



**"Liberating women - removing
barriers and increasing access
to safe abortion care"**

14.-15. September 2018, Nantes, France

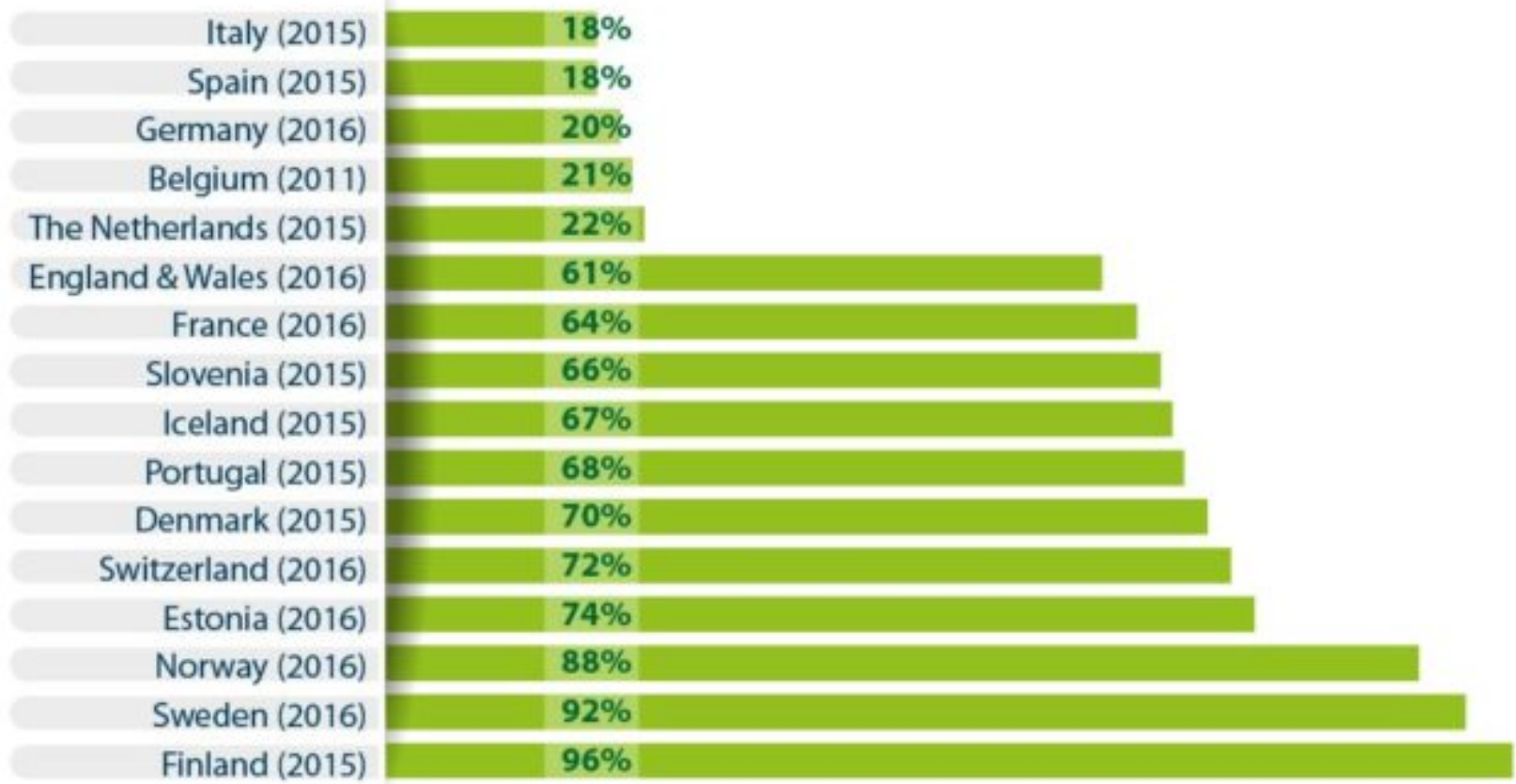
Concurrent session 2: Hot topics in abortion care

