

AALBORG SYGEHUS



Repeated biochemical pregnancy loss – definition, potential causes, prognosis and treatment

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Questions to be addressed

- What is the cause of repeated biochemical pregnancy losses?
- How do biochemical pregnancy losses affect the future pregnancy prognosis?

In theory biochemical pregnancy losses can be

- Death of embryos after implantation in the uterus before visibility by ultrasound

or

- Spontaneously resorbed ectopic pregnancies

Inclusion criteria

- Patients with at least 3 involuntary pregnancy losses before GA 22 weeks confirmed by pregnancy test, plasma hCG, ultrasound or histology after D&C
- Referred to the Danish recurrent miscarriage clinic after January 2000

Exclusion criteria

- Previous birth or stillbirth
- Incomplete pregnancy records
- Age > 42 years at referral
- Lupus anticoagulant, significant uterine abnormality or parental chromosome abnormality
- Irregular menstruations with intervals < 21 or > 35 days
- Pregnancy after IVF/ICSI/FET

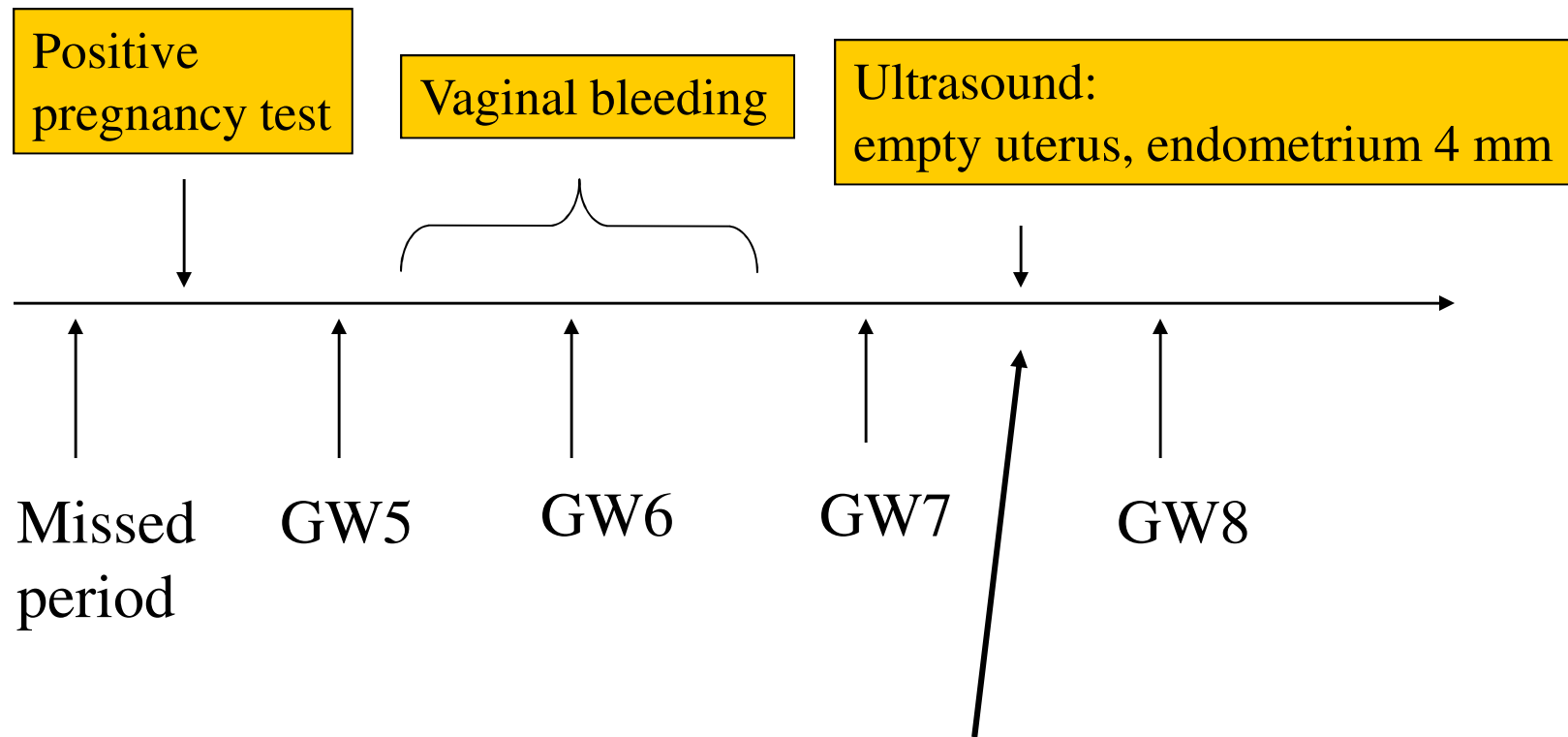
Definition 1

- Miscarriage: intrauterine pregnancy documented by ultrasound and/or histology of tissue from the uterus
- Biochemical pregnancy: loss in the first trimester without documentation of intrauterine pregnancy as above

Definition 2

- Miscarriage: 1) loss after 6th completed GW irrespective of findings by ultrasound/histology or 2) loss prior to 6th week with documentation of intrauterine pregnancy by ultrasound/histology.
- Biochemical pregnancy: loss prior to 6th completed GW with no ultrasound or histology being undertaken or ultrasound showing an empty uterus

Example: 1st pregnancy



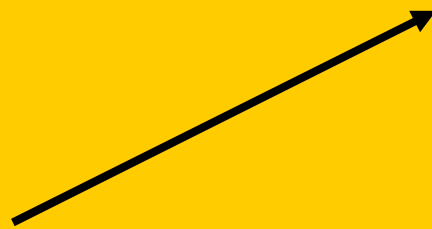
According to definition 1 this is classified as a biochemical pregnancy, according to definition 2 as a miscarriage

Types of intrauterine pregnancies in 204 RM patients

- Definition 1
- 340 biochemical pregnancies
- 469 miscarriages
- Biochemical pregnancy rate = 42.0%

- Definition 2
- 264 biochemical pregnancies
- 545 miscarriages
- Biochemical pregnancy rate = 32.6%

- A possible association between repeated biochemical pregnancies and biomarkers linked to recurrent miscarriage emphasises the belief that repeated biochemical pregnancies are indeed very early deaths of intrauterine pregnancies

