Systemic hormonal contraception initiation after abortion: A systematic review and meta-analysis

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Systemic hormonal contraception initiation after abortion: A systematic review and meta-analysis

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ABSTRACT

Background: Immediate contraceptive initiation, including start of a method before abortion completion, is a convenient option for women seeking abortion care.

Objectives: To evaluate the effect of systemic hormonal contraception initiation on medical abortion effectiveness and the safety of hormonal contraceptive methods following abortion.


Study eligibility criteria: Studies that assessed medical abortion effectiveness after systemic hormonal contraception initiation and the safety of hormonal contraception initiation after abortion.

Participants: Pregnant persons undergoing or who had recently undergone an abortion.

Interventions: Initiation of systemic hormonal contraception post abortion or on the day of the first pill of the medical abortion.

Study appraisal and synthesis methods: We assessed study quality using the US Preventive Services Task Force evidence grading system. We created narrative summaries and calculated pooled relative risks when appropriate.

Results: We identified 16 studies for inclusion, 7 randomized controlled trials, and 9 cohorts. Nine studies assessed medical abortion effectiveness with hormonal contraception initiation and generally found no decreased risk of abortion success or increased risk of additional treatment. One fair-quality study reported a small increase in ongoing pregnancy rate with immediate depot medroxyprogesterone (DMPA) compared with delayed DMPA initiation (3.6% vs 0.9%, risk difference 2.7%, 90% confidence interval 0.4–5.6). We identified no bleeding-related safety concerns following hormonal contraception initiation after medical or surgical abortion. Pooled results were too imprecise to draw firm conclusions.

Limitations: Included studies were poor or fair quality and primarily in high-income or upper-middle-income settings.

Conclusions: Abortion effectiveness did not differ between immediate vs delayed initiation of most systemic hormonal contraceptive methods after a first trimester medical abortion. However, immediate DMPA initiation did show increased ongoing pregnancy. Bleeding effects with hormonal contraception initiation postabortion appeared minimal.

Implications: Initiating a hormonal contraceptive method after an abortion and as early as the same day as the first pill of the medical abortion is an option if contraception is desired. The slight increase in ongoing pregnancy with immediate DMPA initiation highlights the importance of information provision during contraceptive counseling.
1. Introduction

Contraceptive initiation after abortion is important for those who desire delayed or no future pregnancy. Following an induced or spontaneous abortion, ovulation can return as early as 8 to 10 days and usually within 1 month [1-4]. Reports of intercourse within 2 weeks after an induced abortion are common [5]. Moreover, contraceptive counseling and services are considered a human right and should be available and included as a routine component of postabortion care [6-8].

Currently, recommendations in the World Health Organization’s (WHO) Medical eligibility criteria for contraceptive use state that there are no restrictions for the use of combined estrogen-progestogen (combined hormonal) or progestogen-only methods (not including intrauterine devices [IUDs]) immediately following a first trimester abortion, second trimester abortion, or septic abortion (Category 1) [9]. However, current medical abortion regimens that include mifepristone, an antiprogestogen, could have decreased effectiveness with concurrent administration of progestogen-containing contraceptive methods. Additionally, immediate use of hormonal contraceptive methods after an abortion could cause less predictable bleeding patterns, which could affect satisfaction and continuation [10].

The 2 objectives of this systematic review are to assess the effect of hormonal contraception initiation on medical abortion effectiveness (abortion success) and to assess the safety of hormonal contraceptive methods following an induced (medical or surgical), spontaneous, or septic abortion. We focus on non-IUD hormonal methods and will evaluate the effect of timing of hormonal contraception initiation (immediate vs delayed) and hormonal contraception initiation (hormonal method vs non-hormonal/no method).

2. Methods

2.1. Inclusion and exclusion criteria

We included studies that assessed medical abortion effectiveness after hormonal contraception initiation and the safety of hormonal contraception initiation after abortion (Table 1). We included pregnant persons undergoing or who had recently undergone an induced abortion (medical or surgical in the first or second trimester), spontaneous abortion (treated surgically, medically, or expectantly managed), or septic abortion. We focused on systemic hormonal contraception, including combined hormonal methods (oral, patch, ring, or injectable) and progestogen-only methods (oral, injectable, or implant). Nonhormonal comparison groups included individuals using any nonhormonal contraceptive method (e.g., copper intrauterine device [Cu-IUD], barrier method, sterilization) or no contraceptive method. We defined immediate initiation of contraception as: (1) for medical abortion, day of first or second medication use prior to abortion success; (2) for surgical aspiration, the day of or day prior to surgical evacuation for induced, spontaneous, or septic abortion; or (3) for medically or expectantly managed spontaneous or septic abortion, the time of presentation prior to diagnosis of successful outcome. We defined delayed contraceptive initiation as initiation at follow-up (usually between 1 and 4 weeks) after abortion success (all types).