Pain & medical abortion at home

Teresa Bombas

MD. Obstetrician ad Gynecologist
Obstetric Service A, Medical University Hospital of Coimbra
Portuguese Society of Contraception
Portugal

Percentage of medical abortions among induced abortions



Data to be confirmed in Denmark, Finland, Iceland and the Netherlands
No available data for other countries

Medical abortion conditions: 2nd drug taken at home



Women may safely self-administer misoprostol outside of a health facility

Adverse effects of medical abortion¹

Pain

Bleeding

Fever

Nausea and vomiting

Diarrhoea

✓ Pain is reported by 80-90% of women^{2,3,4}

1. Clinical practice handbook for safe abortion . WHO, 2014

2. Cavet S, Fiala C, Scemama A, Partouche H. Assessment of pain during medical abortion with home use of misoprostol. Eur J Contracept Reprod Health Care 2017;22(June (3)):207–11, .

3. Saurel-Cubizolles MJ, Opatowski M, David P, bardy F, Dunbavand A. Pain during medical abortion: a multicentre study in France. Eur J Obstet Gynecol Reprod Biol 2015;194:212–7.

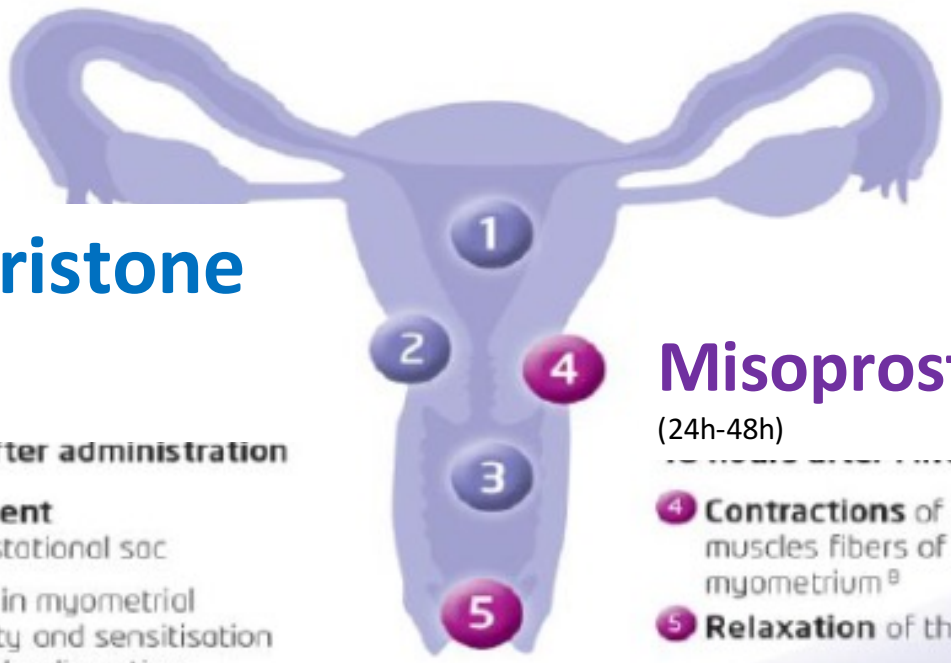
4. Schaff EA, Fielding SL, Weshoff C. Randomized trial of oral vs vaginal misoprostol 2 days after mifepristone 200 mg for abortion up to 63 days of gestation. Contraception 2002;66:247–50.

