Mifegymiso in a Rural Community: How to make it work

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Presenters

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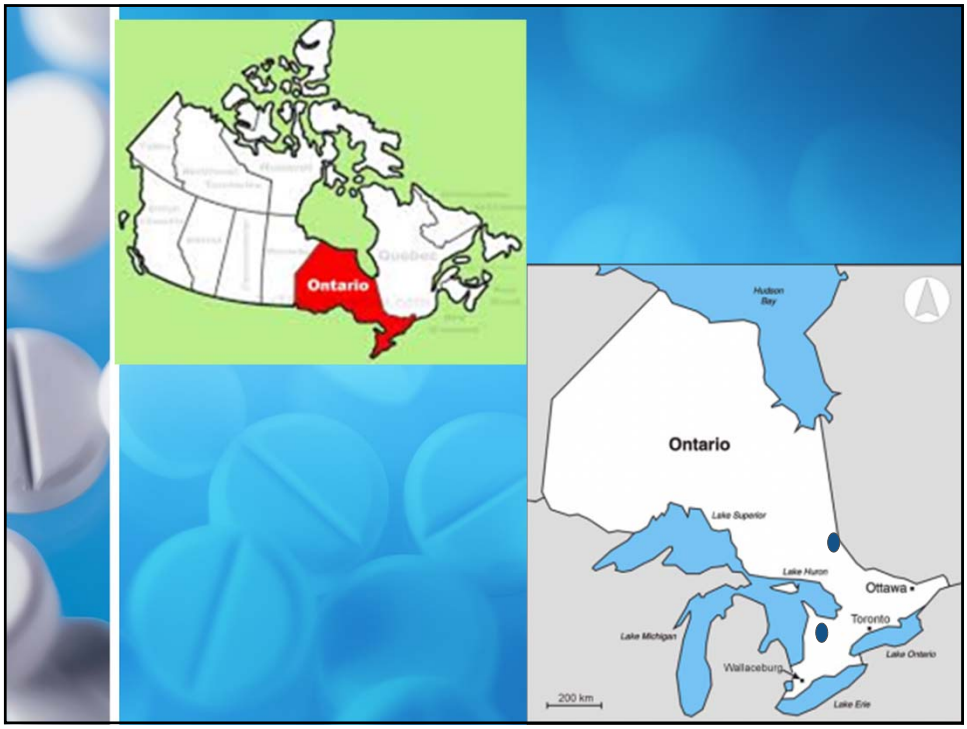

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Objectives

- By the end of this session, you will gain an understanding of:
  - **differences between Medical and Surgical abortion**
  - **advantages of medical abortion**
  - **approval and accessibility of Mifegymiso in Canada**
  - **pharmacology, potential side effects and effectiveness of Mifegymiso**
  - **prescribing Mifegymiso and providing medical abortion care in a rural community**

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Disclosure:

Despite this presentation being specifically about Mifegymiso, we have no affiliation, nor any financial interests with Celopharma.

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Definitions

- Induced Abortion
  - **Surgical Abortion**
    - Removal of pregnancy via instrumentation or aspiration of uterine cavity
  - **Medical Abortion**
    - Use of one or more medications to interrupt a pregnancy

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Statistics

- Stats from CIHI - updated to end of 2017
  - **# Induced abortions in Canada 2017: 94 030**
  - **abortion rate of 13.1/1000 women of childbearing age**
  - **Rates of abortion decreasing since 2011**
- 50% of abortions occur in women under 30 yrs of age, 50% over age 30
- In Quebec and BC, abortion services were nearly equally present in major urban centers and rural locations. Most all other provinces identified services located only in urban centers.

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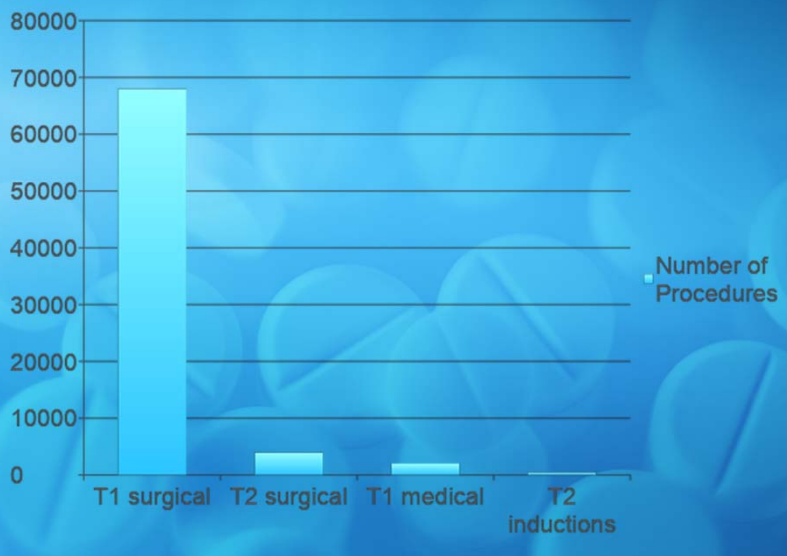
Abortions Performed in 2012 by Type



