Preventing unsafe abortion

R Kulier
Geneva Foundation for Medical Education and Research
March 2004
Definition of Terms

- "abortion" refers to the termination of pregnancy from whatever cause before the fetus is capable of extrauterine life.
- "spontaneous abortion" refers to those terminated pregnancies that occur without deliberate measures.
- "induced abortion" refers to termination of pregnancy through a deliberate intervention intended to end the pregnancy (WHO, 1994).
Definition of unsafe abortion

- "...a procedure for terminating unwanted pregnancy either by persons lacking the necessary skills or in an environment lacking the minimal medical standards of both" which therefore exposes the women to an increased risk of morbidity and mortality.

(WHO, 1993)
Effects of the introduction of the anti-abortion law in Romania (1966)
Unsafe abortion - consequences

- Morbidity, mortality
- Health care sector
Data collection

- Hospital admissions for complications
- Community surveys
- Abortion providers’ surveys
- Mortality studies
- Unsafe abortion database

<table>
<thead>
<tr>
<th></th>
<th>World total</th>
<th>Africa</th>
<th>Asia</th>
<th>Europe</th>
<th>Latin America</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence rate</td>
<td>13</td>
<td>27</td>
<td>11</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>(unsafe abortions per 1000 women 15-49)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence ratio</td>
<td>15</td>
<td>16</td>
<td>13</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td>(unsafe abortions per 100 live births)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated number of deaths due to unsafe abortion</td>
<td>78 000</td>
<td>34 000</td>
<td>38 500</td>
<td>500</td>
<td>5000</td>
</tr>
<tr>
<td>Proportion of maternal deaths (% of maternal deaths due to unsafe abortion)</td>
<td>13</td>
<td>13</td>
<td>12</td>
<td>17</td>
<td>21</td>
</tr>
</tbody>
</table>
Methods

- Surgical
- Non-surgical
- Menstrual regulation (MR)
  - generally used to describe early evacuation of the uterus, after a delayed menses, often without confirmation of pregnancy
Medical methods

- Prostaglandin
- Mifepristone
- Combination, dose, route
  - Methotrexate
  - Tamoxifen
Antigestagen

- Developed during 1960s
- Mifepristone (RU 486)
  - Suppression of folliculogenesis and ovulation
  - endometrium
- Receptors
  - Progesteron
  - Glucocorticoid
Mifepristone

- Action
  - endometrium
  - uterus
  - cervix

- Pharmacokinetics
  - Linear 2-25 mg/day
  - Non-linear above 100 mg/day
Misoprostol, Gemeprost

- Prostaglandin E1 + E2
- Effectiveness: < 90%
- Side effects
Strategy - Cochrane systematic review

- Randomised controlled trials
- Critical appraisal
- Meta-analysis where appropriate
- Search and methods according to Cochrane Fertility Regulation Group Guidelines
Approach

☐ Pregnant women, first trimester (<14 wks)

☐ Interventions
  - Medical
  - Surgical
  - Medical vs Surgical

☐ Outcomes
  - effectiveness, complications, side effects, acceptability
Medical abortion – structure of the review

- Combined regime: mifepristone/prostaglandin
  - Dose, route, time of administration, type of PG, split dose
- Combined regime: methotrexate/prostaglandin
  - Dose, route, timing
- Single vs combined regime
- Others
  - Tamoxifen, laminaria etc

- 14 main comparisons
Medical methods  

- Systematic review
- 39 trials included
- 14 main comparisons
- Main outcome: effectiveness

Kulier 2004
Medical methods  Kulier 2004

Combination:

Mifepristone 200 – 600 mg
followed by
Prostaglandin
  Type
  Dose
  Route
  Time interval
### Medical methods
---