Mifepristone – prostaglandin synergistic mechanism of action

Mifepristone

after administration

- 1 Detachment of the gestational sac
- 2 Increase in myometrial contractility and sensitisation to prostaglandin action
- 3 Opening and ripening of the cervix



Misoprostol

(24h-48h)

- 4 Contractions of smooth muscles fibers of the myometrium[®]
- 5 Relaxation of the cervix[®]

Background

- Women frequently experience pain during MTOP, sometimes even severe.
- Most recent guidelines from National, International Societies give a general recommendation for:
 - **routine use of pain medication:**
 - French Health Authorities (HAS 2010)
 - UK Royal College of Obstetricians and Gynaecologists (RCOG 2015)
 - French national college of obstetricians and gynecologists (CNGOF 2016)
 - International Federation of Gynecology and Obstetrics (FIGO 2011)
 - World Health Organisation (WHO 2014)
 - **only as-needed analgesics :**
 - Executive and Board of the Society of Obstetricians and Gynaecologists of Canada

Problems

- There is a lack of clear and practical guidelines on management of pain associated with first-trimester medical abortion
 - **Assessment or not** the pain in routine practice
 - **Control or not** the risk factors
 - **Best protocol** for management the pain (timing and type of analgesic drugs in use)

Pain Assessment

- According to the WHO, pain assessment should be done in all cases of pain, including an initial evaluation and ongoing reassessment¹.

Pain during medical abortion, the impact of the regimen: A neglected issue? A review

C Fiala, S Cameron, Tbombas, M Parachini, L Saya, K Gemzell-Danielsson

The European Journal of Contraception and Reproductive Health Care, 2014; Early Online: 1–17



Objectives To evaluate pain and other early adverse events associated with different

Methods: The literature was searched for comparative studies of medical abortion using mifepristone followed by the prostaglandin analogue misoprostol. Publications, which included pain assessment were further analysed.

Results:

- 1459 publication on medical abortion up to nine weeks of amenorrhoea only **23** comparative, prospective trials corresponded to the inclusion criteria.
 - Information on pain level was reported in 12/23 papers (52%),
 - information regarding systematic administration of analgesics in 12/23 (52%)
 - information concerning analgesia used was available for only 10/23 (43%).

Conclusion: Neither pain nor its treatment are systematically reported in clinical trials of medical abortion;

Pain management for up to 9 weeks medical abortion – An international survey among abortion providers

C Fiala, S Cameron, T. Bombas, M Parachini, A Agostini, R Lertxundi, K Gemzell-Danielsson

European Journal of Obstetrics & Gynecology and Reproductive Biology 225 (2018) 181–184



Objective: Perform an international survey among medical abortion providers to document the current clinical practice for managing pain in first trimester medical abortion.

- 425 providers were invited by email to complete the survey,
- 362 completed the questionnaires (85%);
- 283 questionnaires were analyzed

Results:

68% (n=173) of respondents did not routinely assess pain

For those who routinely assessed pain, Visual Analogue Scale (VAS) was the most commonly used tool (n = 46, 58%).

Management of pain associated with up-to-9-weeks medical termination of pregnancy (MToP) using mifepristone-misoprostol regimens

Expert consensus based on a systematic literature review

C Fiala, S Cameron, T Bombas, A Agostini, R Lertxundi, Mlubusky, M Parachini, L Saya, Btrumbic, K Gemzell Danielsson

Submitted for publication, PLOS ONE, august 2018

QUESTION EXPERT GROUP STATEMENT	QUESTION EXPERT GROUP STATEMENT
Q5. Should pain be assessed during first-trimester MToP process at all?	It is good clinical practice to assess pain during abortion and before and after any pain intervention. It should also be formally integrated into medical abortion clinical studies.
Q6. If pain must be assessed during first-trimester MToP, should this assessment be systematic or selective?	There was no agreement between the experts regarding the need for a formal assessment in clinical routine. For daily practice, pain assessment could be useful even if not systematic.

Pain management: The value of risk factors ?

