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# Symposium - Spontana aborter Behandling med misoprostol

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# **Missfallsbehandling med misoprostol WHO 2007**

**Inkomplett spontanabort: misoprostol 600 mcg p.o.**

**Missed abortion: misoprostol 800 mcg vaginalt (x2)**

# Miscarriage

## Treatment: surgery

- Until the late 1880ies “less intervention better”
- 1843 - the (sharp) curette
- Since the late 1880ies D&C to reduce bleeding and sepsis
- Incomplete miscarriage often illegally induced abortion
- Surgery standard since more than 50 yrs
- 75% of all emergency gynecological procedures in UK (McKee et al. 1992)

# Miscarriage

Complications to Surgery:

- Incomplete evacuation (2-3%)
- Cervical laceration, Cervical/ Uterine perforation
- Infections (1-10%)
- Adhesions
- Infertility
- Death (0.4/100 000)

**WHY is surgery the standard of care??**

# Miscarriage

## medical vs. surgical vs. expectance

- Three Cochrane reviews:
- Medical vs surgery/ placebo (24 RCT, n=1888)
  - Incomplete spontaneous abortion
  - "Missed abortion"
- Expectance vs. surgery (6 RCT)
- Surgery vs expectance vs medical treatment (2)
- Outcome dependent on several factors

# Miscarriage

## Treatment: Expectance

### Expectance vs. surgery

- 5 RCT , 689 women (Cochrane meta analysis)
- Time to assessment differ

### Conclusion: No clear superiority

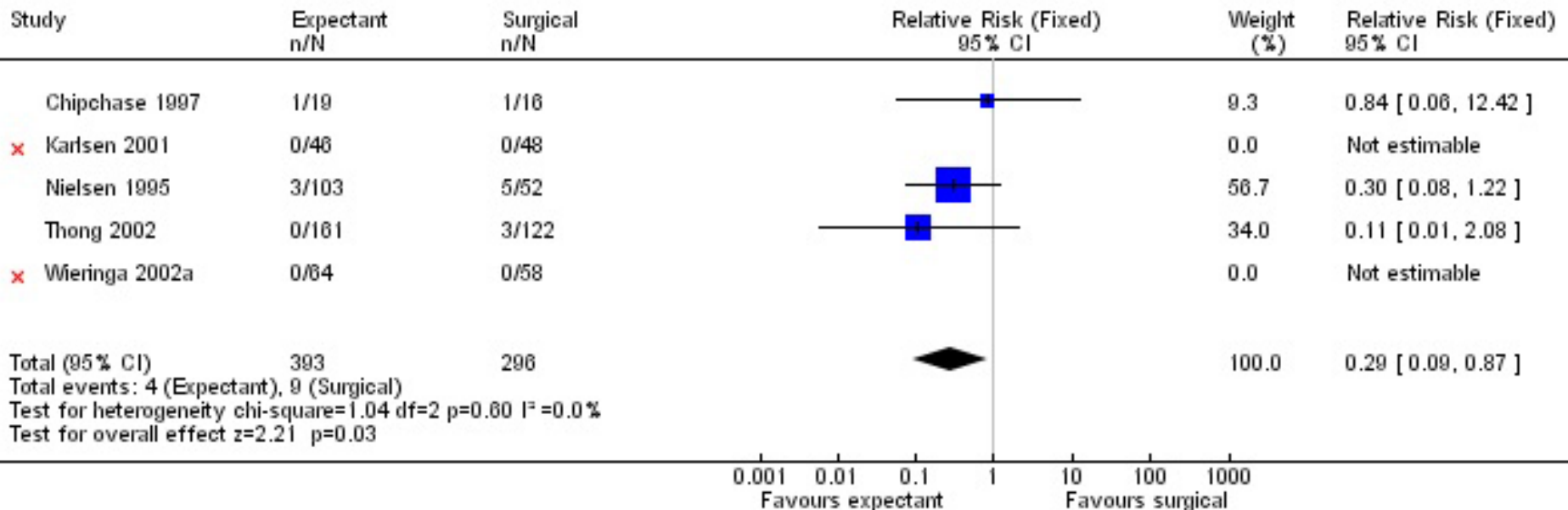
### Expectant management:

