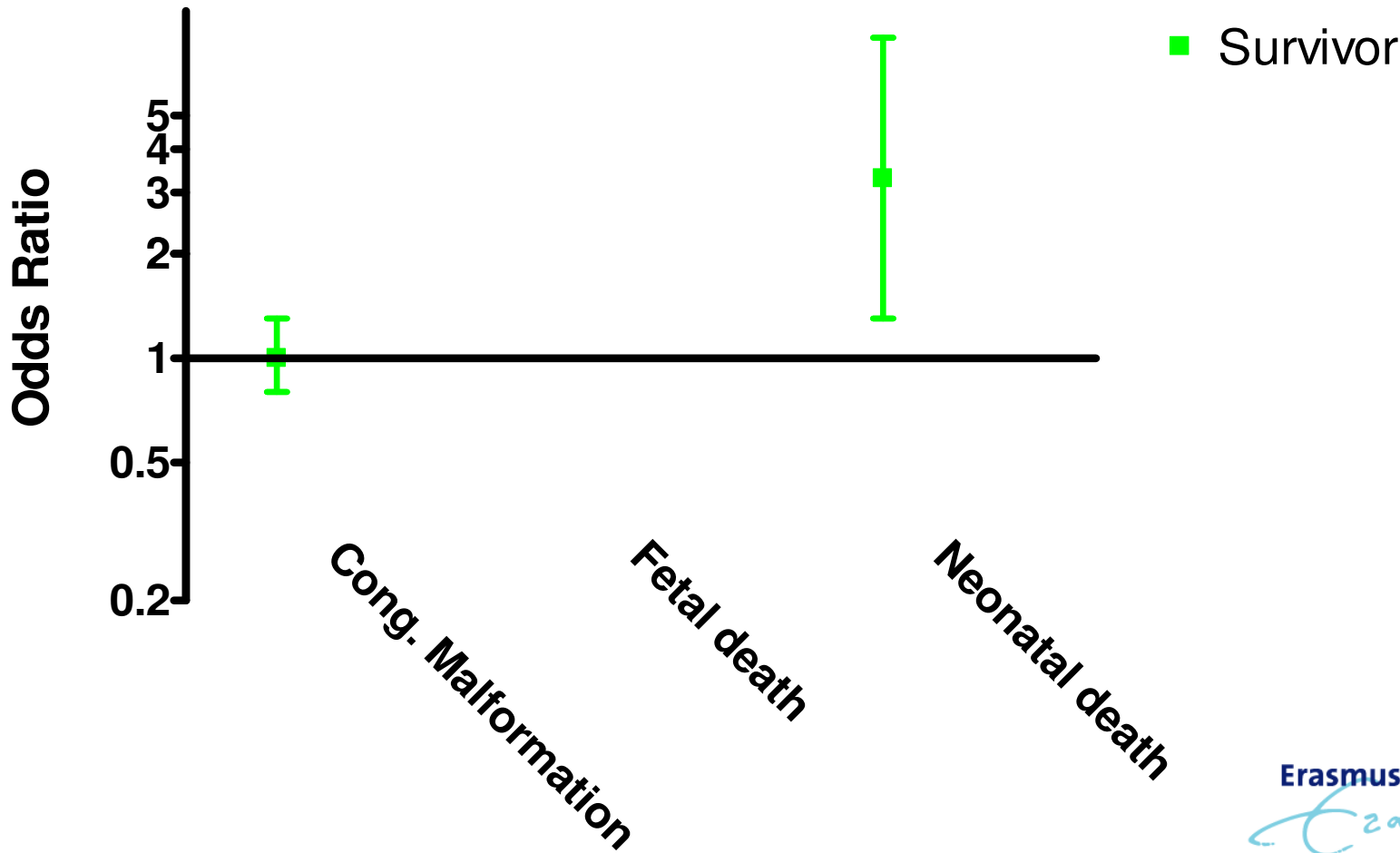


VANISHING TWIN & OBSTETRIC OUTCOME





VANISHING TWIN & PERINATAL OUTCOME



VANISHING TWIN & ADVERSE OUTCOME: ETIOLOGY



- Implantation crowding
 - Could result in unfavorable implantation site¹
- Presence of products segregated after the vanishing twin²
 - Could result in chronic inflammatory reaction
- Vanishing twin could result in blood loss
 - Independent risk factor

