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A Retrospective Cost-Effectiveness Analysis of Mifepristone–Misoprostol Medical Abortions in the First Year at the Regina General Hospital



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ABSTRACT

Objective: In July 2017, mifepristone–misoprostol (mife/miso) became available for medical abortion at the Regina General Hospital's Women's Health Centre (RGH WHC). We investigated whether the proportion of abortions performed medically changed as a result of the introduction of mife/miso, whether using mife/miso instead of the surgical alternative would result in cost savings to the health care system, and whether abortion type differed between patients residing in and outside of Regina.

Methods: We conducted a retrospective chart review of all 306 medical abortions from the RGH WHC between July 1, 2017 and June 30, 2018. We obtained medical and surgical abortion information from that year and the preceding one from an administrative database. Statistical methods were used to calculate the costs of mife/miso, methotrexate-misoprostol (MTX/miso) and surgical abortion, as well as cost-effectiveness ratios.

Results: The proportion of medical abortions increased from 15.4% in 2016/2017 to 28.7% in 2017/2018 ($\chi^2_1 = 54.629$; $P < 0.001$). Calculated costs for mife/miso, with and without complications were CAD \$1173.70 and CAD \$1708.90, respectively, versus CAD \$871.10 and CAD \$1204.10, respectively, for MTX/miso, and CAD \$1445.95 and CAD \$2261.95, respectively, for hospital-based

vacuum aspiration. At a willingness-to-pay threshold of CAD \$318 (the cost of mife/miso), statistical modelling showed a 61.3% chance that mife/miso was more cost-effective than surgical abortion and a 90.8% chance that it was more cost-effective than MTX/miso. Patients from Regina were significantly more likely ($\chi^2_1 = 29.406$; $P < 0.001$) to receive a medical abortion (34.9% of abortions) than those living outside of Regina (19.6% of abortions).

Conclusion: The proportion of abortions completed medically increased significantly over the period studied. Patients from Regina were more likely to receive medical abortion during both time periods. Mife/miso had a >50% probability of cost-effectiveness over both surgical and MTX/miso options.

RÉSUMÉ

Objectif : En juillet 2017, la combinaison mifépristone-misoprostol a été rendue disponible aux fins d'avortement médicamenteux au centre de santé des femmes du Regina General Hospital. Nous avons tenté de déterminer si l'arrivée de la mifépristone-misoprostol avait eu une incidence sur la proportion d'avortements médicamenteux, si le recours à la mifépristone-misoprostol plutôt qu'à l'avortement chirurgical allait engendrer des économies pour le système de santé, et si le type d'avortement pratiqué différait entre les patientes qui habitent à Regina et à l'extérieur.

Méthodologie : Nous avons mené un examen rétrospectif des dossiers médicaux pour tous les avortements médicamenteux réalisés au centre de santé des femmes du Regina General Hospital entre le 1^{er} juillet 2017 et le 30 juin 2018. Nous avons obtenu les renseignements relatifs aux avortements médicamenteux et chirurgicaux réalisés pendant cette année et la précédente à partir d'une base de données administrative. Nous avons utilisé des méthodes statistiques pour calculer les coûts de la mifépristone-misoprostol, du méthotrexate-misoprostol et des avortements chirurgicaux, ainsi que les rapports coûts-efficacité.

Résultats : La proportion d'avortements médicamenteux a augmenté, passant de 15,4 % en 2016-2017 à 28,7 % en 2017-2018 ($\chi^2_1 = 54,629$; $P < 0,001$). Les coûts calculés de la mifépristone-misoprostol, avec et sans complication, étaient de 1173,70 \$ CA et

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1708,90 \$ CA, respectivement, par rapport à 871,10 \$ CA et 1204,10 \$ CA, respectivement, pour le méthotrexate-misoprostol, et à 1445,95 \$ CA et 2261,95 \$ CA, respectivement, pour l'avortement par aspiration à l'hôpital. D'après un seuil de disposition à payer de 318 \$ CA (le coût de la mifépristone-misoprostol), le modèle statistique a révélé que la mifépristone-misoprostol avait 61,3 % des chances d'être plus économique que l'avortement chirurgical et 90,8 % des chances d'être plus économique que le méthotrexate-misoprostol. Les patientes de Regina étaient significativement plus susceptibles ($\chi^2 = 29,406$; $P < 0,001$) de subir un avortement médicamenteux (34,9 % des avortements) que les patientes vivant à l'extérieur de Regina (19,6 % des avortements).