- Increased amount and duration of bleeding
- Higher risk for incomplete abortion and need for back-up surgery
- Lower risk for infection, **no neg effect on fertility**

**Eget val – hög acceptans för båda alt!**

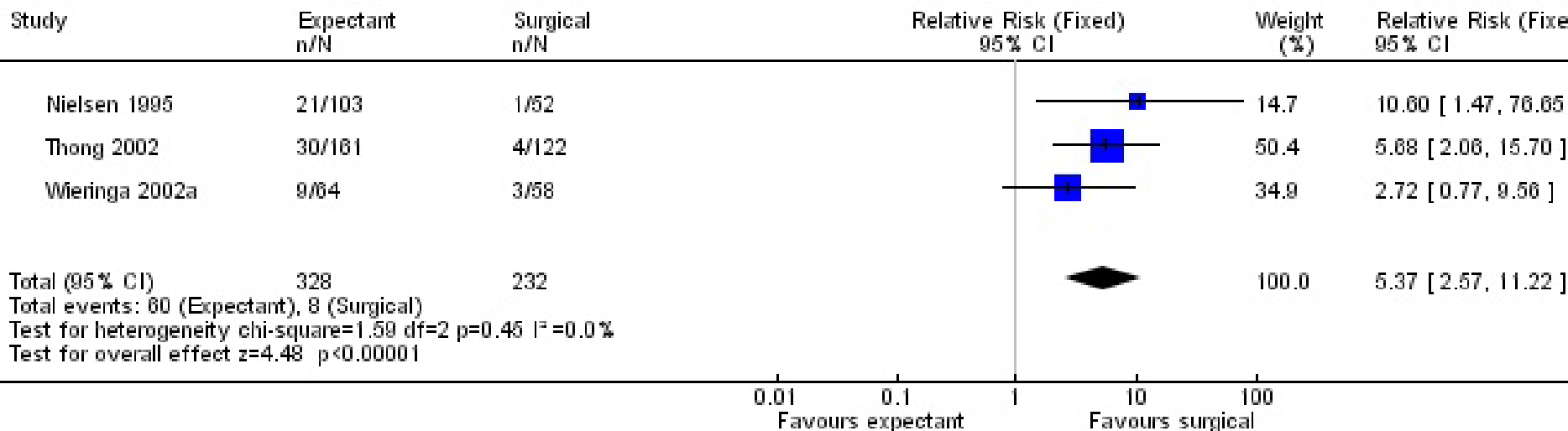
# Meta analysis: Pelvic infection

Review: Expectant care versus surgical treatment for miscarriage  
 Comparison: 01 Expectant care versus surgical treatment for miscarriage  
 Outcome: 04 Localized pelvic infection



# Meta analysis: Incomplete abort (FU to 6v)

Review: Expectant care versus surgical treatment for miscarriage  
 Comparison: 01 Expectant care versus surgical treatment for miscarriage  
 Outcome: 01 Miscarriage not complete (up to 6 weeks)



# Miscarriage

## Treatment: expectance/ medical

Outcome dependent on several factors:

- Type of study: RCT, Observational, pro-/retrospective
- Study population, sample size/ Definition, diagnosis
- Ultrasound
- Time at assessment
- Regimen: Mifepristone/ Misoprostol, dose, route, repeated doses, intervals
- “ Learning curve”