1 Depp, 1996; 2 Pinborg, 2007;

HYPEREMESIS GRAVIDARUM

- Incidence 0.3-1.5%
- Exact etiology unknown; therefore treatment remains symptomatic
- Decreased risk of miscarriage OR 0.3, (95% CI 0.2-0.3)¹

- Hyperemesis gravidarum

- 5 studies

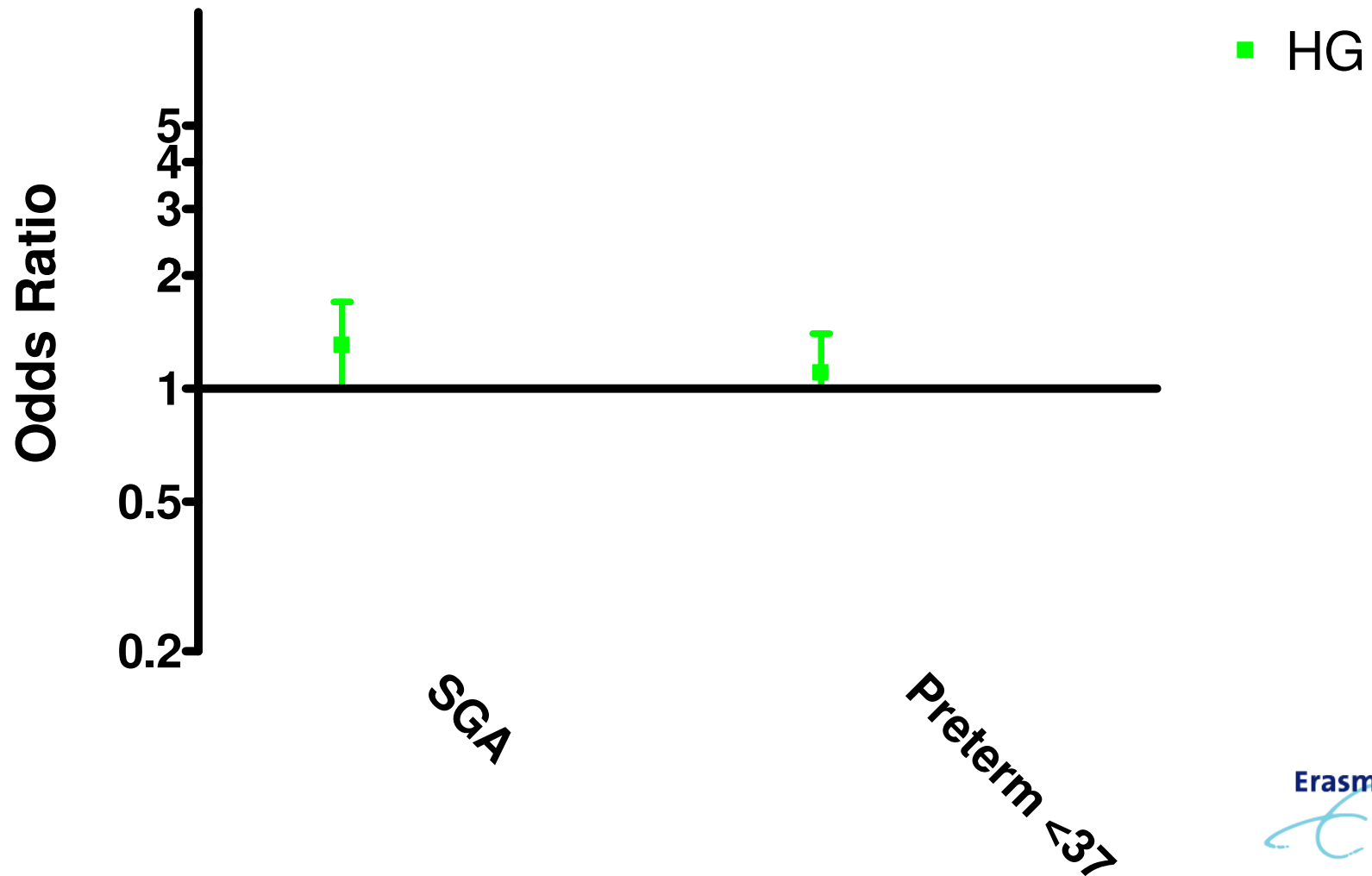
- Two studies controlled for confounders²