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Violence/Harassment & Stigma

- Incidents are rare in Canada
- Picketing without interference most common
- Other: bullying letters, blockade of clinic entrances, violence
- Abortion stigma may be felt by physicians providing abortion care; may be mitigated by
  - **Advocating for the patient's choice**
  - **Pride in performing abortion care**
  - **Connectedness with colleagues**
  - **Integration of abortion care into primary care and women's health**
  - **Capacity to accept conflict as normal and engaging**

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Autonomy & Confidentiality

- In Canada, requiring a partner's consent in order to have an abortion is unconstitutional
- Abortion providers shall not contact the woman's partner or parents about her decision. It is a violation of privacy & confidentiality
  - **Exception: notification of child protection services when laws concerning age of consent are violated**

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Abortion is Common, MA hasn't been

(MA=Medical abortion)

- Abortion services are accessed by nearly **1/3** of Canadian women at some point
- In 2012 only 3.8% were T1 MA; 2017 5.4% (approx 60 registered providers in 94 Canadian facilities)
  - **55% provided service in office; 45% in hospital setting**
  - **87% providers also provide SA**
  - **56% were family physicians**
  - **37% reported providing MA to woman who lived >2hrs away; 6.5% via Telemedicine**

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Advantages of Medical Abortion

- Improves access to abortion care
  - **Service in local community vs driving long distances**
  - **More physicians can provide services**
- Greater privacy
- Mifepristone-containing regimens are up to 98% effective
- Avoids surgery and complications of surgery

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Approval & Accessibility

- Health Canada originally approved Mifegymiso, a two-drug combination as a non-surgical option for early abortion in July 2015
- January 2017 became available to the Canadian public
  - **significant restrictions and red tape made it difficult for providers (physicians and pharmacists) to consider the therapy**
  - **49 day (7 week) cut off for use**

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Approval & Accessibility

- CPSO and OCP (Ontario College of Pharmacists) lobbying with Health Canada regarding their concerns
- Nov 7, 2017 updated regulation
  - **Extended the GA requirement to 63 days (9 weeks)**
  - **Updated dispensing requirements**
  - **Removed mandatory education & registration with the manufacturer**
  - **Physician no longer required to supervise a patient ingesting the medication**
  - **Health Professional Risk Communication document**

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Dispensing Mifegymiso

- There are three ways it can be dispensed according to Health Canada
  1. **Patients can take the prescription to a pharmacy and receive the medication directly from the pharmacist;**
  2. **Patients can take the prescription to a pharmacy and have the medication delivered to the physician's office; or**
  3. **Physicians can sell and dispense the medication to the patient in accordance with CPSO's Dispensing Drugs Policy**

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Training & Education

- Although training is no longer mandatory, Health Canada, SOGC, CPSO and CPA state that the health care provider needs to ensure they have sufficient knowledge, skills, judgment to prescribe medication and supervise care.
- Education program developed (SOGC, CPSO, CPA and Celopharm) available through SOGC e-Learning Portal.
  - **Includes initial Practice Assessment, 6 Module course and Exam**

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Mifegymiso Pharmacology

- MIFE 200 mg po (Day 1)
- MISO 800 mcg buccal (24-48hrs after MIFE)
- For MA up to 63 days (9 weeks) is 87-98% effective
- The risk of ongoing pregnancy is less than 3.5%
- Cost ~ $340.00 per Rx, but no cost to patient

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Mifepristone (MIFE)

- SPRM (selective progesterone receptor modulator)
- Strong anti-progesterone & anti-glucocorticoid activity
- Progestin blockade causing endometrial degeneration, uterine contractility, resumption of prostaglandin production and decreased bHCG
- Cervical softening and dilation via a non-PG pathway (increase of matrix metalloproteinase-2 expression)