Conclusion : La proportion d'avortements médicamenteux a augmenté de manière significative au cours de la période à l'étude. Les patientes de Regina étaient plus susceptibles de subir un avortement médicamenteux au cours des deux périodes. La mifépristone-misoprostol présentait une probabilité de > 50 % de rapport coût-efficacité favorable par rapport à l'avortement chirurgical et l'avortement médicamenteux par méthotrexate-misoprostol.

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INTRODUCTION

Over the last 10 years, approximately 100 000 elective terminations of pregnancy have occurred annually in Canada.¹ Nearly one-third of Canadian women have at least one abortion.² In 2015, Health Canada approved the use of mifepristone plus misoprostol (mife/miso; Canadian brand name Mifegymiso, manufactured by Celopharma), both World Health Organization essential medicines, for medical abortion. The less effective off-label regimen of methotrexate plus misoprostol (MTX/miso) was previously used.³ Until July 2017, this off-label regimen was only used for gestational age (GA) $\leq 7^0$ weeks, according to local practice and not in accordance with Society of Obstetricians and Gynaecologists of Canada (SOGC) or National Abortion Federation (NAF) guidelines,^{3,4} at the Regina General Hospital Women's Health Centre (RGH WHC). The RGH WHC is the main abortion facility and only surgical termination centre for southern Saskatchewan; it performs 900 to 1100 abortions annually.

Mife/miso is safe, effective, and generally considered acceptable by patients and providers.^{3,5–12} It is 95% to 98% effective up to 49 days after last menstrual period and 87% to 98% effective up to 63 days,^{3,6,8–11} and there is emerging evidence of safety and efficacy up to 77 days.^{3,12–15} The first Canadian retrospective case series

of mife/miso implementation found 96.7% effectiveness at a GA of up to 63 days.¹⁶

In addition to medical abortion being considered safe and effective, patients receiving medical abortion (of various regimens) are satisfied with their experience.^{17,18} Some studies show a strong preference for medical abortion,^{17–19} whereas others indicate that surgical abortion is preferable.^{20–22} Research indicates patients are more satisfied when given the ability to choose their preferred method.³

Although it varies among countries, the percentage of abortions in Canada that were medical (vs. surgical) between 2012 and 2017 (before mife/miso's availability) ranged from 4.0% to 5.4%.^{1,23} A Canadian estimate of abortion costs (to both the health care system and patients) calculated costs of \$1233.34 for mife/miso, \$1174.81 for MTX/miso, and \$1779.08 for hospital-based vacuum aspiration.²⁴

History of Mifepristone–Misoprostol at Regina General Hospital

In July 2017, mife/miso became available at the RGH WHC. It was initially only covered for patients with some private plans, who fell under Saskatchewan Formulary coverage or First Nations patients with status, with an out-of-pocket cost of \$356.90 after July 31, 2017. In March 2018, mife/miso was added to the hospital formulary, making it available free of charge to all patients at the WHC.

Research Questions

The study's purpose was to assess the impact of introducing mife/miso at the WHC on both patients and the health care system. Our research questions were as follows:

1. What were the success rates, loss to follow-up rates, and complications during the first year of mife/miso administration at the centre?
2. Was there an increase in the proportion of induced abortions that were completed medically after the introduction of mife/miso in July 2017?
3. What were the potential cost benefits of using mife/miso rather than vacuum aspiration?
4. Did abortion type differ for patients residing in Regina versus those who were required to travel?

METHODS

We conducted a retrospective chart review of all 306 RGH WHC medical abortion patients, plus surgical abortion patients at $\leq 9^0$ weeks who experienced complications, between July 1, 2017, and June 30, 2018. We obtained information about surgical abortions (and medical and surgical abortions during the preceding year) from an

administrative database, and the total number of mife/miso prescriptions dispensed and drug coverage data were obtained from the main Regina pharmacy dispensing it. We obtained ethical approval from the Research Ethics Board of the former Regina Qu'Appelle Health Region (REB-18-58), now part of the Saskatchewan Health Authority.