¹ Maconochie et al., 2007; ² Dodds et al., 2006

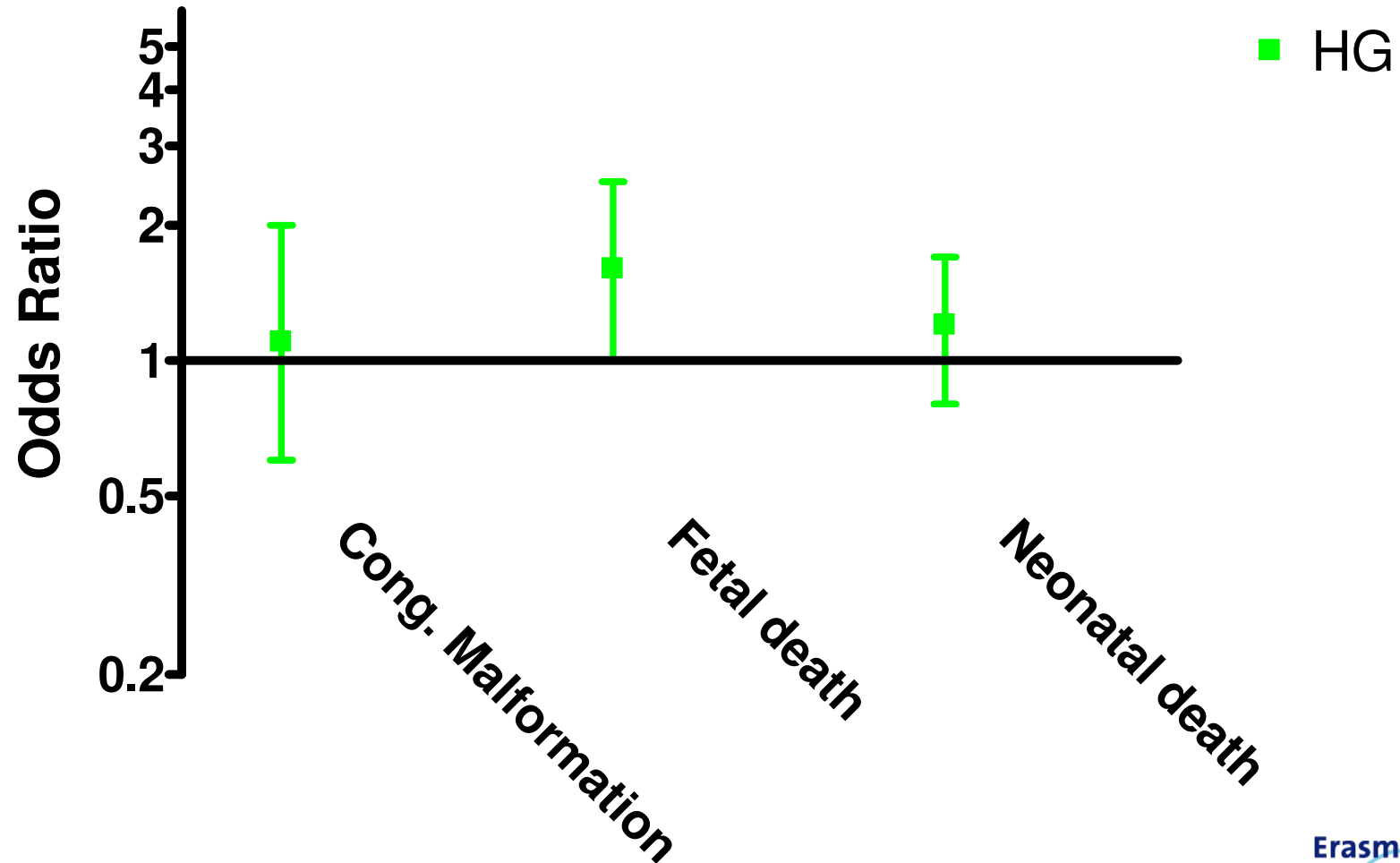


HYPEREMESIS GRAVIDARUM & OBSTETRIC OUTCOME





HYPEREMESIS GRAVIDARUM & PERINATAL OUTCOME





CONCLUSIONS

- Early pregnancy complications are independent risk factors for adverse obstetric outcome in the subsequent or ongoing pregnancy.
- The found increased risks are related to the recurrence and/ or severity of the 1st trimester complication



CLINICAL IMPLICATIONS

- Clinicians have to be vigilant
- Could lead to better risk evaluation to identify women at risk
- Questionable whether this knowledge could prevent obstetric complications to occur
- But possibly, by intensification of care the anticipated detrimental effects can be avoided or reduced

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Erasmus MC



PREVIOUS MISCARRIAGE(S) & TOP

Table I: Early pregnancy events and complications as risk factors for adverse obstetric outcome in the subsequent pregnancy.

Obstetric outcome	Previous miscarriage			Recurrent miscarriage			Termination of pregnancy			
	One	N	Two or more	N	Three or more	N	One	N	Two or more	N
PIH	1.2 (0.6-2.3)	1	2.2 (0.5-7.2)	1	no data	0	1.0 (0.6-1.8)	1	no data	0