# Miscarriage

## Terminology

Spontaneous abortion/ miscarriage

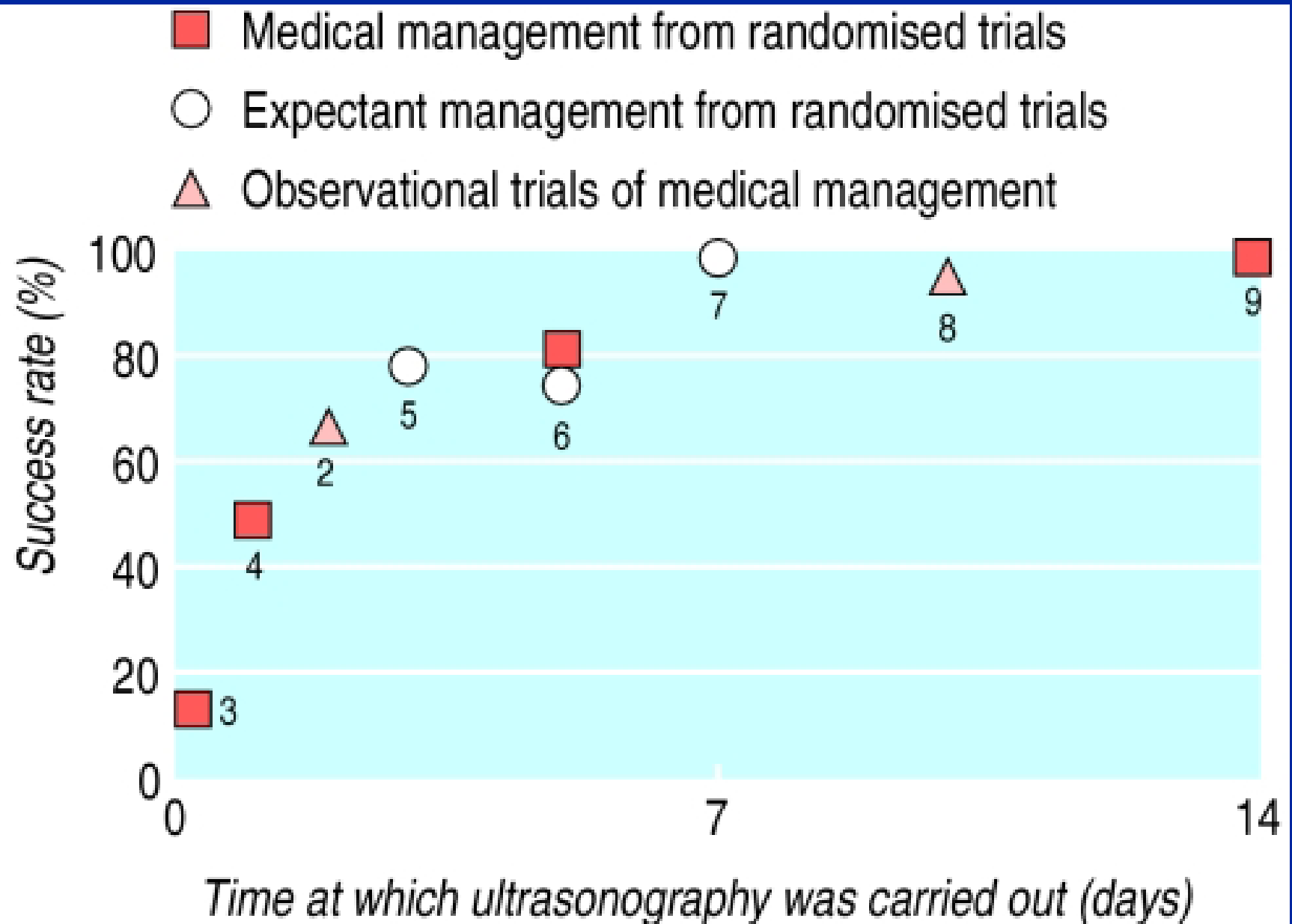
- Complete
- Incomplete; bleeding, passage of tissue but not all
- Inevitable; dilated cervix, no expulsion
- “missed abortion”, non-viable, blighted ovum, fetal demise, embryonic/ foetal death (CRL 5/6mm, </> 8w)
- Anembryonic (empty GS)

RCOG 1997, 2006, ESHRE, 2005

# Outcome dependent on diagnosis

Reference	Treatment	Diagnosis	Evaluation	
			7d.	46d.
Luise-02 Observational study	Expectance	<b>Incomplete</b>	53	91
		<b>Embryonic/ fetal death</b>	30	76
		<b>Anembryonic</b>	25	66
Creinin-05 RCT misoprostol 0.8 mg pv. / VA	Medical	<b>Incomplete</b>	93	-
		<b>Embryonic/ fetal death</b>	88	-
		<b>Anembryonic</b>	81	-