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Mifepristone (MIFE)

- Peak levels in 1-2 hrs
- Elimination 1/2life is 83-90hrs

- Drug interactions (CYP450 3A4 substrate)
  - 3A4 inducers, such as: Glucocorticoids, Macrolides, Rifampin, Carbamazepine, St John's Wort, Benzo's, Barbiturates may result in increased metabolism of mifepristone, and thus possible decreased effectiveness

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Mifepristone (MIFE)

- Drug interactions
  - 3A4 inhibitors, such as: Cimetidine, Erythromycin, Ketoconazole, Spironolactone, Chloramphenicol, Secobarbital, Grapefruit Juice may result in decreased metabolism of mifepristone and increased serum levels (of limited clinical consequence)

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Misoprostol (MISO)

- Synthetic PGE1
  - Cervical ripening, uterine contractions
  - Acts on smooth muscle in GI tract > nausea, vomiting, increased peristalsis, diarrhea
- Pharmacokinetics
  - Varies by route (oral, buccal, SL, vaginal, rectal)
  - For MA, buccal*/SL/vaginal is preferred
    - Results in contractions in about 60 min, sustained action lasting 90 min and declines by 5 hrs
    - *Mifegymiso recommends buccal

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Misoprostol (MISO)

- No known drug interactions
- MISO 800 mcg (4 x 200 mcg tablets) should be self-administered at a convenient time 24-48 hours after taking mifepristone
- For buccal administration, hold 4 tablets between cheek and gums (2 tablets in each cheek pouch) for 30 minutes and then swallow any fragments

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Mifegymiso

- Comparison of 33,000 surgical abortion (SA) vs 17,000 medical abortion (MA) ≤ 63 days:
  - **Ongoing pregnancy**
    - 0.3% (MA) vs 0.1% (SA); p=0.0001
  - **Need for aspiration (incomplete abortion)**
    - 1.3% (MA) vs 0.7% (SA); p < 0.0001
  - **Hospitalization for infection**
    - 0.03% (MA) vs 0.006% (SA); p = 0.048
  - **Transfusion for hemorrhage**
    - 0.02% (MA) vs 0.003% (SA); p = 0.048

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Mifegymiso

- Common side effects
  - **Vaginal bleeding**
    - Amount of bleeding exceeds menses loss
    - Heavier bleeding reported up to 74%
  - **Cramping/pelvic pain**
    - Rated as moderate to severe (>/= 6 on 11-pt scale); may cause significant distress
    - Usually managed with NSAIDs or acetaminophen
  - **Nausea, vomiting, transient fever/chills, headache, breast tenderness, fatigue, hot flushes, dizziness**

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Contraindications

- Known ectopic pregnancy
- Chronic adrenal failure
- Inherited porphyria
- Uncontrolled asthma
- Known hypersensitivity to mifepristone or misoprostol
- Concurrent long term systemic corticosteroid therapy
- Bleeding disorder or on anticoagulant therapy
- Anemia (Hb <95)
- IUD in place (remove first)
- Unconfirmed gestational age
- Ambivalence in the abortion decision

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Breastfeeding & Lactation

- Data is limited.
- In a study of 12 breastfeeding women undergoing MA, levels of MIFE in breast milk ranged from undetectable to 0.913uM/L. The relative infant dose is less than 1.5%. No specific recommendation can be made about breastfeeding following mifepristone.
- Misoprostol is metabolized to misoprostol acid, which is biologically active and excreted in breast milk in small quantities. Theoretically may cause undesirable effects such as diarrhea in breastfeeding infants. No specific recommendation or restriction is made about breastfeeding following misoprostol.

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Providing MA Care

- Prior to prescribing Mifegymiso:
  - **Exclude ectopic pregnancy and confirm GA ideally by u/s;**
  - **Ensure that patients have access to emergency medical care in the 14 days following administration;**
  - **Schedule follow up 7-14 days after patients take the medication to confirm complete pregnancy termination;**
  - **Counsel each patient on the risks & benefits of Mifegymiso, including bleeding, infection and incomplete abortion;**
  - **Obtain the patient's informed consent to take the medication**

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Providing MA Care

- MD to review with patient:
  1. **Mifegymiso Patient Information Brochure**
     - Reviews the medications they will be taking
     - Possible contraindications to review with care provider
     - How to take the medications
     - S&S of the termination
     - Possible adverse effects of the treatment
     - Follow up plans
     - Important contact information

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Providing MA Care

2. Patient Consent Form
   - Mifegymiso is irreversible
   - both steps must be completed
   - must followup with healthcare professional
   - may require surgical followup
   - must have access to emergency care

I have made the decision to end my pregnancy (abortion) after consultation with my health professional. I have made this decision without coercion and on my own free will and being of sound mind.