PF	0.9 (0.8-1.1)	7	1.0 (0.9-1.1)	3	1.1 (0.6-2.0)	2	0.9 (0.7-1.1)	4	0.6 (0.2-1.8)	3
Placental Abruption	1.1 (0.8-1.7)	2	1.5 (1.1-1.7)	1	1.2 (0.4-3.1)	1	no data	0	no data	0
Placenta Previa	1.7 (0.9-3.2)	2	1.7 (1.3-2.3)	1	6.0 (1.6-22.)	1	1.0 (0.7-1.6)	1	1.4 (0.8-2.5)	1
PPROM	1.3 (1.0-1.8)	4	1.6 (1.1-2.1)	4	2.1 (1.5-2.9)	2	1.3 (1.0-1.7)	4	1.8 (1.3-2.6)	2
Preterm <37 weeks	1.3 (1.2-1.4)	13	1.9 (1.7-2.2)	11	2.4 (1.8-3.4)	5	1.3 (1.2-1.4)	12	1.6 (1.4-1.9)	10
Preterm <34 weeks	1.5 (1.3-1.8)	8	2.1 (2.2-3.3)	6	3.8 (1.6-9.0)	3	1.5 (1.3-1.7)	6	2.1 (1.1-3.9)	5
Perinatal outcome										
SGA	1.0 (1.0-1.1)	5	1.3 (1.1-1.5)	3	1.3 (0.9-1.7)	2	1.0 (0.9-1.1)	5	1.1 (0.9-1.3)	5
LBW <2500g	1.2 (1.0-1.3)	5	1.5 (0.9-2.5)	3	2.0 (1.4-2.7)	2	1.2 (1.0-1.4)	6	1.5 (1.2-1.7)	5
LBW <1500g	no data	0	no data	0	no data	0	2.7 (1.1-7.1)	1	no data	0
Cong. malformation	1.3 (1.0-1.7)	2	no data	0	1.8 (1.1-3.0)	1	1.1 (0.9-1.2)	2	1.3 (0.7-2.3)	1
5 min AS <7	1.0 (1.0-1.2)	2	1.0 (0.0-1.4)	1	0.6 (0.3-1.6)	1	1.1 (0.0-1.6)	1	0.0 (0.3-2.0)	1
Fetal death	1.6 (0.9-2.8)	1	no data	0	no data	0	0.5 (0.2-1.1)	2	no data	0
Perinatal death	2.1 (1.0-3.9)	1	1.2 (0.9-1.4)	1	no data	0	1.5 (0.4-6.1)	2	0.5 (0.1-3.8)	1