Mifepristone–Misoprostol Medical Abortion Protocol

Patients were required to self-refer to the RGH WHC. During the study period, the RGH WHC included 9 family physicians and 1 obstetrician who provided medical and surgical abortion services, with one provider working at the clinic per day. Registered nurses discussed pregnancy options at the patient's initial consultation (in person or by phone). Medical abortion was considered an option for patients $\leq 9^0$ weeks GA by ultrasound, which was expanded from 7^0 weeks after the first month of the study period, per Health Canada regulations. Patients were considered ineligible for medical abortion if they had known ectopic pregnancy, GA $> 9^0$ weeks, molar pregnancy, intrauterine device in situ, expressed ambivalence (< 6 of 10 on ambivalence scale), or an inability to complete phone follow-up.

Once the patient was deemed eligible, an initial dating ultrasound (a Health Canada requirement during the study period) and laboratory work were ordered, including complete blood count, renal panel, liver enzymes/bilirubin, quantitative serum beta-human chorionic gonadotropin (β hCG), urine chlamydia and gonorrhea screening, and prenatal serology (including HIV, rubella, hepatitis B/C, and syphilis screens). Only complete blood count and quantitative serum β hCG are recommended in SOGC and NAF medical abortion guidelines^{3,4}; the rest are local protocol. The physician reviewed these results and prescribed mife/miso (mifepristone 200 mg orally and misoprostol buccally 24–48 hours later) directly to the patient at a second in-person appointment. Nurses phoned patients for follow-up; an 80% drop in serum β hCG 7 days after misoprostol administration was considered a complete abortion.

Data Analysis

All charts were deidentified and entered into a REDCap database.²⁵ Descriptive statistics and 2×2 chi-square tests were produced.

Costing

We used a micro-costing (bottom-up) approach from the perspective of the health system, in 2020 Canadian dollars. Because the decision to adopt mife/miso lies with the health care system, the economic analysis was performed from its perspective. This approach entails identifying and

specifying all resources used by individual patients, assuming resource use is the same across each method of abortion, including medication cost, diagnostic and laboratory services cost, staffing, and supplies (Table). We determined unit costs by collecting drug price data from the Saskatchewan Formulary database,²⁶ expenditure records from diagnostic and laboratory services, physician payment from the Saskatchewan Medical Association payment schedule,²⁷ and other facility expenditure records. We determined complication costs using the Canadian Institute for Health Information cost of a standard hospital stay and the resource intensity weight for the case mix group for hospital admissions²⁸; the cost of a single uncomplicated surgical abortion for repeat vacuum aspiration at WHC; and the estimated cost of anesthesia, physician fees, and operating room staffing for repeat vacuum aspiration in the operating room. We did not account for infrastructural cost because this was not collected during micro-costing and because of the complexity associated with estimating such cost.

Economic (Cost-Effectiveness) Analysis

The result of the analysis is expressed as an incremental cost-effectiveness ratio (ICER). We set the willingness-to-pay (WTP) threshold—the maximum amount that our payer, the health care system, would be willing to pay for one additional complete abortion²⁹—at \$318, the cost of mife/miso. Effect was measured as the success rate (i.e., the proportion of complete abortions for each method).

Sensitivity Analysis

We performed a probabilistic sensitivity analysis to determine the robustness of our result in relation to the uncertainty in cost and effect (success rate) estimations. Instead of specific values for the success rate of each abortion method, we chose a uniform distribution with observed minimum and maximum values as the range of distribution to reflect uncertainty in our estimate of the success rate for each abortion method, with equal probability of selection for all values within the specified range. The probability of complete abortion, with minimum and maximum tested based on literature-reported rates, was between 81.7% and 98% for MTX/miso³; between 98% and 99.7% for vacuum aspiration ($\leq 9^0$ weeks, for comparison with the maximum gestation for mife/miso in our study period)³⁰; and between 97.7% and 99.7% (upper boundary for vacuum aspiration) for mife/miso.¹⁵

Similarly, we assumed a uniform distribution for examination of uncertainty in cost estimation. The cost of a single, uncomplicated abortion estimated for each method was the same across patients; we varied this estimate by 10%, an arbitrary number chosen to further examine the uncertainty