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Providing MA Care

- 3. Patient Information Card
  - **Patients are instructed to take their Information Card with them if they visit an emergency room or another health professional who did not Rx Mifegymiso, so that the health professional will be aware that the patient is undergoing a MA**
- 4. Patient Medication Information

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Gestational Age Determination

- By LMP (1st day of LMP)
  - **If u/s not widely available**
  - **If menses is predictable, regular and recorded; occurred at expected time; menses was of expected duration**
- By Ultrasound (gold standard)
  - **Confirms IUP vs ectopic**
  - **If LMP unsure, irregular menses, bleeding or pain in pregnancy or risk factors for ectopic (prior tubal surgery, tubal ligation, assisted reproductive techniques, IUD, hx salpingitis, hx PID)**

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Pregnancy of Unknown Location (PUL)

- Positive pregnancy test with no evidence of IUP nor ectopic pregnancy on US
- Differential diagnosis
  - **Early IUP, multiple pregnancy, pregnancy failure, and ectopic pregnancy**
- In the absence of risk factors/clinical symptoms and no gestational sac, if the βhCG is ≤ 2,000 IU/L OR when a likely gestational sac is present without a yolk sac or fetal pole, it is reasonable to proceed with MA with ectopic precautions

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PUL protocol

- Day 1: Baseline βhCG. Mifepristone.
- Day 2: Misoprostol administered
- Option A: Rapid Follow-Up
  - **Day 3: Follow-Up βhCG**
    - Drop ≥ 50% between first and second βhCG: highly indicative of complete abortion
  - **If βhCG drop is less than 50% at day 3, continue with option B**
- Option B: Standard Follow-Up
  - **Day 7: Follow-up βhCG**
    - Drop ≥ 80%: complete abortion
    - If less than 80%, further investigation required

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Other US findings

- Molar pregnancy
  - **MA is not appropriate; referral**
- Multiple pregnancy
  - **If within GA limits, MA is appropriate**
- Missed/incomplete abortions
  - **Misoprostol alone regime**

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MA in Temiskaming Shores

- Communicated locally with community pharmacy, hospital (ER committee and administration), Chief of Radiology & Public Health Unit.
- For patients presenting to the ED
  - **Medical Directive for RNs in Triage**
    - Pre-printed lab requisition
      - CBC, Group & Screen, quantitative bHCG
    - Pre-printed ultrasound requisition
      - Urgent 24-48hr u/s for Medical Abortion to confirm IUP and GA; with 24-48hr turn around for report (can be verbal from radiologist)
    - Nursing Information Sheet for Education

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Temiskaming Hospital ER Medical Directive

Emergency Room Nurse Initiated Medical Abortion Medical Directive

- This medical directive is to be used by nursing when a patient is triaged requesting information / advice / questions regarding abortion.
- The patient is not required to see the ED physician on call as long as the patient is stable with no active bleeding or cramping.
- Nursing will offer the patient physician consultant options (see list below).

Laboratory

***RN to provide pre-filled outpatient laboratory requisition for the following:

Hematology: **Routine**

☒ CBC

Biochemistry: **Routine**

☒ Quantitative β HCG

☒ Group and Screen

Diagnostics

*** RN to provide pre-filled outpatient ultrasound requisition for the following:

☒ Ultrasound ☒ Urgent – within 24-48 hours and report required within 24-48 hours

Reason: to confirm pregnancy and gestational age for possible medical abortion

Notification to Physician

☒ Copy of the emergency department form with completed medical directive attached to be put in the consult physicians mailbox

☒ Call the consult physician with patient I.D. information

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Nursing Information Sheet

Medical Abortion with Mifegymiso
Nursing Information Sheet

Health Canada has approved the use of Mifegymiso as an option for women wishing to terminate a pregnancy. This is called a Medical Abortion.

Mifegymiso is a prescription that includes Mifepristone 200 mg x 1 tablet + Misoprostol 200 mcg x 4 tablets. The Mifepristone is provided on Day 1, followed by Misoprostol within 24-48 hours.

Women can use this medication as long as they have:

- **a confirmed intrauterine pregnancy**, and
- **are up to 63 days (9 weeks) gestation**.