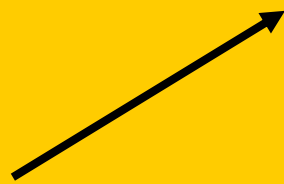


Not addressed in this presentation

Questions to be addressed

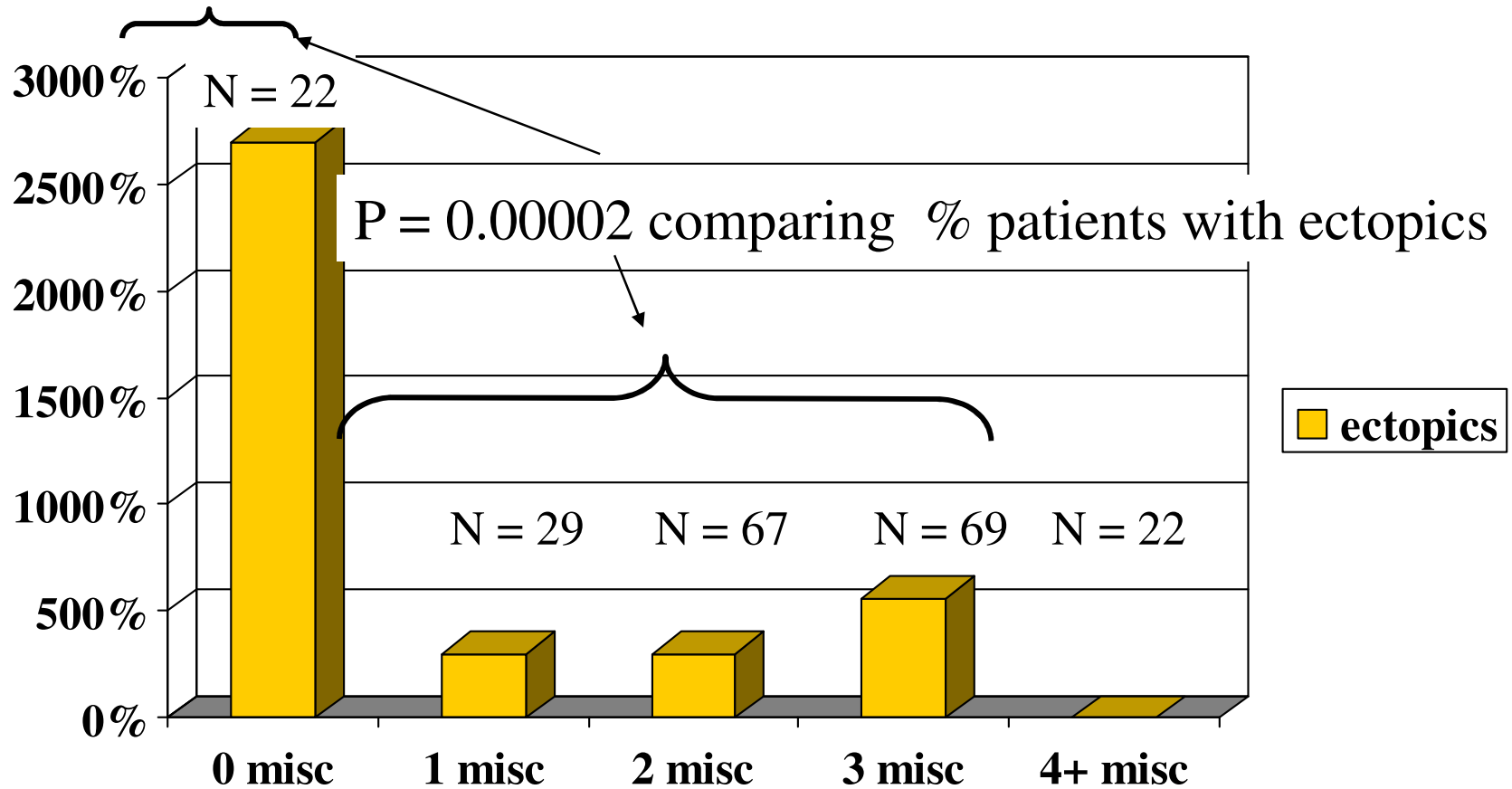
- **What is the cause of repeated biochemical pregnancy losses?**
- How do biochemical pregnancy losses affect the future pregnancy prognosis?

- A possible association between repeated biochemical pregnancies and clinical ectopic pregnancies emphasises the belief that repeated biochemical pregnancies are indeed spontaneously resorbed ectopic pregnancies



Addressed in this presentation

Confirmed ectopics in groups of recurrent miscarriage patients according to no. of prior biochemical pregnancies and confirmed miscarriages (definition 1)



History of the 6 patients with only biochemical pregnancies and ectopics

Birth year	Prior PID	1st	2nd	3rd	4th	5th	6th	7th
1970	Yes	Ex*	Term	Bio	Bio	Bio		
1974	No	Bio	Bio	Bio	Bio	Ex*	Bio	
1969	No	Bio	Ex*	Bio	Bio			
1968	No	Bio	Bio	Bio	Bio	Ex*	Bio	
1978	No	Bio	Bio	Bio	Ex**	Bio	Bio	Bio
1973	No	Bio	Ex*	Bio	Bio	Bio		