## Time at ultrasound assessment vs. success rate



# Medical treatment

## Cochrane meta analysis

### Medical vs. expectance/ placebo or surgery

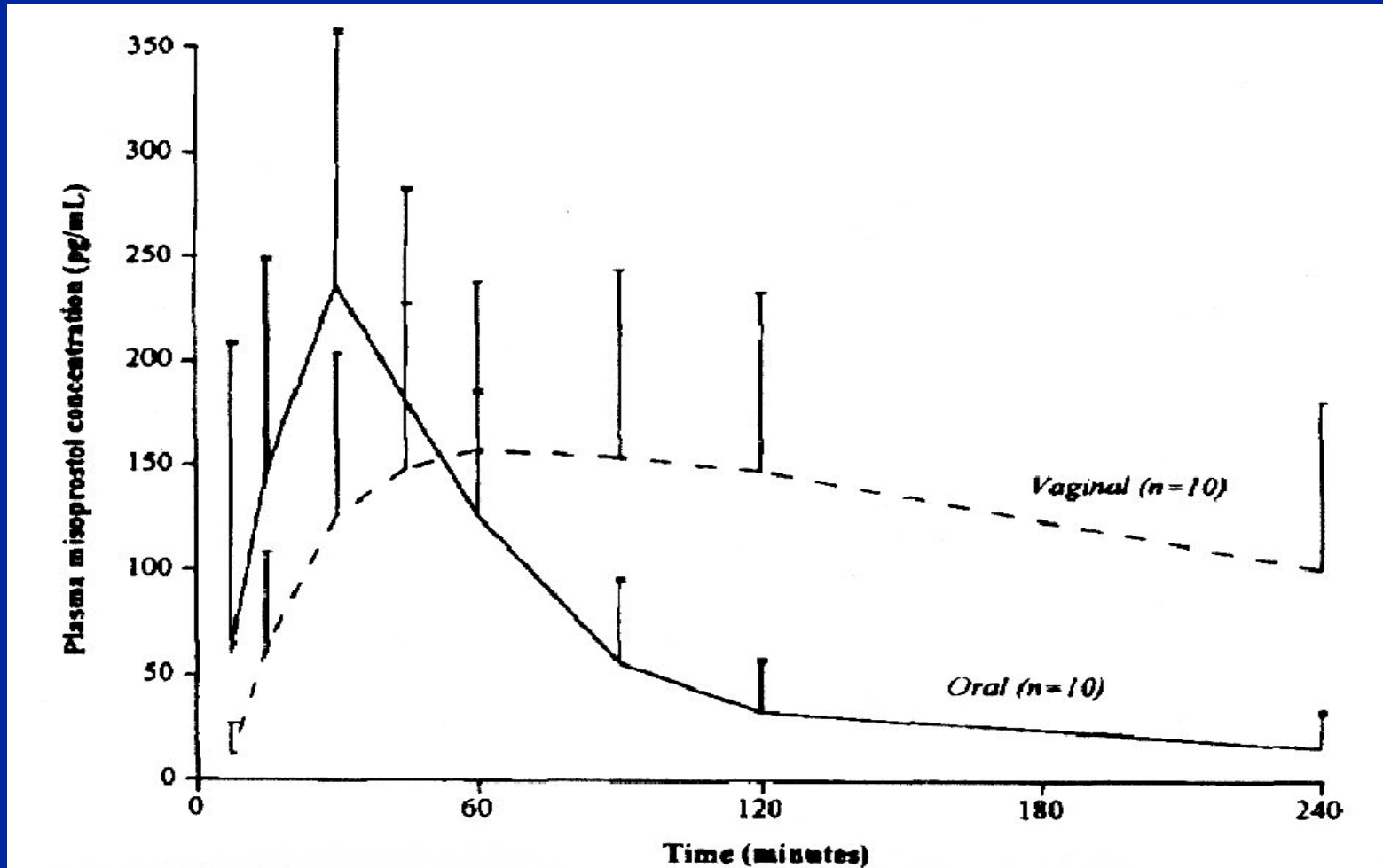
- Missed abortion (embryonic/fetal death, anembryonic)
- 24 RCT (19 RCT I-trimester) n=1888