Table 3 : Factors associated with increased/decreased risk for pain and/or analgesic use as reported in clinical studies

Parameter	Increased risk for pain/analgesic use	Decreased risk for pain/analgesic use
Increasing woman's age		Westhoff 2000b [25], Abdel-Aziz 2004 [40], Suhonen 2011 [44], Kapp 2013 [43], Saurel-Cubizolles 2015 [24]
Increasing parity		Westhoff 2000a [31], Westhoff 2000b [25], Abdel-Aziz 2004 [40], Teal 2007 [45], Lokeland 2014 [22]
Increasing number of previous pregnancies		Suhonen 2011 [44], Saurel-Cubizolles 2015 [24]
Increasing number of previous deliveries		Suhonen 2011 [44], Kapp 2013 [43]
Increasing number of living children		Abdel-Aziz 2004 [40]
Increasing gestational age	Westhoff 2000a [31], Westhoff 2000b [25], Teal 2007 [45], Suhonen 2011 [44]	
Strong pain during normal menstruation /dysmenorrhea	Suhonen 2011 [44], Avraham 2012 [41], Kapp 2013 [43], Saurel-Cubizolles 2015 [24]	
Retroverted uterus	Kapp 2013 [43]	
Married		Westhoff 2000b [25], Abdel-Aziz 2004 [40]
Increased available financial support		Abdel-Aziz 2004 [40]
Asian women		Westhoff 2000a [31], Westhoff 2000b [25]
India		Elul 1999 [42]
Provision of full preliminary information		Kruse 2000 [39]
Decreased mifepristone dosage (200 instead of 600mg)	Saurel-Cubizolles 2015 [23]	

Predictive factors for pain occurrence /intensity

- High gestational age
 - Younger age
 - Low Parity
- There is no difference between misoprostol at home and misoprostol at hospital
 - ✓ **the predictive value of these factors is insufficient to define special/individual pain management**

From:

Bettahar K, Pinton A, Boisramé T, Cavillon V, Wylomanski S, Nisand I, Hassoun D . Medical induced abortion
J Gynecol Obstet Biol Reprod (Paris). 2016 Dec;45(10):1490-1514..

Pain management for up to 9 weeks medical abortion – An international survey among abortion providers

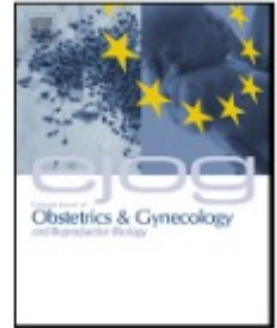
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Results:

- 84% (n = 220) did not change pain management with gestational age
- 67% (n = 173) reported no change according to the place of misoprostol administration.



Pain during medical abortion: a multicenter study in France

Saurel-Cubizolles, M Opatowski, P David, F Bardy, A Dunbavand

European Journal of Obstetrics & Gynecology and Reproductive Biology 194 (2015) 212–217

Objective: To compare the level of pain reported by women by dose of mifepristone, 200 or 600 mg, (in the 5 days after a medical abortion)

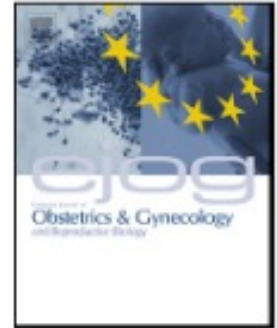
Study design: Observational study in 11 medical centers in France between October 2013 and September 2014.

The protocols were:

Day 1: 200 or 600 mg orally mifepristone

Day 3: 400, 600 or 800 mg orally misoprostol

Women returned a questionnaire that they completed during 5 days following the abortion; pain was recorded on a visual analog scale (0–10) daily.



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Results:

453 women were included; the mean age was 29 years (range 18–49 years).
No difference on pain level with 400 µg, 600 µg, 800 µg of misoprostol

Average Pain (day 3)	Pain average	% Subjects with pain >8/10	Average Pain level in remaining (%) subjects
200 mg Mifepristone	5.1	33% : 8-10	67% : 3.0-3.5
600 mg Mifepristone	4.2	16% : 8-10	84% : 3.0-3.5

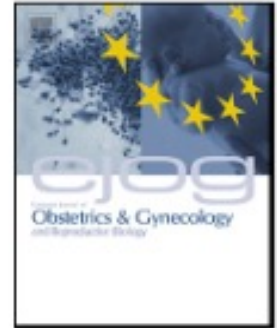
Risk factors for pain:

- women <25 years old,
- gravidity and usual menstrual pain

Risk factors for severe pain

- primigravida women
- women who had painful menstruations

The pain during the 5 days was more frequent for women who had early abortion (<5 weeks) or late abortion (>8 weeks).