* = unilat. salpingectomy; ** tubotomia

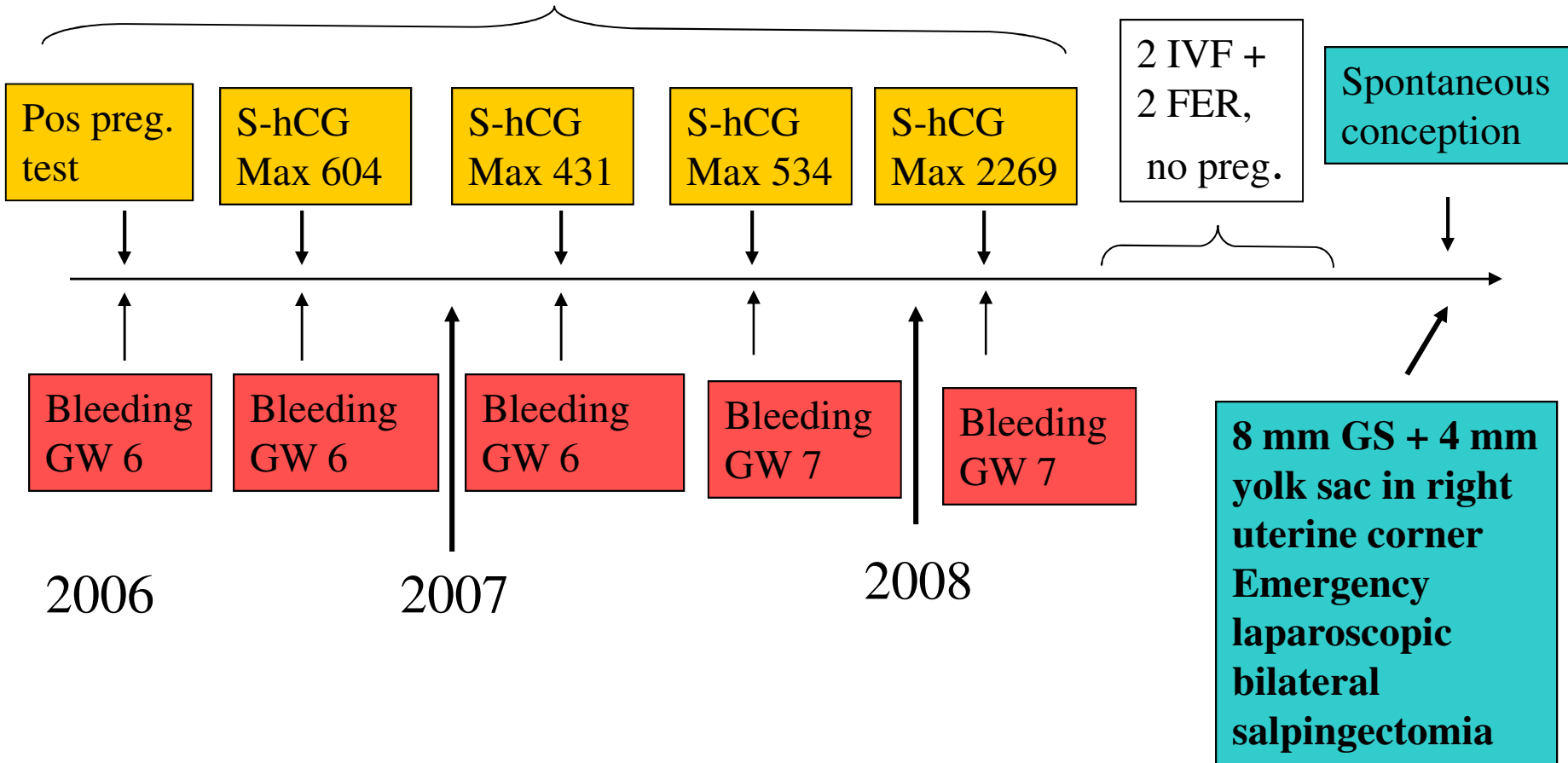
Subsequent pregnancy outcome in 22 patients with only biochemical pregnancies and ectopics

Mean age	No.	Remark	Subsequent treatment	Outcome of first subsequent pregnancy	Final outcome
32	7	1 Mb. Crohn	None/IUI	7 Live births	
34	2		None/IUI	2 Mis/bio	2 Live births
35	6		None	No pregnancy	
32	2	1 Mb Crohn	IVF	2 Live births	
34	4		IVF	4 Mis/bio	2 Live births
33	1	Severe hyperhomocysteinaemia	High dose folate	Live birth	

Cumulative live birth rate in all patients: $14/22 = 63.6\%$

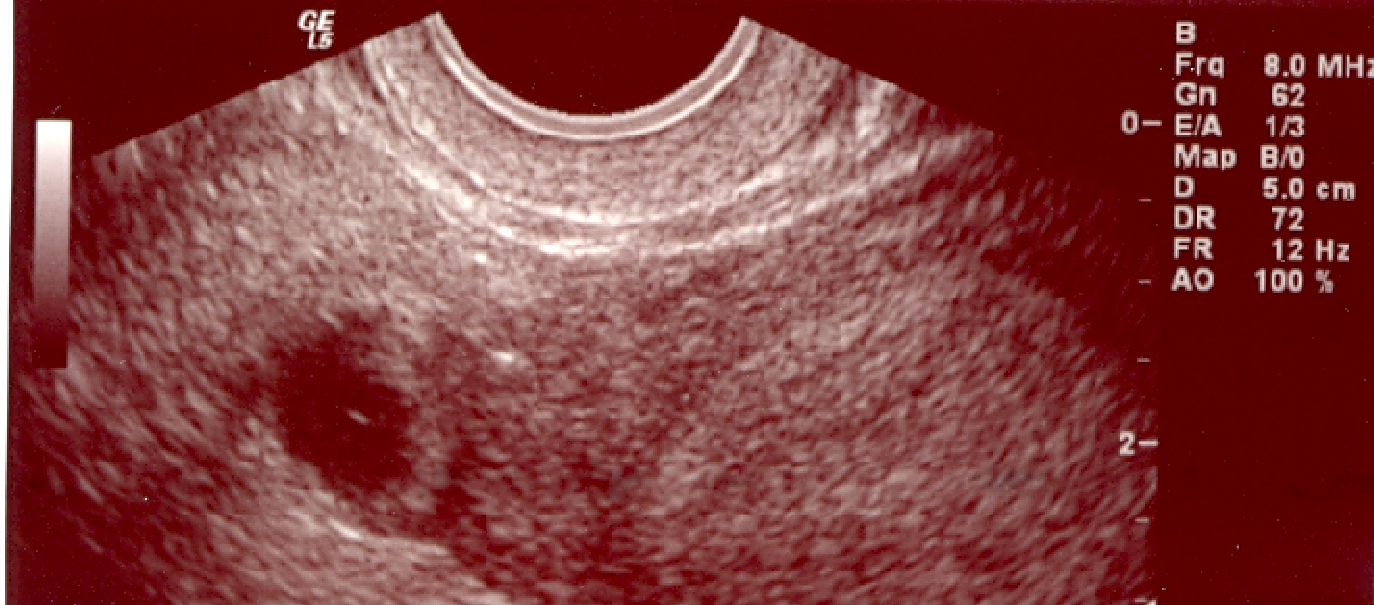
**Born in 1979, reg. cycle 30 days, BMI: 20.4, never clinical salpingitis, normal hysteroscopy, karyotypes 46XX, 46XY
Normal trombophilia screening. No autoantibodies, AMH 33 pmol/l**