Table. Calculated abortion costs for medical and surgical abortions (unique expenses only)

Costs, CAD\$	Vacuum aspiration	Mifepristone–misoprostol	Methoxerate–misoprostol
Base cost (with complication)			
Medication			
Mifepristone + misoprostol	—	318.00	—
Methotrexate + misoprostol	—	—	15.40
Other (misoprostol, naproxen)	7.49	—	—
Diagnostic			
Baseline + follow-up ^a serum β hCG + follow-up		18.23	18.23
Pelvic ultrasound ^b	276.80	276.80	276.80
Other baseline labs	209.20	209.20	209.20
Pathology ^c	146.92	—	—
Pre-procedure consultation			
Nursing consult (30 min/58 h)	29.00	29.00	29.00
MD consult fees: fee codes 40B + 41B + 50P (“counselling” \times 15 min \times 2 + first-trimester abortion) ^d	252.50	252.50	252.50
Nursing direct costs on am of MD consultation (30 min \times 58/h)	29.00	29.00	29.00
Unit clerk support (assume 15 min per patient, \$18.88/h)	4.72	4.72	4.72
Surgical staff			
WHC staff ^e	454.40	—	—
Unit support worker ^f	18.55	—	—
Processing costs	3.64	—	—
Surgical supplies ^g	13.73	—	—
Post-procedure follow-up			
Telephone follow-up ^h	—	36.25	36.25
Total cost (without complication)	1445.95	1173.70	871.10
Complications cost, mean (range)	816.00 (253.00–3124.40)	535.20 (65.00–1961.90)	333.00 (27.80–1445.95)
Average (base cost + complications)	2261.95	1708.90	1204.10

^a Follow-up β hCG was based on \$8.60 \times 1.12 (mean number of follow-up serum β hCG tests).

^b The Health Canada requirement of ultrasound before every mifepristone–misoprostol abortion was removed after our study period.

^c Pathology fees included formalin, pathologist fee, histology staff, clerical staff, reagents/supplies, sanitary pad, and peel packing.

^d The first-trimester abortion billing code was deemed ineligible for medical abortions shortly after our study period.

^e WHC staff included nurses, office administration, nurse manager, and unit coordinator = \$4544.00 per day/2 (for half-day)/5 cases per half-day.

^f Unit support worker cost based on \$18.88 hourly wage \times 80% (for five cases in 4 h) \times 1.228 for 22.8% benefits.

^g Surgical supplies included stanhexidine, syringes, tubing, curettes, sterile gloves, intravenous tourniquet, and control syringe.

^h Cost of nursing calls determined based on median 2.5 calls per patient, which was calculated to be 37.5 minutes of work \times \$58 per hour.

Other baseline laboratory tests across all abortion types included complete blood count, blood group and antibody screen, renal panel, and liver function tests (assume alanine aminotransferase, alkaline phosphatase, bilirubin, sodium, potassium, chloride, bicarbonate, urea, and creatinine).