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✓ The lead clinical investigator of this study considers that 600 mg mifepristone dose is particularly of interest for primigravida women and women who had dysmenorrhea quoted above 5 (i.e. painful menstruations).

Conclusions:

The mean pain severity experienced by women undergoing medical abortion is high;

It is higher with a regimen of 200 mg mifepristone.

The findings emphasize the need to improve analgesic strategies and invite to opt for a protocol of 600 mg instead of 200 mg mifepristone.

Management of pain associated with up-to-9-weeks medical termination of pregnancy (MToP) using mifepristone-misoprostol regimens

Expert consensus based on a systematic literature review

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QUESTION EXPERT GROUP STATEMENT	QUESTION EXPERT GROUP STATEMENT
Q4. Are there predictive factors for first-trimester MtoP associated pain occurrence or intensity?	Several associations between various factors and pain can be found. However, the predictive value of these factors is insufficient to define pain management for an individual woman.

Pain treatment

- ✓ There is insufficient data to determine the optimal analgesic to be used for pain associated with first- trimester
- ✓ FIGO; WHO; RCOG, HAS and CNGOF recommend the use of NSAIDs
- ✓ NSAIDs were demonstrated not to have any negative impact on efficacy of medical abortion or the duration of the procedure

MEDICAL ABORTION

- Respectful, non-judgmental communication
- Verbal support and reassurance
- Thorough explanation of what to expect
- The presence of a support person who can remain with her during the process (if the woman desires it)
- Hot water bottle or heating pad

- Analgesia (NSAIDs, e.g. ibuprofen 400–800 mg)
- Anxiolytics/sedatives (e.g. diazepam 5–10 mg)
- Adjuvant medications may also be provided, if indicated, for side-effects of misoprostol (e.g. loperamide for diarrhoea).
- **>12 weeks' gestation**
In addition to NSAIDs, offer at least one or more of the following:
 - oral opioids;
 - intramuscular (IM) or intravenous (IV) opioids; epidural anaesthesia.

- Paracetamol is not recommended to decrease pain during abortion.
- To ensure that oral medications will be most effective at the time of the procedure, administer them 30–45 minutes before the procedure.

Pain management for up to 9 weeks medical abortion – An international survey among abortion providers

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Results:

- 94% (n=267) reported analgesic prescription for all women
- 82% (n= 233) before pain onset
- 6% (n = 16) of respondents reported that they never provided analgesia
 - 97% (226) prescribed -WHO-Step I analgesics (NSAIDs, paracetamol)
 - 89,5% (205) It was initiated shortly before or after misoprostol intake
 - the median treatment duration was 2 days [1–20 days]