Spontaneous conception

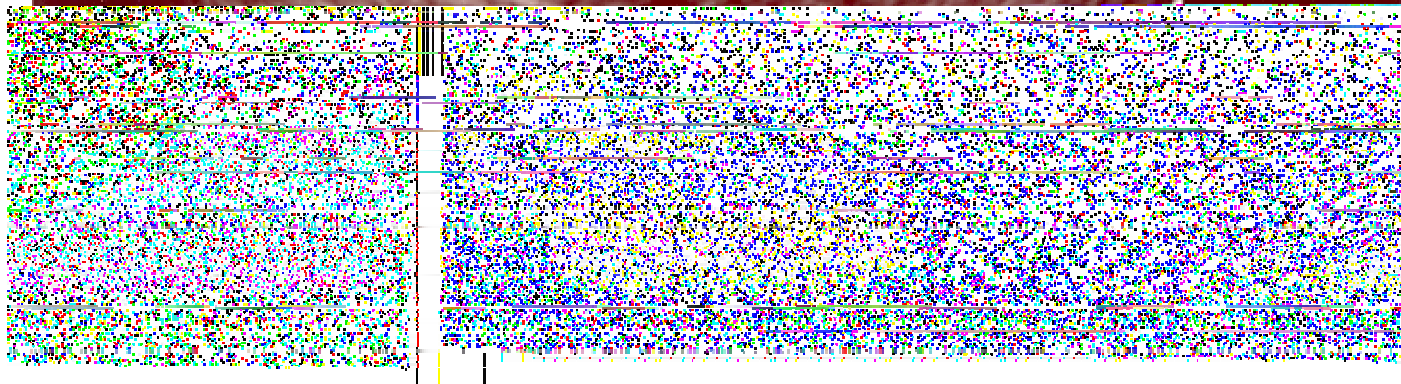


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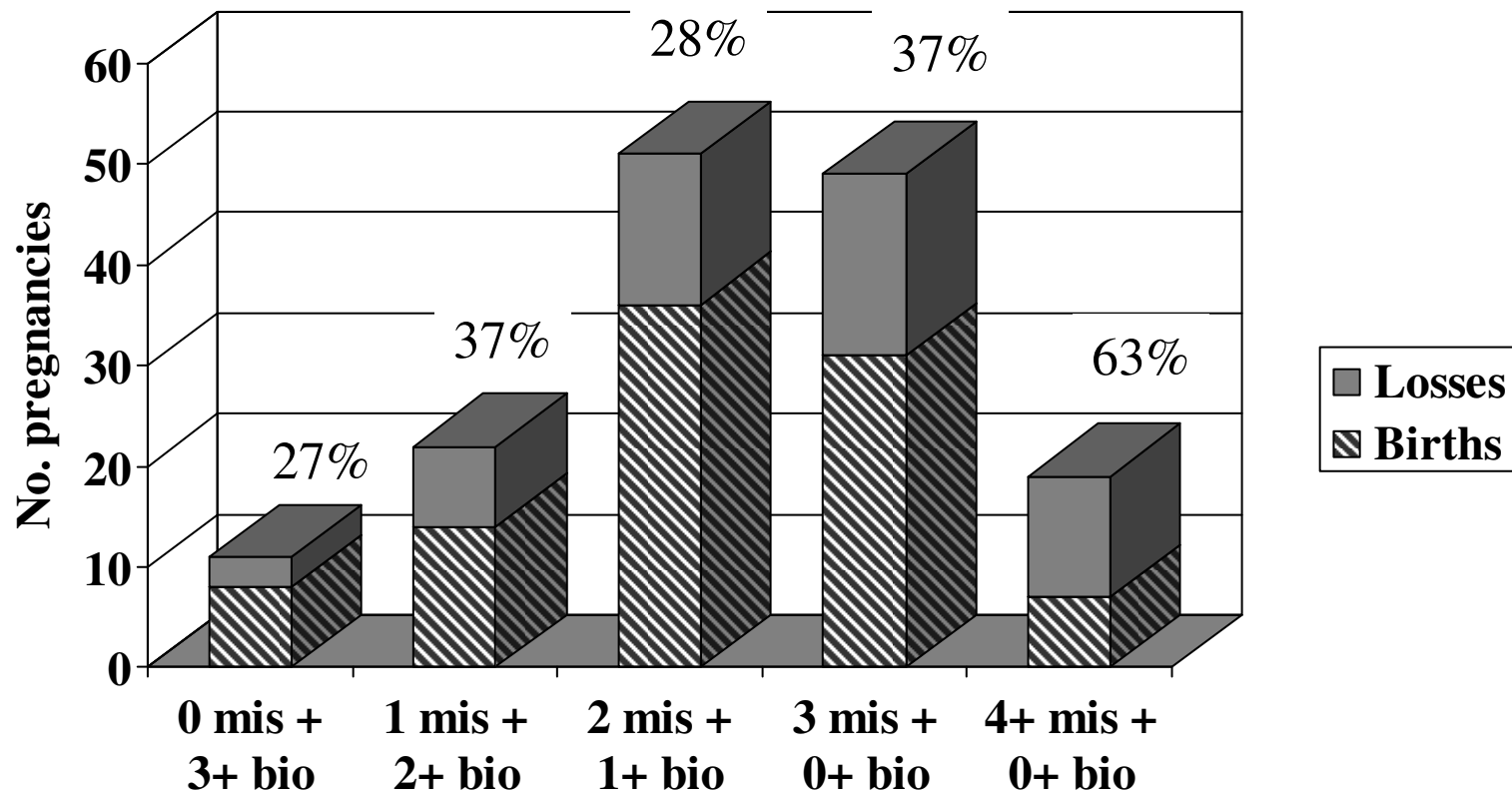