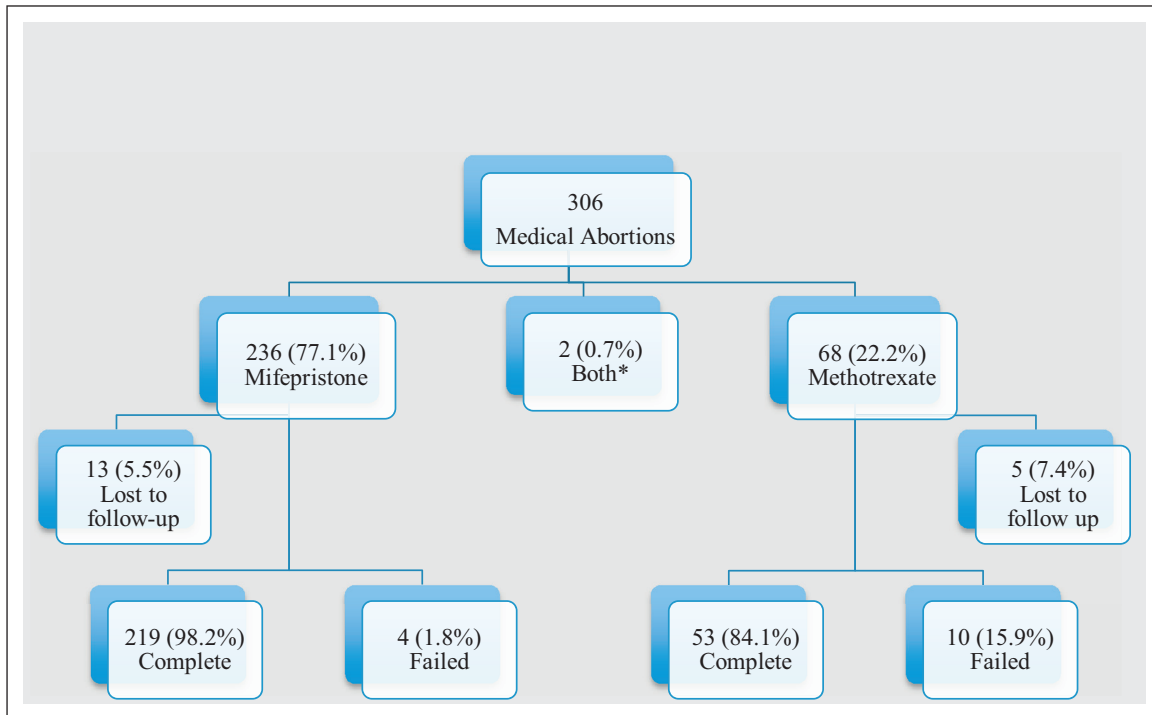
β hCG: beta-human chorionic gonadotropin; WHC: Women's Health Centre.

in this estimate. Total cost estimates for complications were allowed to vary probabilistically within their estimated minimum and maximum intervals. We summarized the cost and effectiveness of each abortion method based on 10 000 probabilistic simulations of cost and effects. The analysis was performed using R software. The results are graphed as an incremental cost-effectiveness (CE) plane and CE acceptability curve with a specified WTP range.

RESULTS

A statistically significant improvement in abortion completion rate was observed when using mife/miso rather than MTX/miso: 98.2% versus 84.1% ($\chi^2_1 = 23.790$, $P < 0.001$; Figure 1). A total of 20 (6.5%) vacuum aspirations were performed after medical abortion: 4 after mife/miso, 15 after MTX/miso, and 1 after both.

Figure 1. Summary of medical abortions performed at the Women's Health Centre between July 1, 2017, and June 30, 2018.



*In the first case, the patient who received mifepristone–misoprostol had a 79% decrease in β hCG at the 1-week follow-up. There was an increase in subsequent β hCG levels, which was ordered per clinic guidelines because an 80% decrease was not seen at 1 week. She was asymptomatic but was given methotrexate for possible ectopic pregnancy owing to rising β hCG level. She presented to the emergency department 1 week later and ultimately decided to have a vacuum aspiration, which was completed. The second patient had a pregnancy of unknown location on ultrasound with a gestational age of 7 weeks by last menstrual period. She was given mifepristone but had rising β hCG levels on follow-up. Repeat ultrasound at that time indicated a true or pseudogestational sac at 5 weeks gestational age. Methotrexate was given at that time, which resulted in complete abortion.
 β hCG: beta-human chorionic gonadotropin.

The overall mife/miso complication rate was 8.5% (20 of 236 with follow-up). Overall, 15 medical abortion patients (4.9%) visited the RGH emergency department. Eleven patients (4.7%) had retained products of conception, 2 had infections (0.8%), 6 had significant bleeding noted (2.5%), and 4 underwent dilation and curettage (1.7%; 1 in the main operating room by the gynaecologist on call, the rest at WHC under conscious sedation by family physicians). One patient had iron infusions for a hemoglobin level of 77 (0.4%), but none had a blood transfusion.

Eighteen medical abortion patients (5.9%) were lost to follow-up during our study period, with 4 being from rural communities. Nurses performed a total of 932 follow-up calls for MTX/miso and mife/miso patients (median 2.5 per patient; interquartile range 2.0–3.5; range 1–16), requiring an estimated 37.5 minutes per patient (assuming 15 minutes per nursing call, including charting) for a cost of \$36.25 per medical abortion. Further follow-up costs came from a mean of 1.12

(standard deviation 0.76) follow-up serum β hCG tests (range 0–8) per patient.