### Conclusion:

- Misoprostol p.v. faster than expectance/ placebo
- Less need for curettage
- GI side effects similar
- Vaginal more effective than p.o, sublingual similar, more diarrhoea
- Higher dose of misoprostol more effective (800 mcg)
- Mifepristone - not enough/ conflicting data

# Why is vaginal administration of misoprostol more effective?

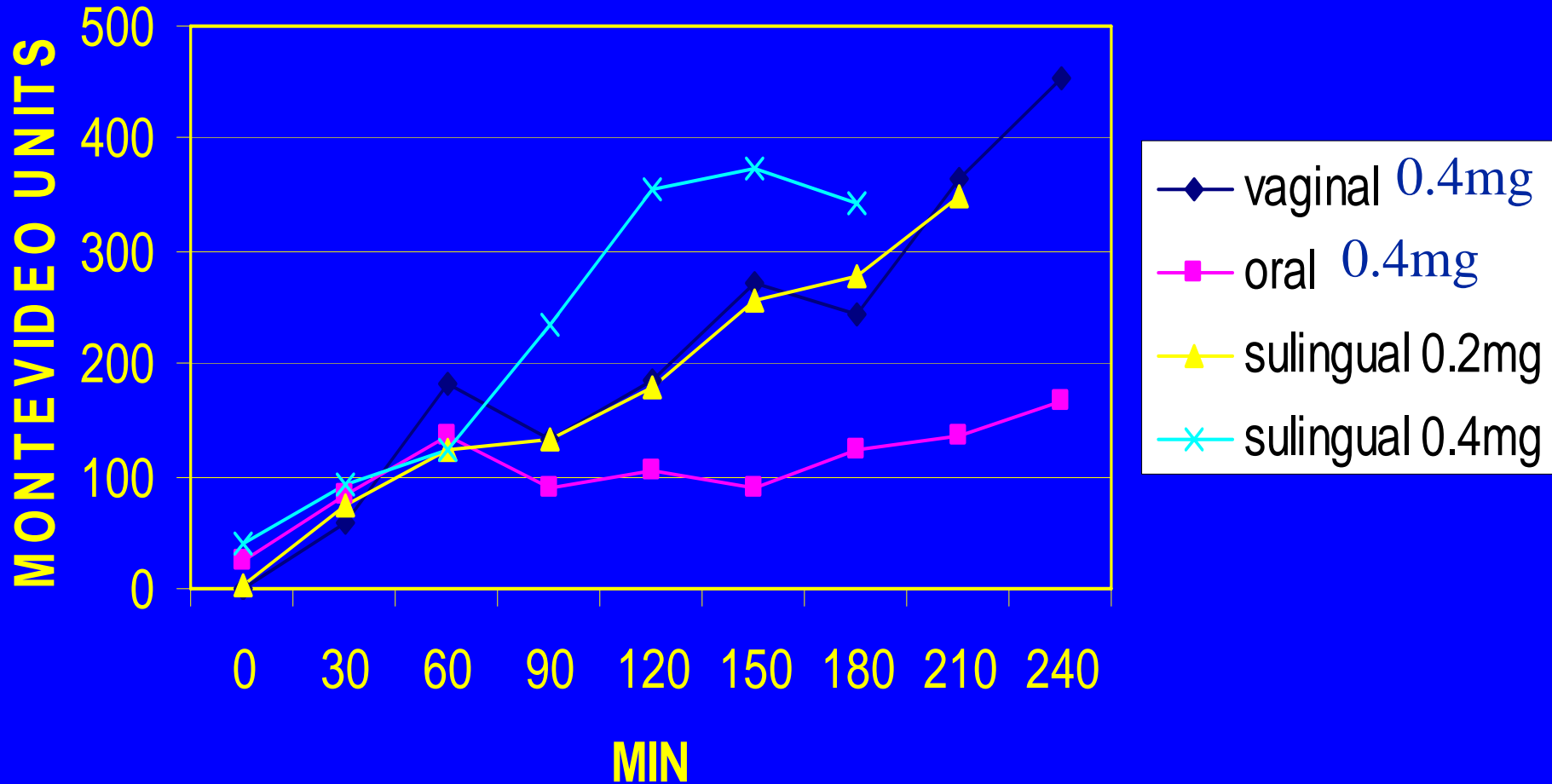
# Oral vs. vaginal misoprostol



Zieman et al. 1997

Early miscarriage, K Gemzell Danielsson

# Effect on Uterine Contractions



Aronsson et al., 2004

# Recommended regimens

- For women presenting with uterine size equivalent to a gestation through 12 weeks LMP.
- Missed abortion
- Incomplete miscarriage/ abortion

# Missed abortion

Embryonic/fetal death or anembryonic-

Regimens:

- Misoprostol 800 mcg vaginally (Evidence level 1)
- Alternative: 600 mcg sublingually
  
- Treatment may be repeated twice with a 3h interval but more studies are needed to evaluate the efficacy of repeated doses of misoprostol

WHO 2007

# Incomplete miscarriage/ abortion

- **600 mcg oral misoprostol** (Evidence level 1) or
- **400 mcg sublingual misoprostol**  
several ongoing trials: as safe and effective

The current evidence does not support repeated doses

# Miscarriage

- Course of treatment:
  - Day 1. Administration of misoprostol
  - Day 7-14. Follow up to confirm that the uterus is empty
- Effects and side effects:  
bleeding, cramping,  
fever/ shivering,  