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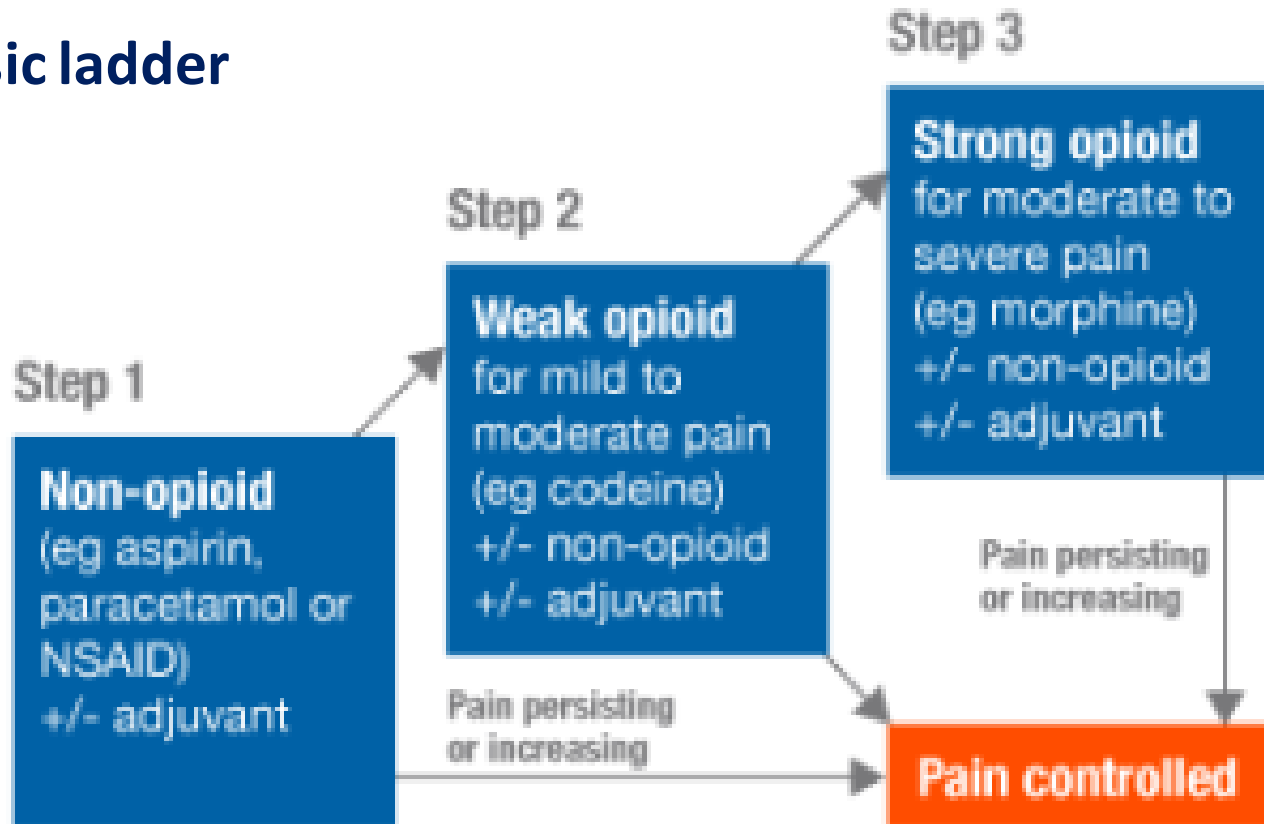
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Conclusions:

- Most providers do provide analgesia routinely to women undergoing medical abortion up to 9 weeks gestation.
- There were widespread variations in analgesic regimens used.
-

WHO analgesic ladder



WHO Model List of Essential Medicines, 20th edition, 2017

Non-opioids: acetylsalicylic acid, ibuprofen, paracetamol

Weak opioides: codeine,

Strong Opioides: fentanyl, morphine, methadone

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Q14. Which are the most appropriate pharmacological agents?	<p>There was little evidence in the literature regarding the most appropriate pharmacological agents. Therefore, the experts' consensus is:</p> <ul style="list-style-type: none">– First line: prophylaxis: ibuprofen, 400 to 800 mg (use of second line in case of contraindications to NSAIDs)– Second line: opioids: codeine, dihydrocodeine, or morphine. <p>According to the WHO, patients with severe pain can start with step 3, and morphine is still the first choice for severe pain.</p>

Should analgesic treatment be prophylactic or curative?

