Ökad autonomi i abortvården -aktuell forskning

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Disclosures:

Gemzell-Danielsson has been invited to present /an expert /advisory board byr Merck (MSD), Bayer, Exelgyn, Actavis, Gedeon Richter, Mithra, Exeltis, Ferring, Natural Cycles, Campus Pharma, Ciqle,MedinCell and HRA-Pharma

Reproductive Health Research
From bench - to bed - to the hands of women
to improve women's health

Abortion related deaths can be prevented !!!!

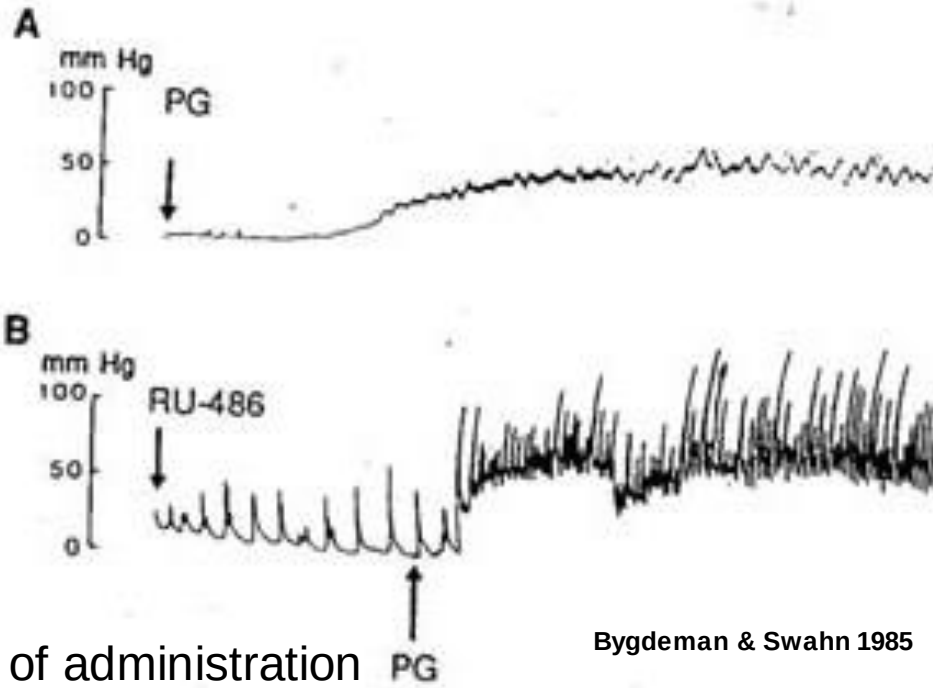
- Recognize abortion as a major contributer to materna mortality,
  Politicians, doctors, nurses (FIGO),Religious leaders etc.
- **Stop outdated methods. Increase access to safe abortion** VA, MA, ”menstrual regulation”, PAC
- Increase emergency service för abortion related complications (midlevel providers, doctors, MVA, drugs)
- Contraceptive councelling and contraception also for young/unmarried women
- Information on SRHR
- Remove stigma
- Empower women!

Effective contraceptive methods and safe abortion care - are prerequisites for Reproductive Health

Medical abortion

Development of medical abortion

- 70ies, Prostaglandin analogues (PG) discovered by prof Sune Bergström and his team at KI, Awarded the Nobel Price in 1982
- Induced uterine contractions and cervical ripening;
- Shown to act in synergy with progesterone receptor modulator;
- Mifepristone (RU486) E Baulieu, Fr



Bygdeman & Swahn 1985

→Medical abortion (1988)

- Optimal mifepristone dose
- Optimal prostaglandin- type, dose, route of administration
- Gestational length vs efficacy
- Acceptability

Bygdeman M, Gemzell Danielsson K, Marions L: JAMWA 55: 3: 195-6, 2000.