**Kulier 2004**

**dose of mifepristone**

**Review:** Medical methods for first trimester abortion

**Comparison:** 01 combined regimen mifepristone/prostaglandin: dose of mifepristone: 600mg vs 200mg

**Outcome:** 01 failure to achieve complete abortion

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>RR (fixed)</th>
<th>Weight</th>
<th>RR (fixed)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 all</td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>McKinley M600po</td>
<td>7/110</td>
<td>7/110</td>
<td>4.66</td>
<td>1.00</td>
<td>[0.36, 2.78]</td>
<td>B</td>
</tr>
<tr>
<td>WHO 01 GPI pv</td>
<td>37/447</td>
<td>34/449</td>
<td>22.58</td>
<td>1.09</td>
<td>[0.70, 1.71]</td>
<td>A</td>
</tr>
<tr>
<td>WHO M400po</td>
<td>95/797</td>
<td>85/792</td>
<td>56.76</td>
<td>1.11</td>
<td>[0.84, 1.46]</td>
<td>A</td>
</tr>
<tr>
<td>WHO 00 GPI pv</td>
<td>22/389</td>
<td>24/388</td>
<td>16.00</td>
<td>0.91</td>
<td>[0.52, 1.60]</td>
<td>A</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1743</td>
<td>1739</td>
<td>100.00</td>
<td>1.07</td>
<td>[0.87, 1.32]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 0.40, df = 3 (P = 0.94), I² = 0%
Test for overall effect: Z = 0.53 (P = 0.59)

---

**Total events:** 161 (Treatment), 150 (Control)

Test for heterogeneity: Chi² = 0.40, df = 3 (P = 0.94), I² = 0%
Test for overall effect: Z = 0.53 (P = 0.59)
Medical methods Kulier 2004
misoprostol po vs pv

Review: Medical methods for first trimester abortion
Comparison: 05 combined regimen mifepristone/prostaglandin: misoprostol po vs pv
Outcome: 01 failure to achieve complete abortion

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>El-Refaey M600M600</td>
<td>17/130</td>
<td>7/133</td>
<td>64.36 2.48 (1.07, 5.79)</td>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Schaef M800M200</td>
<td>29/548</td>
<td>4/596</td>
<td>35.64 7.89 (2.79, 22.28)</td>
<td></td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>678</td>
<td>729</td>
<td></td>
<td>100.00</td>
<td>4.41 (2.32, 8.38)</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 46 (Treatment), 11 (Control)
Test for heterogeneity: Chi^2 = 2.97, df = 1 (P = 0.08), I^2 = 66.3%
Test for overall effect: Z = 4.53 (P < 0.00001)
Medical methods Kulier 2004
mifepristone alone vs combined

Review: Medical methods for first trimester abortion
Comparison: 07 mifepristone alone vs combined regimen mifepristone/prostaglandin
Outcome: 01 failure to achieve complete abortion

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron M160CP1pv</td>
<td>8/20</td>
<td>1/19</td>
<td>6.30 7.60 (1.05, 55.14)</td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swahn M120CP1co</td>
<td>6/14</td>
<td>11/28</td>
<td>45.06 1.09 (0.51, 2.33)</td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zheng M600PG2pv</td>
<td>45/95</td>
<td>8/97</td>
<td>48.64 5.74 (2.86, 11.53)</td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>129</td>
<td>144</td>
<td>100.00 3.76 (2.30, 6.15)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 59 (Treatment), 20 (Control)
Test for heterogeneity: Chi² = 12.06, df = 2 (P = 0.002), I² = 83.5%
Test for overall effect: Z = 5.29 (P < 0.00001)
### Medical methods