WHC performed 161 medical abortions in the year before mife/miso's introduction, compared with 306 medical abortions in the year after its introduction. The number of surgical abortions decreased from 884 to 766, and the proportion of medical abortions increased from 15.4% to 28.7% ($\chi^2_1 = 54.629$, $P < 0.001$).

After the addition of mife/miso to the hospital formulary in March 2018, 121 mife/miso abortions were provided, compared with only 6 MTX/miso abortions. Patients were more likely to receive mife/miso (95.3%) over MTX/miso (65.4%) when it was provided free of charge to them ($\chi^2_1 = 38.459$, $P < 0.001$).

The largest proportion of patients receiving medical abortions resided within Regina (73.5%). Patients from Regina were significantly more likely ($\chi^2_1 = 29.406$, $P < 0.001$) to

receive a medical abortion (34.9% of all abortions) than patients from outside Regina (19.6%).

Using data obtained from the main Regina community pharmacy dispensing mife/miso, only 45 of 136 patients (33%) paid entirely out of pocket for their mife/miso prescription up to April 2019. The Saskatchewan Ministry of Health announced in June 2019 that it would provide universal coverage of mife/miso.^{31–33}

Cost-Effectiveness

We observed a 98.2% rate of complete abortion at $\leq 9^0$ weeks with mife/miso, versus 84.1% for MTX/miso and 99.6% after vacuum aspiration. This translated into an incremental effect of 14.80% for mife/miso over MTX/miso and -1.34% over vacuum aspiration, with costs delineated in the Table. Incremental cost for mife/miso relative to using methotrexate is \$302 for a single, complete abortion without complication and $-\$272$ versus vacuum aspiration. This demonstrates an increased cost of \$302 for a 14.8% increase in the effect of mife/miso over MTX/miso.

The ICER for mife/miso relative to MTX/miso is \$2149 for a single, uncomplicated abortion and \$20 317 for mife/miso versus vacuum aspiration. Similarly, the ICER for mife/miso relative to MTX/miso for a single, complicated abortion is \$3585 (\$41 272 vs. vacuum aspiration).

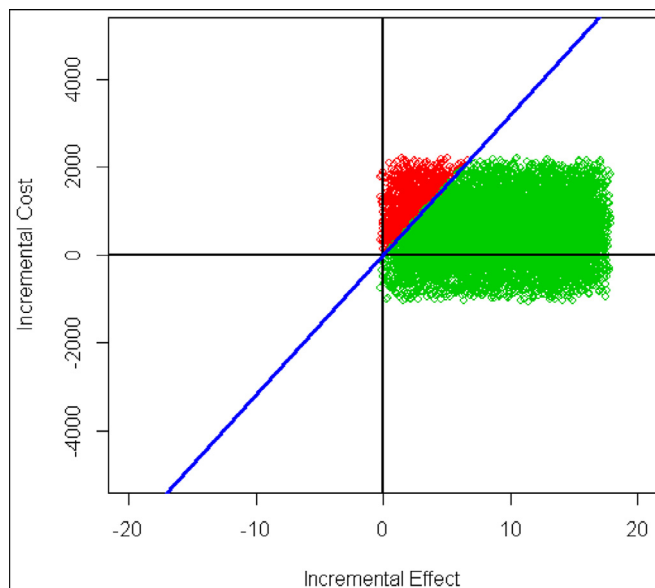
Sensitivity Analysis

On the CE plane for mife/miso relative to MTX/miso (Figure 2), the line through the origin represents the set WTP threshold at \$318, the estimated price of mife/miso. The CE plane suggests that mife/miso is likely to be more costly and more effective or less costly and more effective than MTX/miso. At \$318 WTP, the probability that mife/miso would be cost-effective relative to MTX/miso is 90.8%, and the probability is 61.4% relative to vacuum aspiration (see Figure 3, CE acceptability curves).