Medical abortion

Recommended regimen (WHO, RCOG) to 10 weeks

mifepristone 200 mg +

misoprostol 800 mcg pv/sl/bc

24h - 48h interval

+ 400 mcg - Increased efficacy (Ashok et al., 2002)

Pain medication: NSAID + paracetamol, opioid if needed

verify expulsion/home test

- Rh prophylaxis not recommended in Ist trimester
- General antibiotics prophylaxis not recommended
- Same dosage irrespective of BMI

Medical abortion

Recommended regimen (WHO, RCOG) > 10 weeks

mifepristone 200 mg +

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Pain medication: NSAID + paracetamol, opioid if needed

verify expulsion/home test

- Rh prophylaxis not recommended in Ist trimester
- General antibiotics prophylaxis not recommended
- Same dosage irrespective of BMI

Medical abortion

- Highly effective, safe and accepted method
- Can be used for all gestational lengths (not limited to 9 w)
- Can replace surgical abortion
- Mifepristone –
  - Limited availability
  - Approved in about 60 countries
  - Expensive
- Misoprostol– alone highly effective
- But priming with mifepristone increases efficacy, allows lower dose and less side effects

How can we increase access to high quality, safe abortion care?

Development and implementation of simplified medical abortion

1. ”Home use” of misoprostol
2. Telemedicine/ self managed abortion
3. Task - shift / - sharing
4. Simplified procedures for Follow Up
5. Post Abortion Contraception, quickstart
6- Post Abortion Care (mPAC)
7. Expanding access (from very early to > 12 weeks)

Ongoing studies:

V EMA
I NTRAM
P RIMA

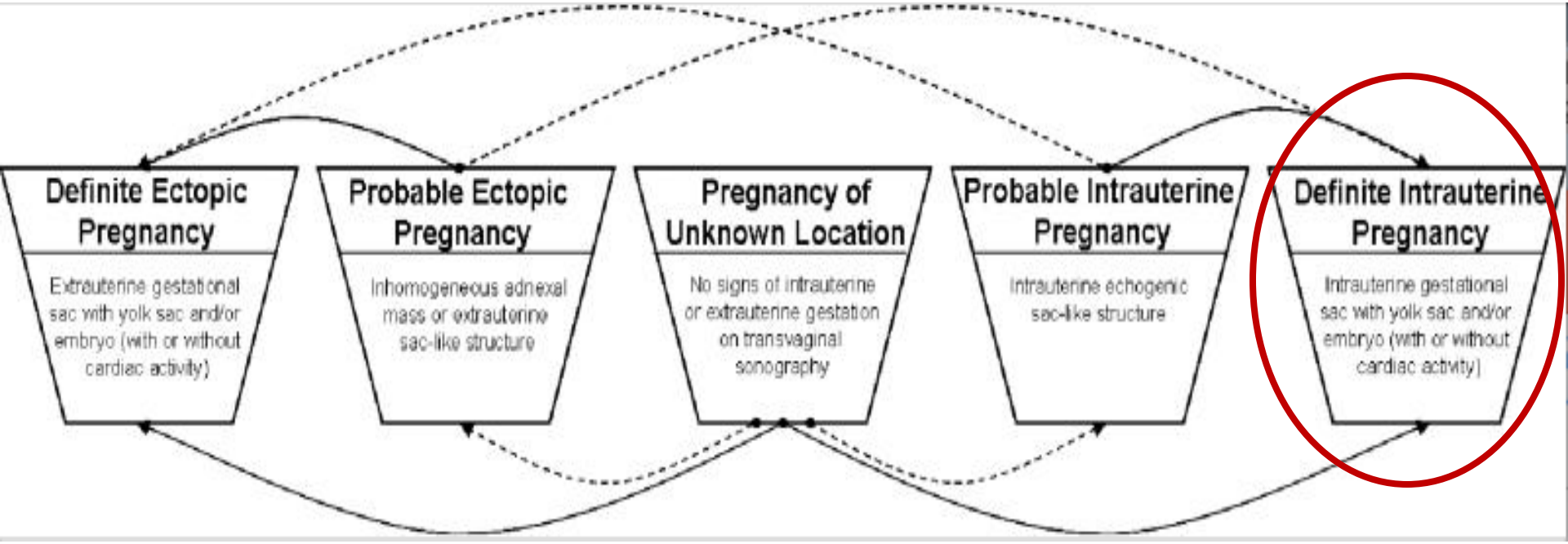
LOWE
wow!

From very early….