**prostaglandin vs combined regime**

Kulier 2004

**Review:** Medical methods for first trimester abortion

**Comparison:** Prostaglandin alone vs combined regimen (all)

**Outcome:** Failure to achieve complete abortion

<table>
<thead>
<tr>
<th>Study/or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 al</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheng PGE1&amp;T</td>
<td>36/76</td>
<td>20/75</td>
<td></td>
<td>54.11</td>
<td>1.78 [1.14, 2.77]</td>
<td>A</td>
</tr>
<tr>
<td>Creinin M800&amp;MT</td>
<td>16/30</td>
<td>3/31</td>
<td></td>
<td>7.93</td>
<td>5.51 [1.79, 17.00]</td>
<td>A</td>
</tr>
<tr>
<td>Jain M800&amp;MI</td>
<td>15/125</td>
<td>5/119</td>
<td></td>
<td>13.77</td>
<td>2.86 [1.07, 7.61]</td>
<td>A</td>
</tr>
<tr>
<td>Jain M900&amp;TM</td>
<td>7/75</td>
<td>6/75</td>
<td></td>
<td>13.44</td>
<td>1.40 [0.47, 4.21]</td>
<td>B</td>
</tr>
<tr>
<td>Ozeren MF900&amp;MT</td>
<td>15/36</td>
<td>4/36</td>
<td></td>
<td>10.75</td>
<td>3.75 [1.38, 10.21]</td>
<td>A</td>
</tr>
<tr>
<td>02 ≤ 45 days gestation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jain M800&amp;MI</td>
<td>9/80</td>
<td>3/75</td>
<td></td>
<td>100.00</td>
<td>2.81 [0.79, 10.00]</td>
<td>A</td>
</tr>
<tr>
<td>03 &gt; 45 days gestation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jain M800&amp;MI</td>
<td>6/45</td>
<td>2/44</td>
<td></td>
<td>100.00</td>
<td>2.93 [0.63, 13.76]</td>
<td>A</td>
</tr>
</tbody>
</table>

**Favours treatment**

**Favours control**
Methotrexate

☐ Folic acid antagonist
☐ Toxic on trophoblast
☐ Combination with prostaglandin
  ■ Effectiveness ~ 95%
☐ Fetal anomalies
Conclusions - medical methods

- Combined regimes are more effective
- Mifepristone 200 mg seems adequate in the combined regime
- Vaginal prostaglandin is more effective compared to oral
- Prostaglandin side effects are common
Medical methods - unresolved issues

- No firm conclusion:
  - Effectiveness: dose, type or time of prostaglandin, splitting of dose
  - Acceptability po vs pv
  - Methotrexate: dose, time, route of PG
- Early vs late?
Medical vs Surgical Say 2002

- 5 randomised controlled trials
- 4 comparisons:
  - Prostaglandin vs vacuum aspiration
  - Mifepristone vs vacuum aspiration
  - Mifepristone/prostaglandin vs vacuum aspiration
  - Methotrexate/prostaglandin vs vacuum aspiration
## Medical vs Surgical

### Comparison: Prostaglandin vs Vacuum Aspiration

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Controls</th>
<th>Peio OR (95% CI, Fixed)</th>
<th>Weight</th>
<th>Peio OR (95% CI, Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amonorrhea 49 days or less</td>
<td>1 / 35</td>
<td>0 / 16</td>
<td>4.3</td>
<td>4.55 [0.07, 295.14]</td>
<td></td>
</tr>
<tr>
<td>VACO 1997</td>
<td>16 / 203</td>
<td>6 / 216</td>
<td>98.7</td>
<td>2.63 [1.03, 6.32]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95%)</td>
<td>16 / 234</td>
<td>6 / 234</td>
<td>100.0</td>
<td>2.69 [1.14, 6.35]</td>
<td></td>
</tr>
<tr>
<td>Chi-square 0.06 (df=1) Z=2.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Amonorrhea 63 days or less

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Controls</th>
<th>Peio OR (95% CI, Fixed)</th>
<th>Weight</th>
<th>Peio OR (95% CI, Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtotal (95%)</td>
<td>0 / 0</td>
<td>0 / 0</td>
<td>0.0</td>
<td>Not Estimable</td>
<td></td>
</tr>
</tbody>
</table>

### Total (95%) (df=1) Z=2.25

<table>
<thead>
<tr>
<th>Events</th>
<th>Controls</th>
<th>Peio OR (95% CI, Fixed)</th>
<th>Weight</th>
<th>Peio OR (95% CI, Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 / 234</td>
<td>6 / 234</td>
<td>100.0</td>
<td>2.69 [1.14, 6.35]</td>
<td></td>
</tr>
</tbody>
</table>
### Medical vs surgical

Say 2003

<table>
<thead>
<tr>
<th>Outcomes: Duration of bleeding</th>
<th>Prostaglandin vs vacuum aspiration</th>
<th>WMD (95% CI Fixed)</th>
<th>Weight %</th>
<th>CI (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anenorrhoea less than 43 days</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WMC 1867</td>
<td>203</td>
<td>6.90 (0.90)</td>
<td>216</td>
<td>3.70 (1.40)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>203</td>
<td>216</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chi-square 0.00 (df=0) Z=45.49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anenorrhoea less than 63 days</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chi-square 0.00 (df=0) Z=0.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>203</td>
<td>216</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chi-square 0.00 (df=0) Z=45.49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Surgical methods