nausea, vomiting, diarrhea

## Additional information

- The woman should be informed where to seek help in case of heavy bleeding or signs of infection.
- Following vaginal administration of misoprostol unsolved tablets may be found in the vagina at an examination. This doesn't affect the absorption of misoprostol
- No contraindication to breastfeeding (Abdel-Aleem 2002)

# Misoprostol Indications

**Approved:** Treatment and prevention of Gastric ulcers under treatment with NSAIDs  
Induction of labour (Brazil, 25µg, vag. suppository)  
Medical abortion following mifepristone

## **British National Formulary recommends:**

### **Induction and augmentation of labour:**

“Misoprostol is given orally or by vagina for the induction of labour (unlicensed indication).”

### **Induction of abortion:**

“Misoprostol is given by vaginal administration to induce medical abortion (unlicensed indication); intravaginal use ripens the cervix prior to surgical abortion (unlicensed indication).”

## Why are women dying?

“Women are not dying because of diseases we cannot treat. They are dying because societies have yet to make the decision that their lives are worth saving.”

Mahmoud Fathalla, MD, PhD, 1997  
as cited by IPAS ([www.ipas.org](http://www.ipas.org))

# Why are women dying?

- **Haemorrhage** **25%**
- **Sepsis** **15%**
- **Unsafe abortions** **15% (-30%)**
- **Hypertension/Eclampsia** **12%**
- **Prolonged labour** **8%**
- **Pre-existing disorders** **20%**