Very Early Medical Abortion (VEMA)

VEMA, very early medical abortion

- An increasing number of women present very early for their abortion.
- Different protocols in clinical routine
- **Alt 1** Start treatment only if confirmed intrauterine pregnancy (IUP) (ultrasound)
- **Alt 2.** Start without delay irrespective of confirmed IUP or not (VEMA)
  - Follow up-when and how
  - Definition of IUP



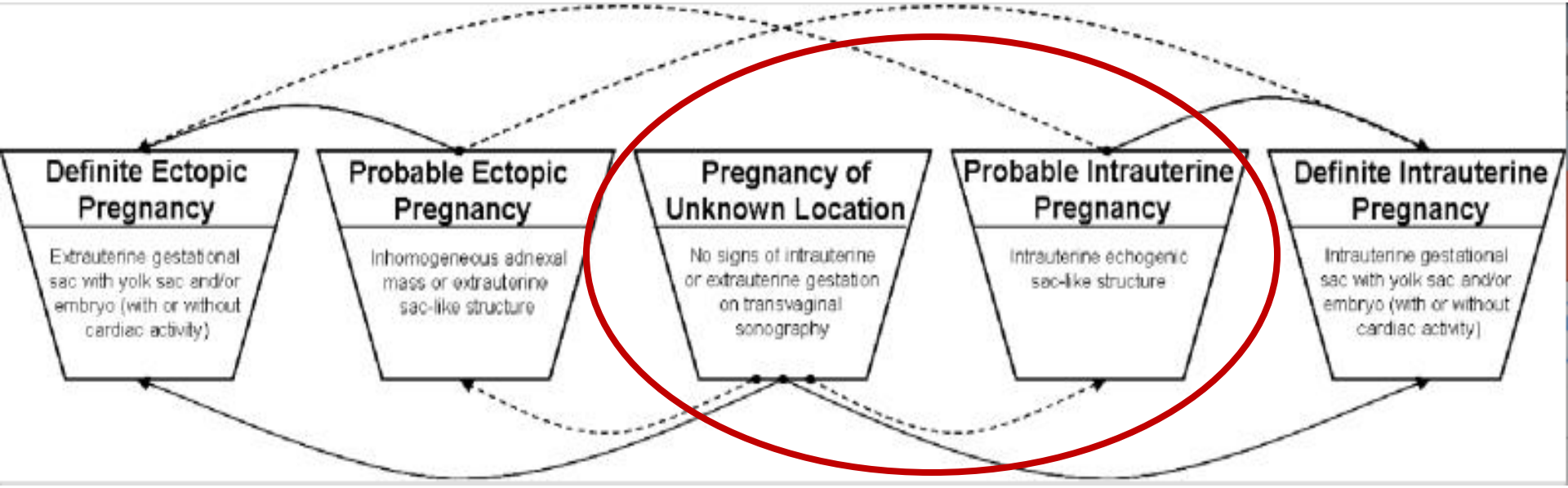
Barnhart et al, 2012

Confirmed IUP –

Definite Intrauterine Pregnancy

Gestational sac with: 1) yolk sac and /or

2) fetal structure, with or without cardiac echo



Barnhart et al, 2012

Not confirmed IUP

- Empty cavity (PUL)
- Intrauterine sac like structure (Probable IUP)
  - Irrespective of location
  - Irrespective of decidualisation

Potential disadvantages

- Limited data on VEMA
- Is it less effective vs confirmed IUP ?
- Is it safe?
  - Fear of a missed ectopic pregnancy
- Is it more inconvenient?
  - More expensive?
  - Repeat u/ s-hcg, US

Potential advantages

- psykological
- physiological:

→less pregnancy symptoms

→less bleeding

→less pain

- possibility to discover and treat an ectopic pregnancy early, before rupture

(WHO. Safe abortion, 2012) (Rodger MW et al. Contraception 1989)

Previous studies?

- 3 studies on VEMA
  (Goldstone et al.Contraception, 2013, Shaff et al.Contraception,2001, Heller R, Cameron S. Fam Plann Reprod Health Care, 2015)

- No missed ectopic pregnancy

- In 2 of the studies lower efficacy in VEMA (ongoing pregnancy and incomplete aboriton)

BUT

- Small studies. The largest included 125 VEMA patients

Study design

Register based multicenter cohort study

To assess the efficacy and safety of medical abortion in women with very early pregnancy and no confirmed intrauterine pregnancy - VEMA.