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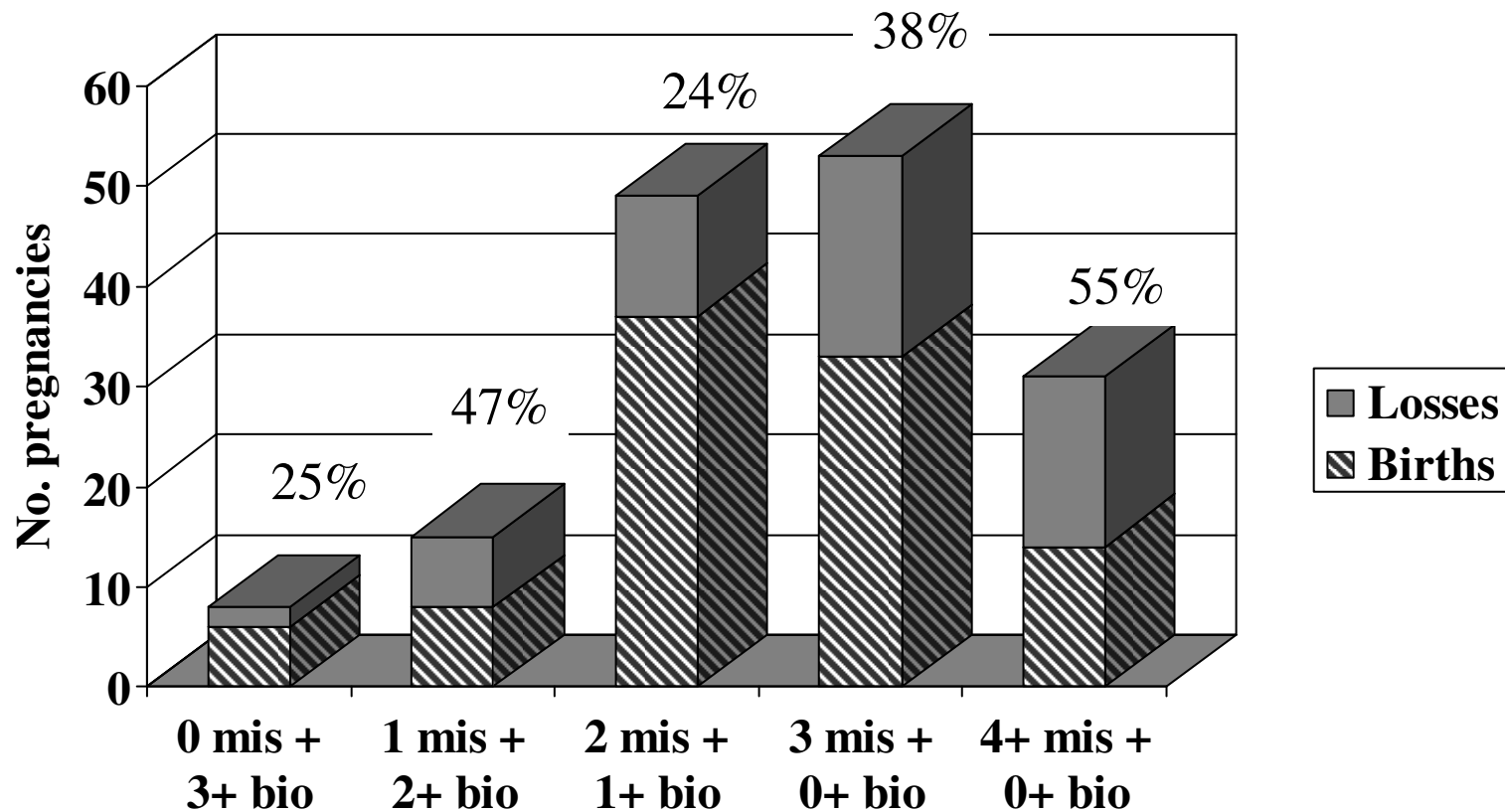
A very relevant clinical question: does the presence of biochemical pregnancies in the reproductive history affect the chance of a subsequent live birth?

Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with RM according to no. of previously confirmed miscarriages (definition 1)



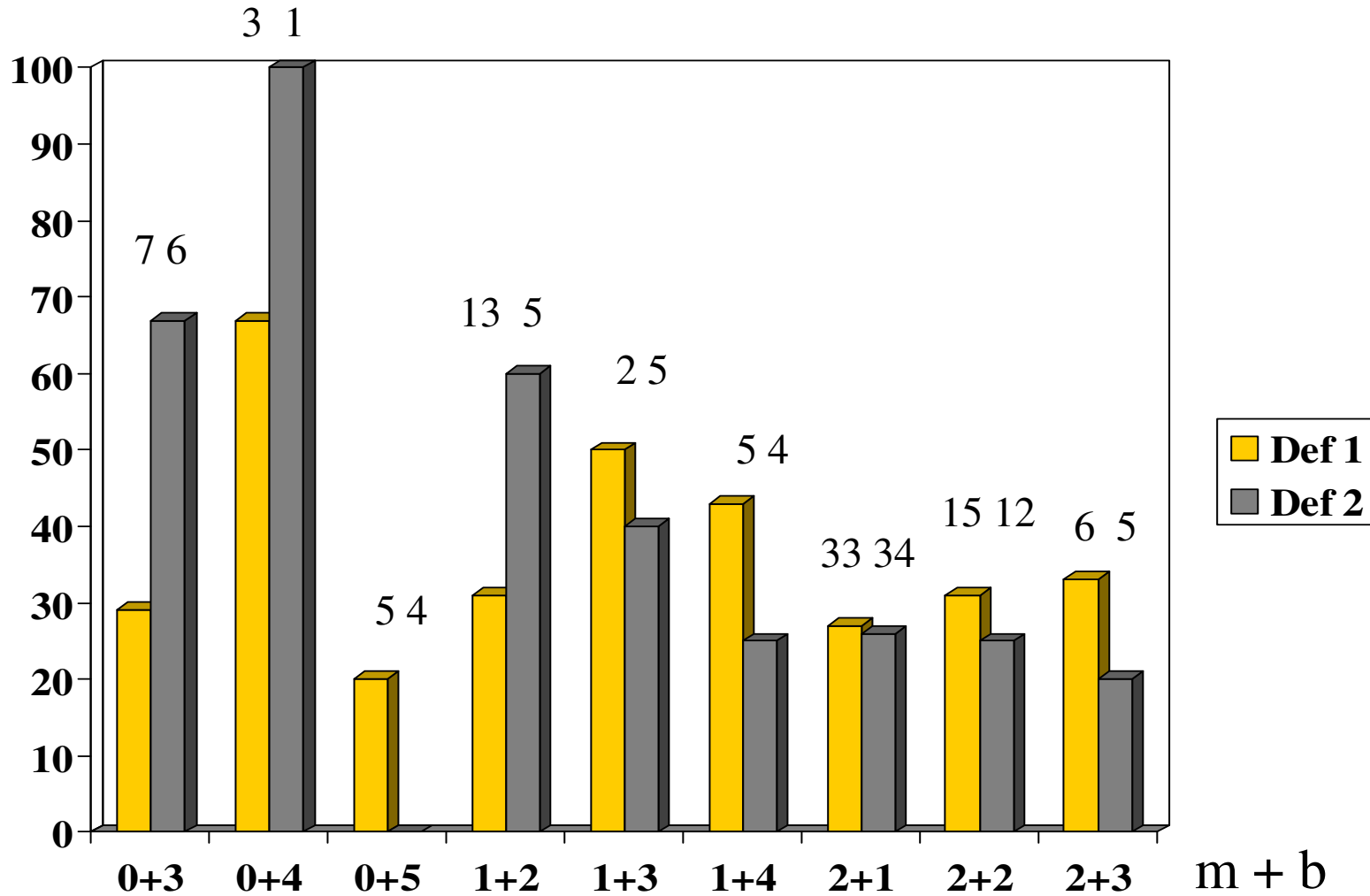
No significant differences between loss rates in different groups

Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with RM according to no. of previously confirmed miscarriages (definition 2)



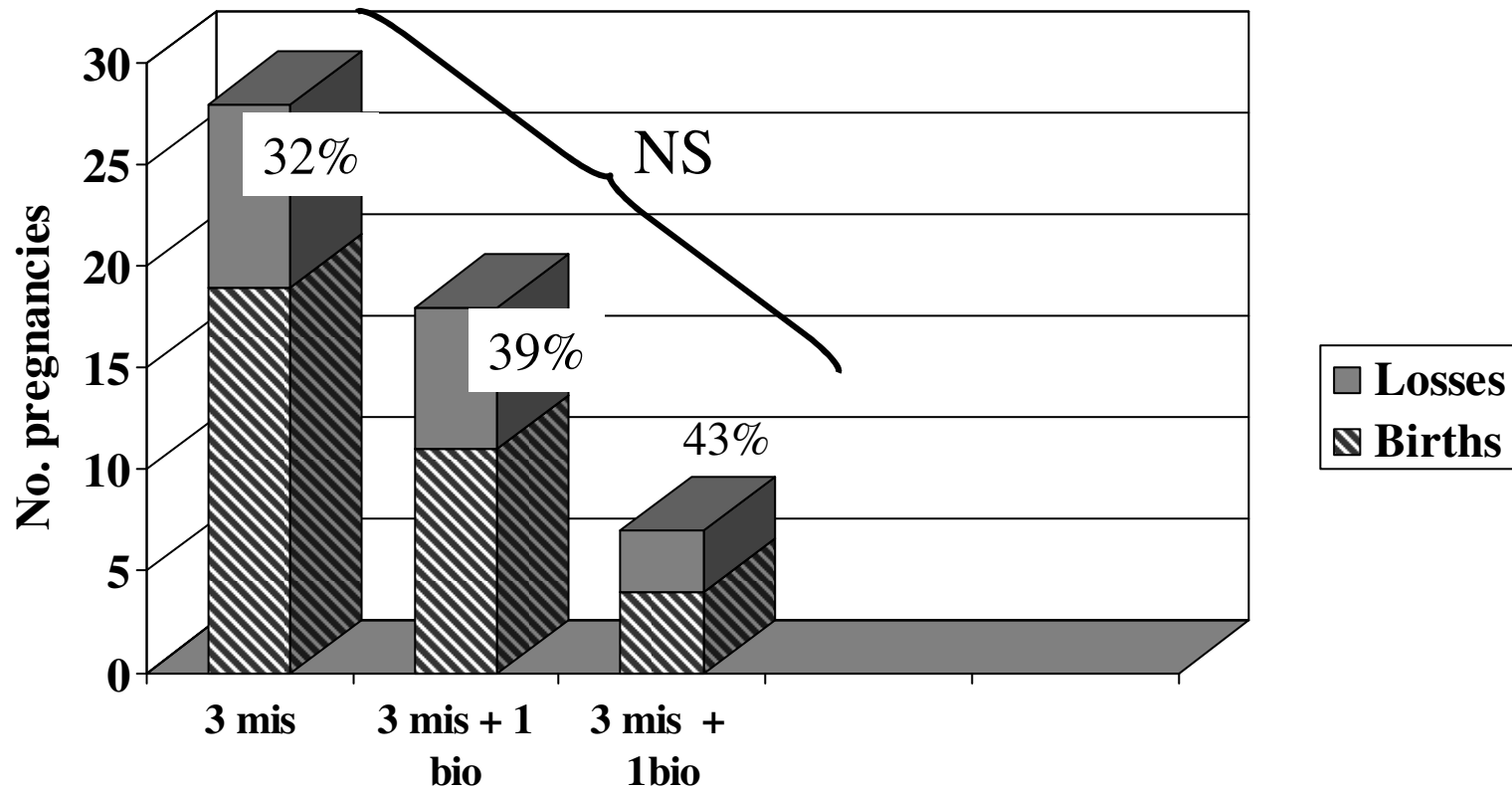
No significant differences between loss rates in different groups

Loss rates in first pregnancies after referral of patients with < 2 prior miscarriages according to previous number of miscarriages (m) and biochemics (b)