The patient must see a physician in consultation to determine if they are eligible, to provide education on medical abortion, medication information, possible side effects and appropriate follow up.

Upon a patient presenting to the ER department, the triage RN can institute the **Medical Directive for Medical Abortion**. It outlines necessary blood work, ultrasound requisition and arranging a consultant physician for the patient. The patient does not need to see the ER physician as long as the patient is stable (vital signs stable, not actively bleeding or cramping). The patient can see the ER physician if they request to be seen.

Once the patient meets the consultant physician and determines the patient wants to proceed with medical abortion and is eligible, the patient will take their prescription to Findlay's Drug Store to fill their prescription and take the medication as instructed. It is mandatory for the consultant physician to book a follow up visit with their patient within 7-14 days after taking the prescription. This is the physicians' responsibility to arrange.

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MA in Temiskaming Shores

- For patients presenting to the ED
  - **Medical Directive for RNs**
    - Patient can choose provider listed for MA
    - RN will call provider with Patient ID information and place ER sheet in mailbox
    - Patient does not have to see the ER doc on call unless the patient requests, if VS are stable and no concerning symptoms (bleeding, cramping, abdominal pain, abnormal vaginal discharge)

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MA in Temiskaming Shores

- Provider will call patient directly to schedule a timely consultation to review results, counseling/education and provide Rx.
- If a patient presents to the PHU, or to another health professional
  - **Can directly refer to local provider (timely)**

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MA in Temiskaming Shores

- Provider will schedule a follow up visit within 7-14 days.
  - **Confirm completion of MA**
    - Serial bHCG +/- u/s if indicated
  - **Discuss contraception (ovulation can start within 8 days post MA)**
    - Highly suggested to plan for IUD insertion at the follow up visit

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Re-presenting to the ED

- Patients are provided the following information:
  - **Contact your health professional for immediate medical attention if you experience:**
    - Heavy vaginal bleeding (soaking 2 (or more) thick sanitary pads per hour for 2 consecutive hours or have large fist-sized clots)
    - Prolonged heavy bleeding or severe cramping (expected for 11-14 bleeding; heavier on the first few days)
    - Cramping not improved by pain relief medication
    - Fever/chills/malaise lasting >6 hrs

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Re-presenting to the ED

- Abnormal vaginal discharge
- Severe abdominal pain
- Feeling sick (including weakness, nausea, vomiting, diarrhea, abdo pain, cramps, fatigue, chills) with or without a fever more than 24 hours after taking misoprostol tablets

- Appropriate measures
  - Anxiolytics/sedatives
  - Adjuvent medications (ie loperamide for diarrhea)
  - IM or IV analgesics
  - Removal of tissue from cervical os if present

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Failed MA

- Misoprostol may be used off label for the management of retained products or ongoing pregnancy when diagnosed at the first follow up visit in a woman who is clinically stable and desires to avoid surgical management.
- Misoprostol 800mcg Buccal or Vaginal may be considered.
- At a subsequent follow-up, if retained products or ongoing pregnancy continue, surgical management is advised.

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Temiskaming Shores Data

- 26 cases in 16 mos (1.6 referrals/month)
- Avg GA 7.5 wks (range 6-9wks)
- Avg age 29 (range 19-44; 60% <30yrs)
- Referral received from
  - **MD/NP office 11 (42%)**
  - **Health Unit 8 (31%)**
  - **ED 4 (15%)**
  - **Self 3 (12%)**
- 23% first pregnancy
- 15% previous terminations (all surgical)
- 100% patients qualify for MA; all <9wks GA
  - **2 didn't return call for booking**
  - **1 decided to keep pregnancy**

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Temiskaming Shores Data

- 27% no show rate for follow up visit; most still completed their f/u bloodwork (3 did not)
  - **of those with follow up visits and/or bloodwork completed = 0% failure rate**
- 2 went to ED
  - **1-pain; 2-bleeding/passed tissue in ED**
- Birth control
  - **large variety if using birth control or not and various types**
  - **majority were "about to start" (BCP, IUD booking appt, tubal ligation appt)**
  - **4 (15%) interested or planning on IUD after termination**

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Final Messages

- ⅓ Canadian women will seek abortion services at some point in their lifetime
- Mifegymiso is a safe and effective form of medical abortion
- Minimal resources are required for rural providers to offer this service
- Pre arranged medical directives and policies can help ensure that women may access the services in a timely and safe manner

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