- Comparing 1500 women with no IUP with women with IUP
- Gestations ≤ 49 days
- Matched in regard to age, parity, initiation of abortion treatment
- MedGyn, Austria and Sahlgrenska, Sweden

Results

VEMA failure (ie ongoing pregnancy or incomplete abortion)

- NOT more likely in women with no confirmed IUP compared to confirmed IUP, gestations ≤ 49 days
- Significantly lower rate of treatment for incomplete abortion
- Findings support that VEMA is effective and safe

Recommendation

Avoid unnecessary delay!

Offer medical abortion accordingly

on time complete correct™

VEMA Protocol

→* positive pregnancy test

→* Inform about signs and symtoms – to seek care

→* S-hCG on the day of mifepristone-before taking the tablet

→* FU S-hCG after 1 week

→* If konc.fall >80% no further intervention needed

- If symtpoms of ectopics, spontaneous abortion or molar pregnancy, discripancy between LMP and US →investigate pathological pregnancy

- If the initial s-hCG- > 5000 consult a specialist..

Study Title

Efficacy of Very Early Medical Abortion – a randomized controlled non-inferiority trial

- EuraCT number 2018-003675-35
- Sponsor's protocol number WV 2018 VEMA 1.0
- Clinical study phase Phase IV

Study objective:

- To investigate if the efficacy of VEMA is non-inferior within a non-inferiority margin of 3 percent to delayed abortion treatment initiated when an intrauterine pregnancy (IUP) can be confirmed on ultrasound?

- Trial sites:

Sweden, Nepal, Australia, NZ, USA, DK, Norway, Scotland, Austria

Ectopic pregnancy

- A protocol for Very Early Medical Abortion may further improve outcomes and help to detect ectopic pregnancy before rupture.
- Symptomatic women with signs of or suspected ectopic pregnancy have been identified and treated as per clinical routine.
- The rate of asymptomatic women with an ectopic pregnancy is similar to that reported earlier of approximately one percent.
- All asymptomatic ectopic pregnancies have been identified and
- treated before rupture and according to the proposed trial protocol and procedures.

…To much later.

Medical abortion > 12 weeks

Complications following induced abortion

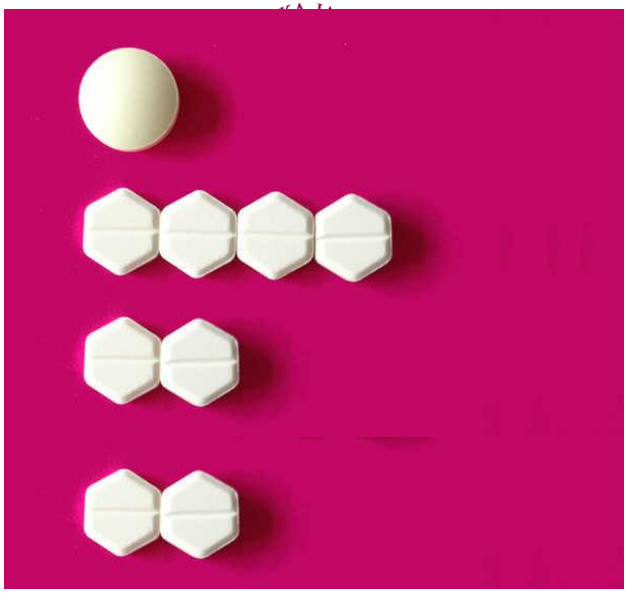
Second trimester abortion constitute

10-15% of all induced abortions but are responsible for

two thirds of all major complications.

WHO 1997

Medical abortion > 12 weeks



- Start early!

- Mean time to expulsion 5-7 hours
- Median dose of misoprostol: 1200 mcg
- 97% abort within 5 doses of misoprostol (= within 15 hours)
- Wait for the placenta if no bleeding, Examine before descision on surgery!
- Need for surgical intervention: 2-15%

Contraception. 2004 Jan;69(1):51-8.
Midtrimester medical termination of pregnancy: a review of 1002 consecutive cases.
Ashok PW1, Templeton A, Wagaarachchi PT, Flett GM.