Numbers in subgroups too small for valid comparisons

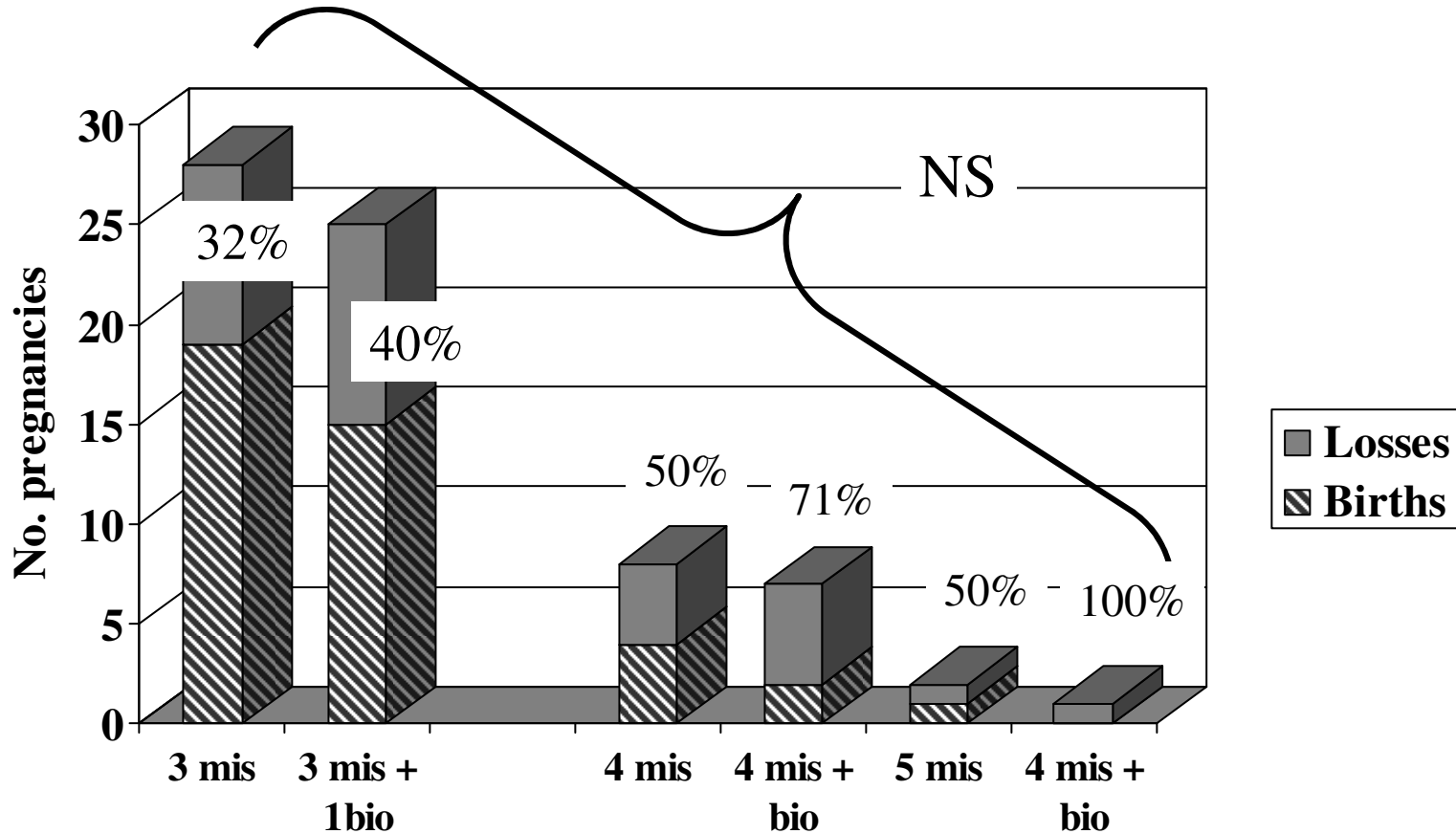
Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with 3 confirmed miscarriages according to no. of previous biochemicals (definition 1)



No significant differences between future loss rates in different groups

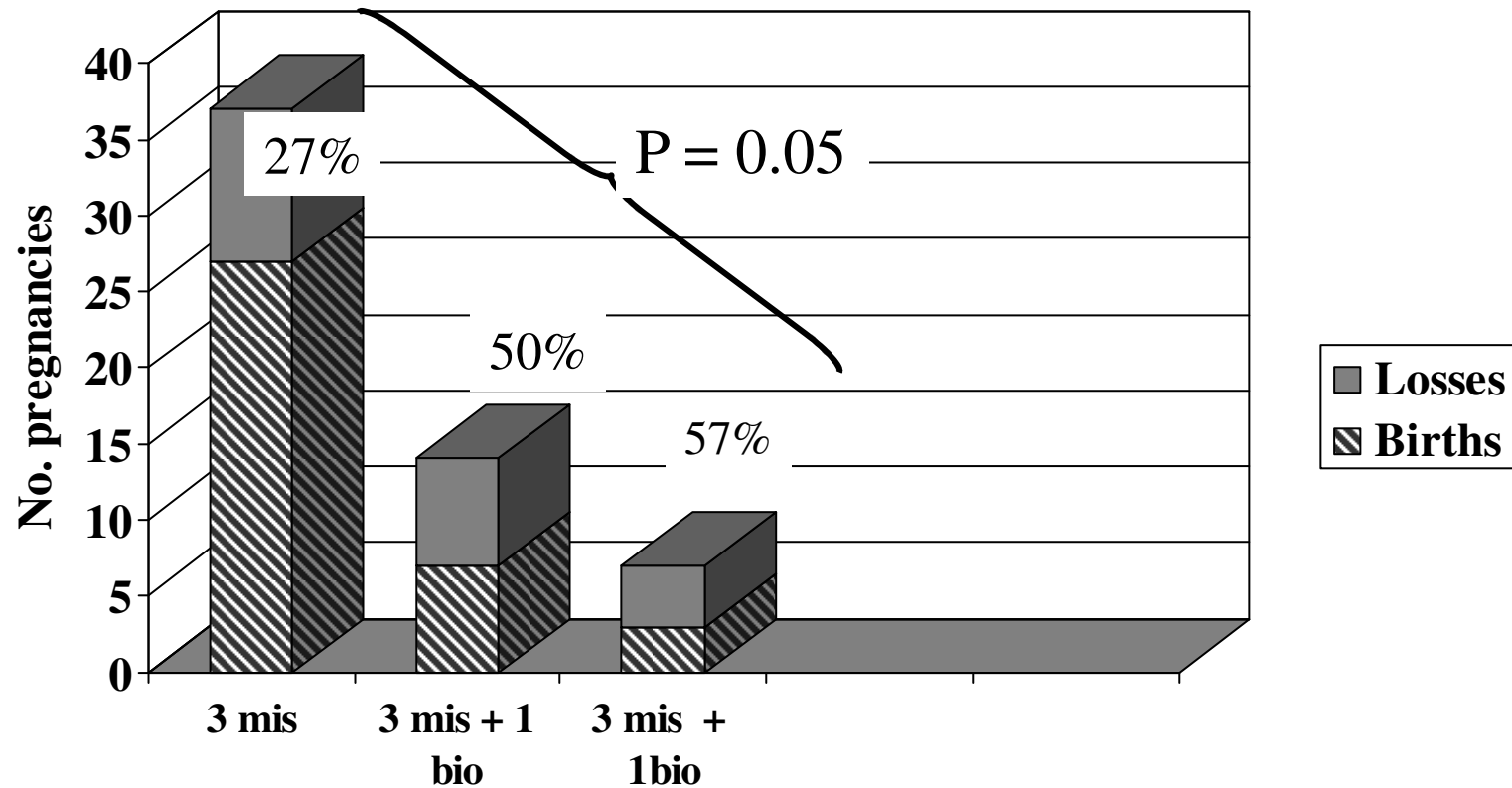
Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with RM according to no. of previous miscarriages and