DISCUSSION

The proportion of medical abortions increased significantly from 15.4% to 28.7% of all induced abortions at WHC after mife/miso's introduction in July 2017. There was a significant improvement in completion rate when using mife/miso rather than MTX/miso. Our calculated completion rate of mife/miso was 98.2%, comparable to other studies.^{3,5–14,16–18} Patients were more likely to choose mife/miso over MTX/miso after the addition of mife/miso to the hospital's formulary in March 2018, when it was free of charge to all WHC patients. As expected, we found

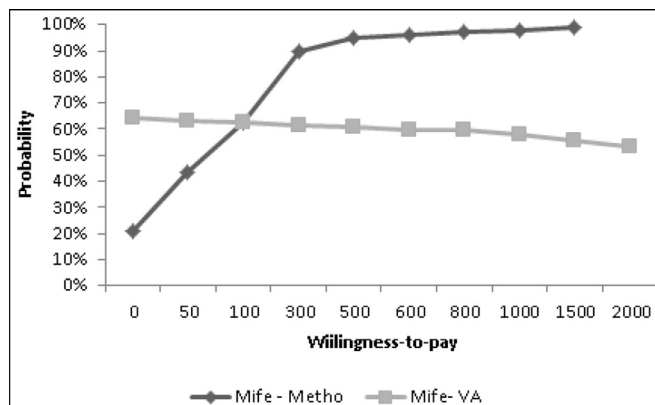
Figure 2. Cost-effectiveness plane for mifepristone versus methotrexate at willingness to pay of \$318.



medical abortion to be cheaper than surgical abortion, with an ICER suggesting cost-effectiveness.

Our loss to follow-up rate of 5.9% was lower than reported rates of 9% to 30%.^{8,9,11,12,17,21} Our low rate may be a result of requiring quantitative β hCG testing and phone follow-up versus in-person appointments or ultrasounds. Although previous studies have not found a significant difference in loss to follow-up for remote versus in-clinic visits, one study did find that patients prefer the remote follow-up option.³⁴ The substantial nursing staff effort, a median of 37.5 minutes of follow-up per medical abortion, could also account for our low rate. Of the 18 patients lost to follow-

Figure 3. Cost-effectiveness acceptability curves for mifepristone relative to methotrexate and vacuum aspiration.



up, only 4 were from rural populations. The relatively low loss to follow-up rates among rural patients support mife/miso as a safe and effective option for rural patients, despite the potentially challenging follow-up care. Fewer rural patients received a medical abortion than patients from Regina, accounting for approximately one-quarter of such cases. Given that medical abortion is safe and effective for rural patients, province-wide expansion of medical abortion provision is of great importance.

Since fall 2018, no physician fee code exists for medical abortion in Saskatchewan. For the expansion of medical abortion to occur, given our calculated median of 37.5 minutes of follow-up per patient, compensation for community family physicians, nurse practitioners, and gynaecologists providing this service is necessary, especially outside Saskatchewan's two urban surgical abortion centres, Regina and Saskatoon. Tele-abortion is another feasible option for expansion. This has been successfully implemented in the United States and in other Canadian provinces, such as British Columbia.^{9,35} A provincial centralized nursing line for all Saskatchewan patients would be an efficient and cost-effective way to provide follow-up care for medical abortions. Before the COVID-19 pandemic, Regina was the only place in Saskatchewan that offered both nursing pre-abortion consultations and follow-up by phone; this has been expanded during COVID-19 and hopefully will continue afterwards.

There were several limitations to our study and our cost-effectiveness analysis. With Health Canada now abolishing the universal ultrasound requirement, costing \$276.80, many medical abortions carry an additional cost savings of \$276.80. Our calculations also assumed five surgical procedures per WHC clinic, which is often no longer the case with the advent of mife/miso, making staffing resource use higher per surgical procedure. We also assumed physician costs to be the same for both medical and surgical abortion, and Saskatchewan now has no billing code for medical abortion. Surgical abortions may cost less outside our hospital setting. Other important limitations include potentially limited generalizability based on mife/miso's first year at one centre (with extra baseline laboratory tests from NAF and SOGC guidelines) and only accounting for complications that presented to Regina's two hospitals.

CONCLUSIONS

We found mife/miso's rate of complete abortion to be 98.2%, with 5.9% lost to follow-up and 8.5% having complications. The proportion of medical abortions increased

significantly with the introduction of mife/miso. Compared with patients from outside Regina, patients from Regina were significantly more likely to receive a medical abortion. At a threshold WTP assumption of \$318 (the cost of the drug), mife/miso had a >50% chance of increased cost-effectiveness over both MTX/miso and surgical options.

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