Hum Reprod. 2005 Aug;20(8):2348-54. Epub 2005 May 5.
A randomized trial of mifepristone in combination with misoprostol administered sublingually or vaginally for medical abortion at 13-20 weeks gestation.
Hamoda H, Ashok PW, Flett GM, Templeton A.

Study Title

PRIMA - Medical abortion from day 85 to 153 of gestation: A randomized comparison between administration of the initial dose of misoprostol at home or in the clinic

- EudraCT: 2018-000964-27
- Ethical approval: 171220, Regionala etikprövningsnämnden, Stockholm Dnr. 2017/2312-31/2
- Protocol Code number: WP2018
- N=900

Study objective:

- To investigate the proportion of women who are treated as day-care patients (day-care being defined as 9 hours from time of admission) while performing a medical abortion from day 85 to day 153 of gestation.

Post abortion contraception

(INTRAM, LOWE)

Background

LARCs (long acting reversible contraception) ie IUDs and Implant

- are the most effective methods to prevent unwanted pregnancy
- IUDs have the highest satisfaction, and continuation rates

Women want something that is effective, safe and with few side effects

Yet % OCC >> %LARC

Winner et al, N Engl J Med, 2012 United Nations DoEaSA, Population Division. Trends in Contraceptive Use Worldwide 2015. Peipert et al, Obstetr Gynecol ,2011 Kopp-Kallner PlosOne 2014
Hellström et al., Eur J Contra RH 2019

Recommendation on immediate insertion of implants –

Quickstart resulted in higher use and lower rates of repeat uplanned pregnancy.

It is most effective in settings where women do not come for follow up

BUT

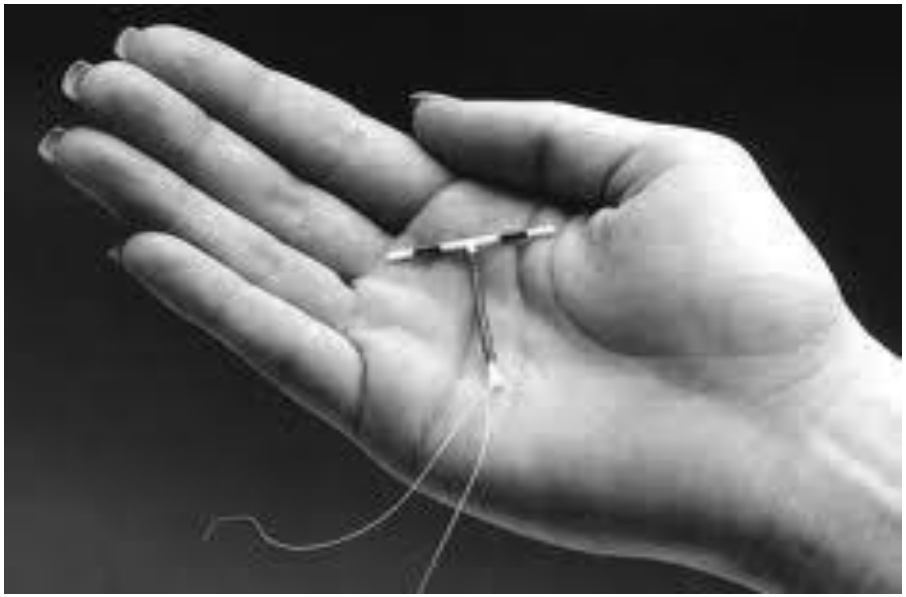
There is sufficient evidence to implement it in ALL settings as there are no negative consequences

Women preferred quickstart **p<0.001**

Hognert H, et al.,Hum Reprod. 2016

IUD/IUS and medical abortion

- RCT (N= 129) → 9w
- **Chose IUD or IUS**
- Early (5-9 days) vs delay (2-3 wks):
- Higher insertion (1.5% vs.11.5%
- No perforation
- Low infection (N= 1 delayed gr)
- Expulsion similar (10% vs. 7%)
- Expulsion not assoc with ultrasound endometrial thickness
- Timing not affect bleeding
- IUS fewer days heavy bleed