biochemicals (definition 1)



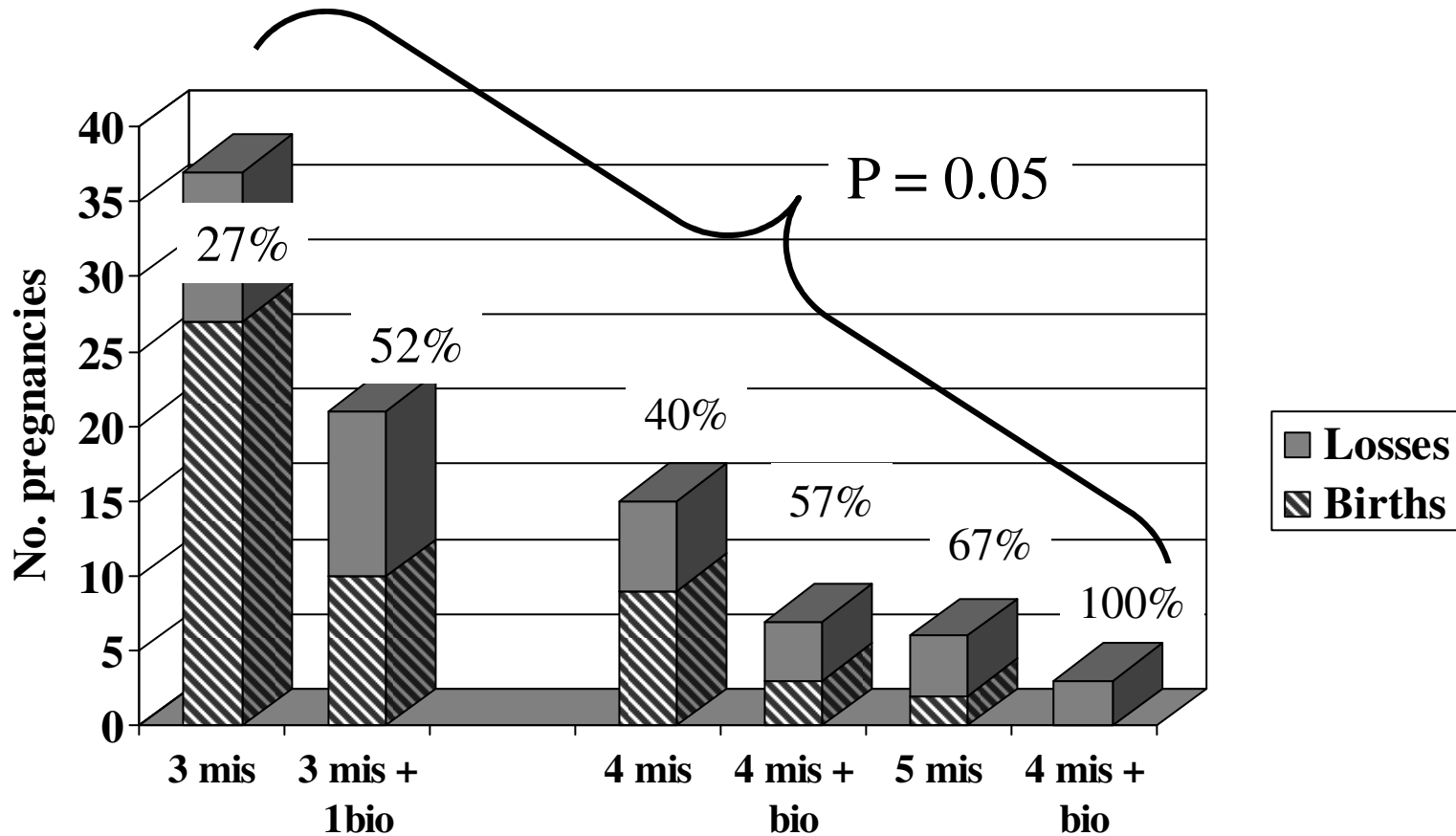
No significant difference between future loss rates in different groups

Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with 3 confirmed miscarriages according to no. of previous biochemicals (definition 2)



P = 0.05 for the difference between future loss rates in different groups

Frequency of miscarriage/biochemicals/ectopics in the next pregnancy among women with RM according to no. of previous miscarriages and biochemicals (definition 2)



P = 0.05 for the difference between future loss rates in different groups

Conclusion 1

- Biochemical pregnancies comprise a significant proportion (33-42%) of pregnancy losses among Danish patients diagnosed with recurrent miscarriage

Conclusion 2

- Among patients with exclusively biochemical pregnancies the risk of a clinical ectopic pregnancy is considerable (27%)
- Among other patients with a diagnosis of recurrent miscarriage the risk of a clinical ectopic pregnancy is much lower and at the same level as in the background population

Conclusion 3

- The risk of a new miscarriage/biochemical loss seems to be independent of the number of biochemical pregnancies included in the patient's reproductive history in patients with less than 3 confirmed miscarriages

Conclusion 4

- In patients with 3 or more confirmed miscarriages each additional biochemical loss significantly increases the risk of new pregnancy loss

Conclusion 5

- In patients diagnosed with recurrent miscarriage but with exclusively repeated biochemical pregnancies, IVF may be the best treatment option

Thank you for
your attention