- Vacuum aspiration
- Dilatation/curettage
- Manual vacuum aspiration (MVA)
Surgical methods for first trimester abortion  
Kulier 2003

- 3 trial included
- 2 comparisons:
  - Vacuum aspiration vs dilatation & curettage
  - Metal vs plastic cannula for vacuum aspiration
- N = 767
### Surgical methods for first trimester abortion

Kulier 2003

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of trials</th>
<th>No of participants</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive blood loss</td>
<td>2</td>
<td>257</td>
<td>1.02 (0.21-4.95)</td>
</tr>
<tr>
<td>Febrile morbidity</td>
<td>2</td>
<td>467</td>
<td>0.84 (0.26 – 2.71)</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>2</td>
<td>467</td>
<td>0.67 (0.11 – 3.95)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2</td>
<td>467</td>
<td>2.03 (0.38 – 10.97)</td>
</tr>
</tbody>
</table>
Surgical methods

VA vs MVA

- RCT; < 56 days of amenorrhoea
  - MVA n = 91
  - VA n = 88
  - Effectiveness
  - Complications
## Surgical methods

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MVA (n=91)</th>
<th>VA (n=88)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing pregnancy</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Re-curettage</strong></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>infection</strong></td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
Mifepristone

- Second trimester
- Cervical ripening
- Induction of labour
- Postcoital contraception
- Endometriosis/Uterine Leiomyomata
- Hormone dependent tumors
- Antiglucocorticoid action
Medical vs surgical  Say 2003

- Small sample sizes
- Medical:
  - Longer duration of bleeding
  - Single regimes less effective than vacuum
- acceptability
Medical vs surgical  

- n = 363, partially randomised
- < 63 days
- Mifepristone 600 mg/gemeprost 1 mg/48 h
- vs
- Vacuum aspiration
### Medical vs surgical

Henshaw 1994

<table>
<thead>
<tr>
<th></th>
<th>Medical n = 172</th>
<th>Vacuum aspiration n = 191</th>
<th>95% CI for difference between proportions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete abortion</td>
<td>94.2%</td>
<td>97.9%</td>
<td>-0.003 to 0.078</td>
</tr>
<tr>
<td>Minor complications within</td>
<td>11.0%</td>
<td>15.7%</td>
<td>-0.116 to 0.023</td>
</tr>
<tr>
<td>Requiring uterine curettage</td>
<td>5.8%</td>
<td>2.1%</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

- Safe and effective methods for first trimester abortion are available
- Acceptability data scarce
- Medical methods:
  - Longer duration of bleeding
  - Single regimes less effective
- Serious complications are rare
Collaborators

- Linan Cheng
- Anis Feki
- Metin Gülmezoglu
- Justus Hofmeyr
- Lale Say
In circumstances where abortion is not against the law... to ensure that abortion is safe and accessible."

(Key actions ICPD+5, paragraph 63)

"In all cases, women should have access to quality services for the management of complications arising from abortion."

(Key actions ICPD+5, paragraph 63)
• F1. Promote policy dialogue on unsafe abortion, and provide guidance to countries on how to develop, implement and evaluate programmes to prevent and address unsafe abortion.

• F2. Promote the effective management of abortion complications and postabortion care, including its integration within other reproductive health services.

• F3. Develop and promote interventions to improve access to quality care in circumstances where abortion is not against the law, with special emphasis on underserved populations.

UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)
References

- [http://www.cochrane.org/cochrane/revabstr/ab003037.htm](http://www.cochrane.org/cochrane/revabstr/ab003037.htm)
- [http://www.cochrane.org/cochrane/revabstr/ab002900.htm](http://www.cochrane.org/cochrane/revabstr/ab002900.htm)
- [http://www.popcouncil.org/rhfp/pac.html](http://www.popcouncil.org/rhfp/pac.html)
- [http://www.who.int/reproductive-health/hrp/practices/dissemination.html](http://www.who.int/reproductive-health/hrp/practices/dissemination.html)
- [http://www.cochrane.org](http://www.cochrane.org)
References