Saav et al Plos One 2013

Impact of counselling

- To date, there are no consistent recommendations or models on how to provide effective contraceptive counselling.
(bias, coercion)

- Various counselling strategies to improve uptake of LARCs have failed to result in reduction in unintended pregnancy especially post abortion

The LOWE trial

To evaluate the effect of structured contraceptive counselling on:

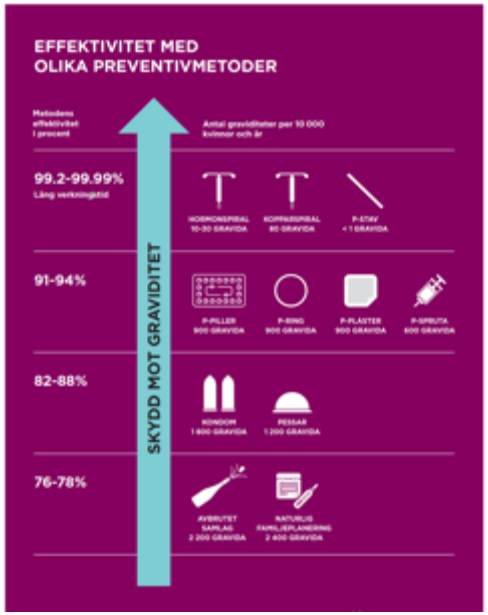
- uptake of LARCs in a real life setting, ie maintained cost and access
- pregnancy rates

Uptake defined as choice + initiation

- Cluster randomized trial (intervention vs standard), Sept 2017 –May 2020
- 1338 patients: ≥18 years, needing contraception

Intervention package

Educational Video



Effectiveness chart

Demo-box

Key questions intended to

I) reflect on how to deal with a pregnancy if it were to occur at the moment

II) specify for how long contraception planned to be used and to

III) describe menstrual bleeding patterns and IV) pain

LOWE – impact of counselling intervention

An intervention package of structured counselling, focusing on the effectiveness of contraceptive methods

→ resulted in a higher uptake of LARCs

→ fewer pregnancies among those recruited at abortion clinics at 12 months follow-up compared with routine counselling

→ High satisfaction among participants and HCP

→ Time saving

Emtell Ivarsson et al., BJOG accepted April 2021

Medical abortion provided by telemedicine

Telemedicine MA

- www.womenonweb.org
- Telemedicine service
- Online consultation with a medical doctor
- MA provided
- Helpdesk

www.womenonweb.org

Gomperts RJ, et al., Using telemedicine for termination of pregnancy with mifepristone and misoprostol in settings where there is no access to safe services. BJOG. 2008 Aug;115(9):1171-5

Effectiveness and acceptability of medical abortion through telemedicine – a non-inferiority RCT

- Women On Web (WOW) - Online abortion counselling service since 2006, offers MA to women pregnancy <10+0 weeks
- Safe, acceptable and effective (Gomberts et al. BJOG 2008 Aug115(9):1171–5, Aiken et al BJOG 2017 Jul;124(8):1208-15, Les et al Eur J Contracept Reprod Health Care 2017 Oct;22(5):360-2)
- Covid pandemic with increasing need for telemedicine also where abortion is legal (eg UK, April 2020)
- No RCTs on the subject

DOI: 10.1111/j.1471-0528.2008.01787.x
www.blackwellpublishing.com/bjog

Short communication

Using telemedicine for termination of pregnancy with mifepristone and misoprostol in settings where there is no access to safe services

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[a]Women on Waves, Amsterdam, the Netherlands [b]Women's Wallet, Amsterdam, the Netherlands [c]Women on Web, Minneapolis, MN, USA [d]Department of Woman and Child Health, Karolinska Institutet, Stockholm, Sweden [e]Department of Obstetrics and Gynaecology, Hevoziekenhuis, Almere, the Netherlands

Correspondence: RJ Gomperts, Women on Waves, PO Box 15683, 1001 ND, Amsterdam, the Netherlands. Email gomperts@womenonwaves.org