Data are reported as Odds Ratio (OR) with 95% Confidence Interval (CI)

FIRST TRIMESTER COMPLICATION

Table II: Early pregnancy events and complications as risk factors for adverse obstetric outcome in the ongoing pregnancy.

Obstetric outcome	Threatened miscarriage		Intrauterine haematoma		CRL discrepancy		Vanishing twin		Hyperemesis gravidarum	
	OR	N	OR	N	OR	N	OR	N	OR	N
Haemorrhage	1.8 (1.7-1.9)	2	no data	0	no data	0	0.9 (0.5-1.5)	1	no data	0
PIH	1.4 (1.1-1.8)	1	2.1 (1.5-2.9)	1	1.0 (0.8-1.2)	1	1.2 (0.6-2.1)	1	1.0 (0.9-1.3)	1
PE	1.2 (0.9-1.6)	2	4.0 (2.3-7.0)	1	no data	0	1.8 (0.7-4.9)	2	no data	0
Abruption	1.8 (1.1-2.9)	3	6.4 (3.4-12.2)	2	no data	0	1.9 (1.0-3.5)	1	no data	0
Placenta previa	1.5 (0.8-2.9)	3	no data	0	no data	0	1.1 (0.5-2.4)	1	no data	0
PPROM	1.3 (1.0-1.7)	3	0.7 (0.1-3.2)	1	no data	0	no data	0	no data	0
Preterm <37 weeks	1.6 (1.4-1.8)	8	2.4 (1.7-3.3)	4	1.0 (0.7-1.5)	1	1.4 (1.1-1.7)	6	1.1 (1.0-1.4)	4
Preterm <34 weeks	2.5 (1.6-3.9)	4	no data	0	2.0 (1.1-4.0)	1	2.3 (1.5-3.6)	5	no data	0
Perinatal outcome										
IUGR	no data	0	no data	0	2.8 (1.9-4.3)	1	no data	0	no data	0
SGA	1.4 (1.0-1.9)	2	2.1 (1.4-3.3)	3	1.1 (1.0-1.2)	1	1.7 (1.0-2.9)	5	1.3 (1.0-1.7)	4
LDW <2500g	1.6 (1.1-2.2)	5	no data	0	1.0 (1.2-2.3)	1	1.7 (1.3-2.2)	3	1.5 (1.3-1.7)	2
LBW <1500g	2.7 (1.4-5.2)	3	no data	0	no data	0	2.0 (1.3-3.2)	3	1.4 (1.0-2.0)	1
Cong. malformation	1.5 (1.1-2.0)	2	1.6 (0.5-5.1)	1	no data	0	1.0 (0.8-1.3)	1	1.1 (0.6-2.0)	3
5-Min Apgar score < 7	1.1 (1.0-1.3)	1	5.7 (2.5-12.7)	1	no data	0	no data	0	1.2 (0.8-1.7)	3
Fetal death	1.1 (0.8-1.4)	4	2.8 (0.9-8.4)	2	no data	0	no data	0	1.6 (1.0-2.5)	2
Perinatal death	2.1 (1.0-4.4)	4	2.1 (0.8-5.4)	2	0.8 (0.2-3.3)	1	3.3 (1.3-8.4)	1	1.2 (0.8-1.7)	4

Data are reported as Odds Ratio (OR) with 95% Confidence Interval (CI); no data, no available study