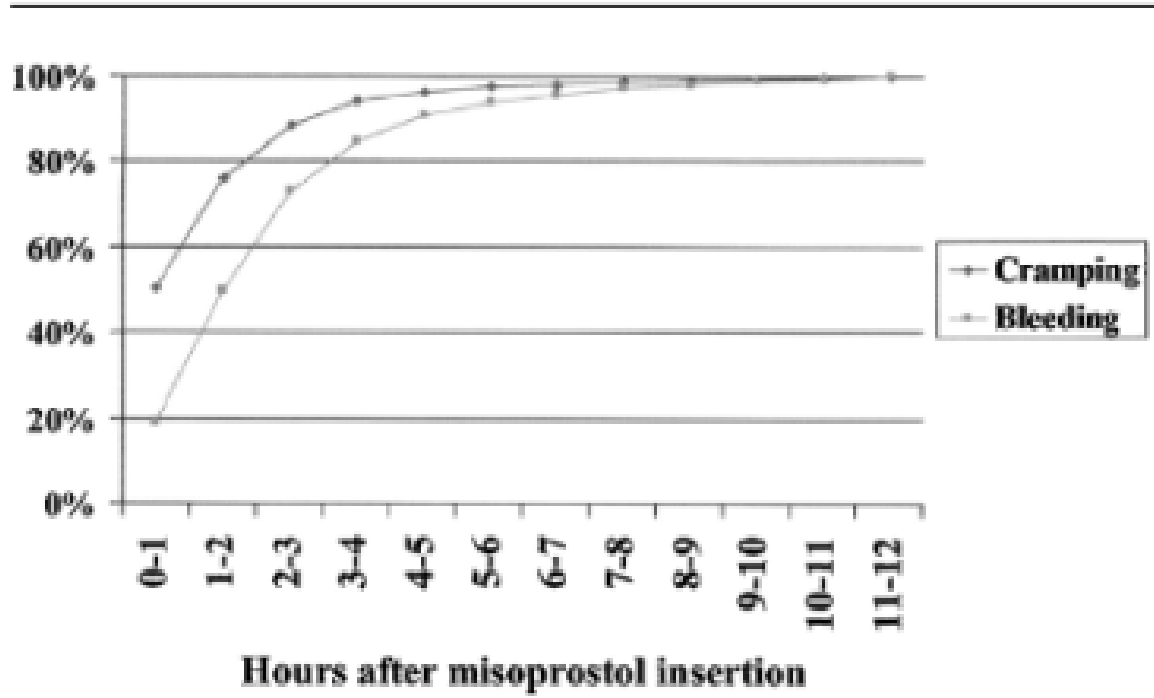
Misoprostol: Pharmacokinetic parameters according to the route of administration

Route	Oral	Buccal	Sublingual	Vaginal
Instruction for use: pills are	...swallowed	...placed between the cheek and gums and swallowed after 20-30 min	...placed under the tongue and swallowed after 10 min	...placed in the vagina
AUC	Low	Moderate	Moderate	High
Cmax	High	Moderate	Very high	Moderate & variable
Tmax	≈ 30 min	≈ 60 min	≈ 10 min	≈ 60 min

AUC: area under the curve; Cmax: maximum plasma concentration; Tmax: time to reach maximum plasma concentration

There are 2 periods of high pain: near the intake of misoprotol and at the expulsion

Bledding and pain after misoprostol administration



There is a pic of pain between 1 and 3 h after misoprostol in take

Jackson AV, Dayananda I, Fortin JM, et al. Can women accurately assess the outcome of medical abortion based on symptoms alone? Contraception 2012;85:192–7.

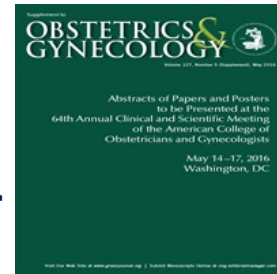
Should analgesic treatment be prophylactic or curative?