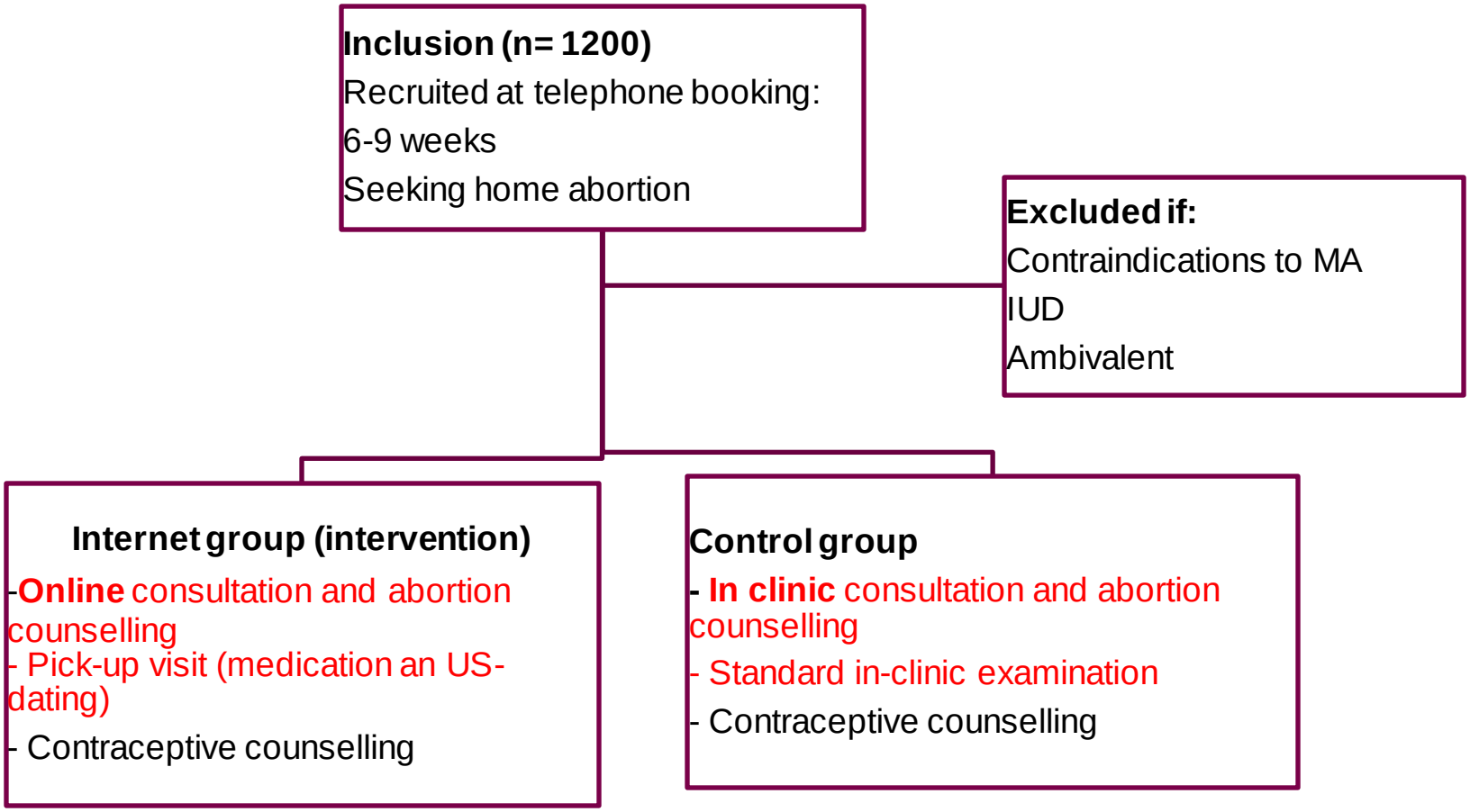
Accepted 25 February 2008.

Women on Web is a service that uses telemedicine to help women access mifepristone and misoprostol in countries with no safe care for termination of pregnancy (TOP). This study reviews the telemedicine service. After an online consultation, women with an unwanted pregnancy of up to 9 weeks are referred to a doctor. If there are no contraindications, a medical TOP is conducted by mail. After maximising the follow up from 54.8 to 77.6%, 12.6% decided not to do the TOP and 6.8% of the women who did the medical TOP at home needed a vacuum aspiration. Telemedicine can provide an alternative to unsafe TOP. Outcomes of care are in the same range as TOP provided in outpatient settings.