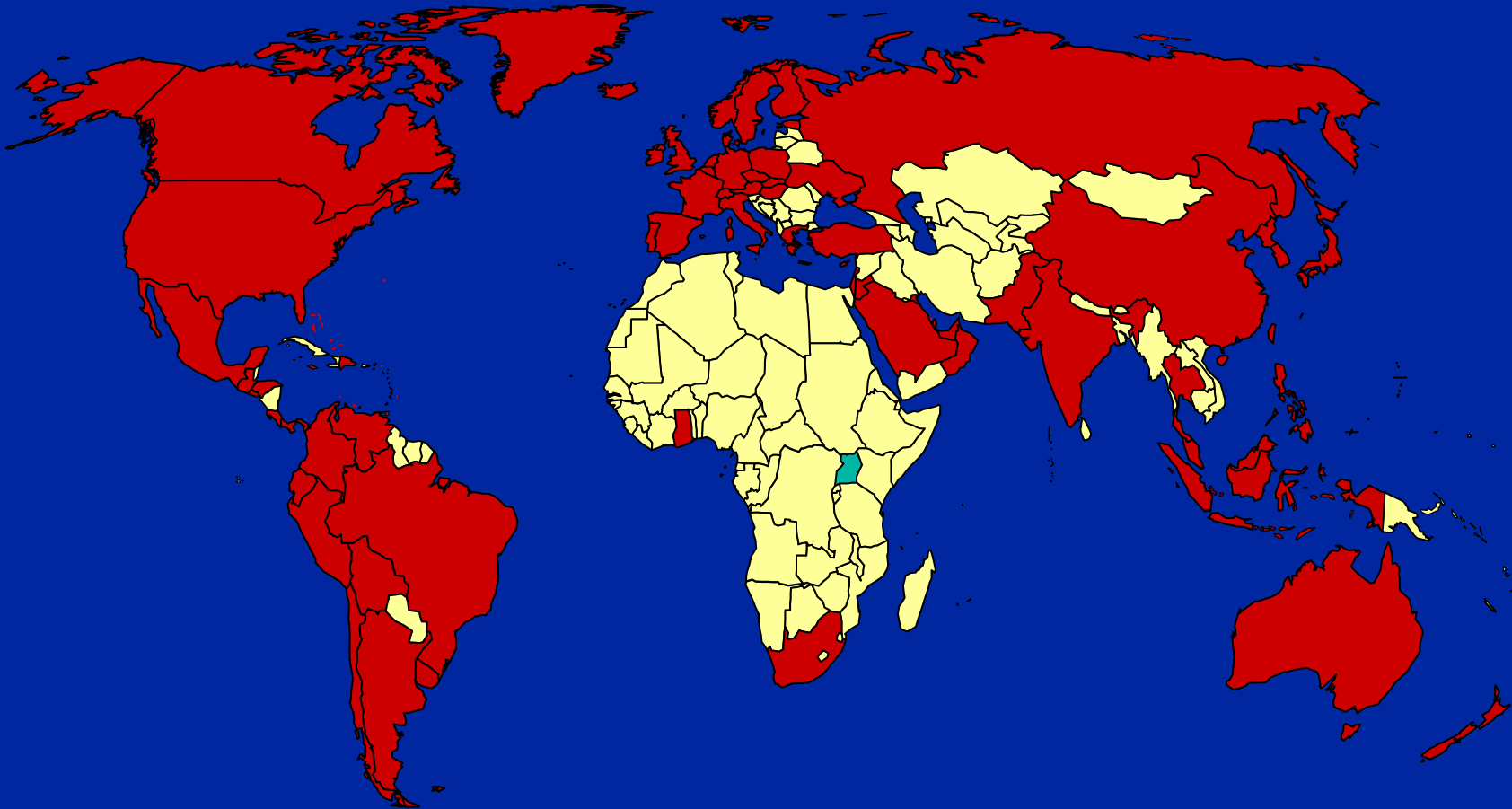
**(Anaemia, malaria, heart diseases)**

Source: WHO 1999

# What is Misoprostol?

- An orally active prostaglandin E1 analogue
- Prostaglandins are the most basic drugs in obstetrics
- Leads to uterine contractions and cervical softening, acts very fast
- Misoprostol has several advantages over the other prostaglandins (safer, stable at room temperature, oral/vaginal application, cheaper)
- Marketed in 1985 and approved in >87 countries
- Has the potential to reduce maternal mortality by 50%

# Misoprostol gap



Misoprostol availability 2002

## Conclusion

### For closing the gap

- Misoprostol has most properties of an ideal, life-saving drug. But it is not available in those countries, which would need it most.

“... societies have yet to make the decision that their lives are worth saving.”

# Misoprostol use in OB/Gyn

## A. Uterine evacuation after pregnancy failure

Incomplete spont. abortion

Missed abortion

IUFD

## B. Labour induction

## C. Postpartum haemorrhage,

Prevention,

Treatment

## D. Cervical ripening for gynaecological procedures

Surgical abortion, Hysteroscopy, ET, IUD-insertion, curettage etc

## E. Induced abortion

1st trimester

2nd trimester

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**[www.misoprostol.org](http://www.misoprostol.org)**

Misoprostol in Obstetrics & Gynaecology

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**Let each patient choose from  
expectant, surgical or medical  
management**