Analgesic therapy for medical abortion

Drug	Ibuprofen	Opioid: Paracetamol+ codeine	Tramadol
Posology	400mg-600 mg (4-4h) max 6 per day	1 -2 cp (400 mg/30mg) Max 4 per day	100 mg (6 -6 h) max 4 per day
Contra-indication	LES severe Cardiac disease Hepato-celular disease Gastric ulcer	Asma Hipersensibilty to codeine	Lung disease Severe Hepato- celular disease
Time for clinical effect	90 minutes	60 minutes for codeine	120 minutes

From:

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J Gynecol Obstet Biol Reprod (Paris). 2016 Dec;45(10):1490-1514..



Prophylactic Compared With Therapeutic Ibuprofen Analgesia in First Trimester Medical Abortion: A Randomized Controlled Trial

Elizabeth G. Raymond, MD, MPH, Mark A. Weaver, PhD, Kamen S. Louie, MS, MPH, Gillian Dean, MD, MPH, Lauren Porsch, MPH, E. Steve Lichtenberg, MD, MPH, Rose Ali, PA-C, MS, and Michelle Arnesen, MPAS, PA-C

OBSTETRICS & GYNECOLOGY, VOL. 122, NO. 3, SEPTEMBER 2013

Randomized participants: 250

- **Prophylactic group** 123 (follow-up data: 111 (90%))

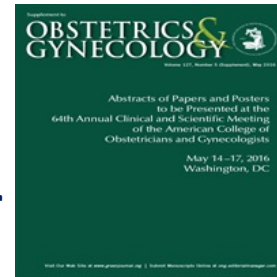
(1h before misoprostol, Take 800 mg ibuprofen, and one additional tablet every 4–6 hours for 48 hours)

- **Therapeutic group** : 127 (follow-up data: 117 (92%))

(every 4–6 hours as needed starting at the onset of pain):

Max 4 tables per day

200 mg mifepristone orally in the clinic followed by 800 micrograms 1–2 days later at home



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OBSTETRICS & GYNECOLOGY, VOL. 122, NO. 3, SEPTEMBER 2013

Results:

The mean **maximum pain scores:**

the prophylactic 7.1 (standard deviation 2.5)

therapeutic groups were 7.3 (standard deviation 2.2), ns

No evidence that pretreatment with high-dose ibuprofen followed by around-the-clock administration offered any advantage over ibuprofen as needed in reducing pain in first-trimester medical abortion in duration of pain, average daily pain, recalled maximum pain, qualitative pain description, acceptability of pain, and use of alternative analgesic agents

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QUESTION EXPERT GROUP STATEMENT	QUESTION EXPERT GROUP STATEMENT
Q11. Should analgesic treatment be systematic or selective?	Treatment for pain associated with first-trimester MToP should be systematic. In addition, women should have easy access to additional stepwise pain treatment.
Q12. Should analgesic treatment be prophylactic or curative, and at what time should it be taken?	Limited data suggest that prophylactic treatment is not better than only curative, But, expert's recommendation is that best principles would advise giving prophylactic analgesia

Nonpharmacological strategies

- Giving detailed information to women on the procedure
- Respectful, non-judgmental communication
- Verbal support and reassurance
- The presence of a support person who can remain with her during the process (only if she desires it)
- Allowing home intake of misoprostol
- Ensuring a relaxing and supporting environment
- Hot water bottle or heating pad

1. Safe Abortion: Technical and Policy Guidance for Health Systems. 2nd ed. Geneva: World Health Organization; 2012

2. **Bettahar** K, Pinton A, Boisramé T, Cavillon V, Wylomanski S, Nisand I, Hassoun D. Medical induced abortion *J Gynecol Obstet Biol Reprod (Paris)*. 2016 Dec;45(10):1490-1514..

Take home messages

- *There is a clear need for standardized evidence based regimens for management of pain associated with first trimester medical abortion*
- Good counselling is important
- The use of analgesic by routine
- Prophylactic use or at time of misoprostol intake
- Step the needs
 - 1^o line: ibuprofen
 - 2^o line: codeine /tramadol
 - 3^o line morphine
- Include non-pharmacologic strategies

FIAPAC 13º Congress, 2018
Pain & medical abortion at home

From Coimbra, Portugal

Thank you