Keywords Abortion, buccal misoprostol, e-health, home-use, mifepristone, self-administration, telemedicine.

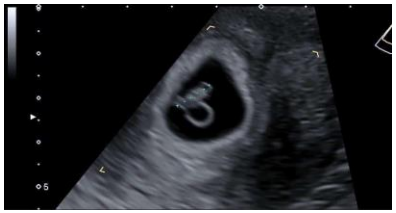
Effectiveness and acceptability of medical abortion through telemedicine – a randomised controlled non-inferiority trial

Method



Sub-study: Is US necessary to determine gestational length?

- Correlation between US/LMP-dating



Results (n=173)

Mean difference LMP vs US

-2.1 days

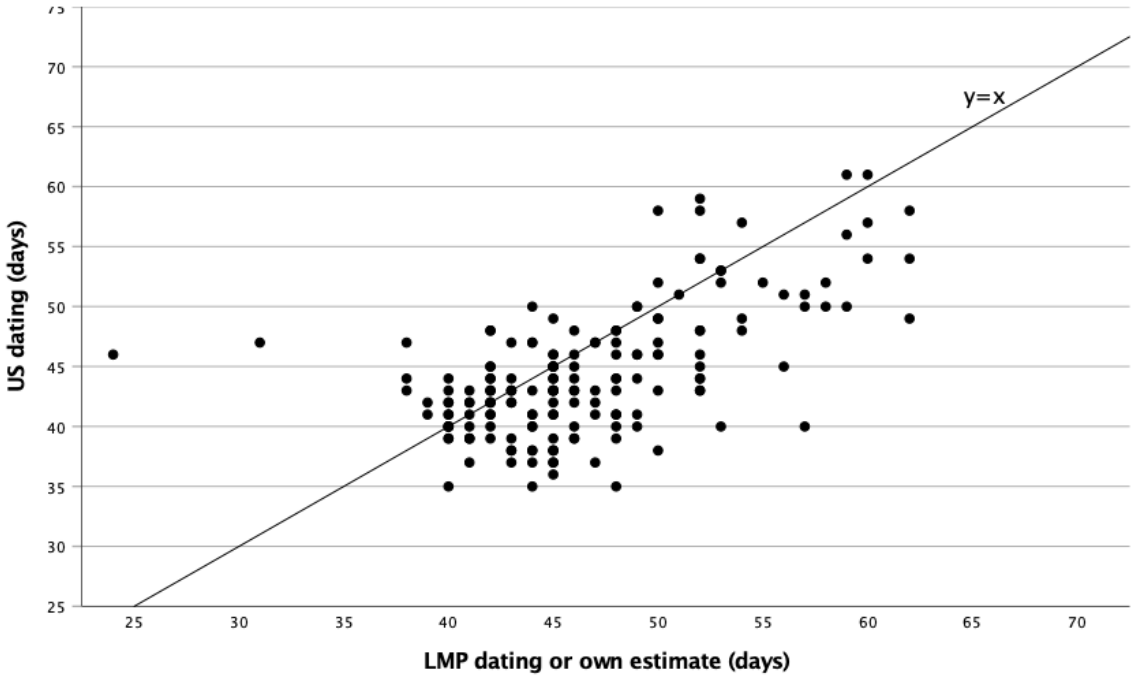
Understimate >7 days

2.3% (4)

Correlation

- **LMP vs. US, r=0.61**
- Own estimare vs US, r=0.54

(Previous studies r = 0.30-0.70)



US-dating not always necessary to decide gestational length in TM

Conclusion

- Looking forward to results from our ongoing RCTs
- THANKS to all collaborators for your hard work and support!

Lowe V-I-P wow!

Research Group on Post-Ovulatory Methods for Fertility Regulation, UNDP/UNFPA/WHO/ World Bank Special Programme of Research, Development and Research Training in Human Reproduction, WHO, and KI/K team
Swedish research council, FORTE, ALF, KI/K

THANK YOU!

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