The main outcomes of interest included medical abortion effectiveness following systemic hormonal contraception initiation and safety of systemic hormonal contraception with medical, surgical, spontaneous, or septic abortion. We accepted any measurement of abortion success for medical abortion effectiveness (e.g., surgery to complete abortion, additional surgical or medical treatment, ongoing pregnancy). Safety outcomes included adverse health events: thromboembolic events (by self-report or clinical diagnosis), bleeding outcomes up to 12 weeks after abortion (changes in hemoglobin/hematocrit, bleeding related method discontinuation, or other self-reporting methods), and pelvic infection up to 12 weeks after abortion.

2.2. Sources

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance [11]. We searched PubMed, Popline, Cochrane Library, and ClinicalTrials.gov for all primary peer-reviewed research from database inception through January 6, 2020 and included randomized controlled trials [RCTs], cohort studies, and case-control studies in any language (Appendix A). We examined previously published systematic reviews and key review reference lists for relevant articles.

2.3. Study selection

Three authors (CK, AN, and EBB) independently screened all titles, abstracts and full texts identified from the initial search to determine eligibility for inclusion. We used a standard template for data abstraction (Tables 2 and 3).

2.4. Quality assessment

Two authors (CK and AN) assessed the quality of each individual study using the United States Preventive Services Task Force grading criteria [12,13]. We rated study quality as good, fair, or poor based on evaluation criteria that included random sequence generation and allocation concealment (for RCTs), selection of participants (for cohort and case-control studies), maintenance of comparable groups, participation rate, extent of loss to follow-up, rigor and completeness of exposure and outcome measurements, adjustment for potential confounders, sample size and precision, and clear definition of interventions and consideration of all important outcomes. We resolved any disagreements between authors for selection, abstraction, or quality assessment by discussion.

2.5. Data synthesis

All authors participated in summarizing and systematically assessing the evidence. We synthesized findings descriptively. We pooled study results when we found comparable study aims, design and outcomes with little statistical heterogeneity. We performed the meta-analysis using Review Manager 5.3 Software (Cochrane Collaboration, Oxford, UK). We pooled data from RCTs on the number of abortion outcome events and number of participants assigned to each treatment group and used a Peto fixed-effect model to calculate pooled odds ratios and 95% confidence intervals (95% CI). We used the standard Cochrane $\chi^2$ to assess statistical heterogeneity and $I^2$ to evaluate magnitude of heterogeneity (greater than 75% indicates considerable heterogeneity) [14,15].
Table 1
Inclusion criteria of studies to assess medical abortion effectiveness after systemic hormonal contraception (HC)\textsuperscript{*} initiation and safety of systemic HC initiation after abortion

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>Included studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical abortion</td>
<td>Immediate HC</td>
<td>Delayed HC initiation</td>
<td>Abortion success</td>
<td>5 (4 RCTs, 1 cohort)</td>
</tr>
<tr>
<td>Individuals undergoing medical abortion</td>
<td>HC initiation at any time</td>
<td>No HC initiation</td>
<td>Abortion success</td>
<td>5 (3 RCTs, 2 cohort)</td>
</tr>
<tr>
<td>Surgical abortion</td>
<td>Immediate HC</td>
<td>Delayed HC initiation</td>
<td>Adverse events</td>
<td>1 RCT</td>
</tr>
<tr>
<td>Individuals undergoing surgical abortion</td>
<td>HC initiation at any time</td>
<td>No HC initiation</td>
<td>Adverse events</td>
<td>6 cohort</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>Immediate HC</td>
<td>Delayed HC initiation</td>
<td>Adverse events</td>
<td>None</td>
</tr>
<tr>
<td>Individuals with spontaneous abortion</td>
<td>HC initiation at any time</td>
<td>No HC initiation</td>
<td>Adverse events</td>
<td>None</td>
</tr>
<tr>
<td>Septic abortion</td>
<td>Immediate HC</td>
<td>Delayed HC initiation</td>
<td>Adverse events</td>
<td>None</td>
</tr>
<tr>
<td>Individuals with septic abortion</td>
<td>HC initiation at any time</td>
<td>No HC initiation</td>
<td>Adverse events</td>
<td>None</td>
</tr>
</tbody>
</table>

RCT, randomized controlled trial.
\textsuperscript{*}HC, hormonal contraception is defined as systemic hormonal contraception and includes combined hormonal methods (oral, patch, ring, or injectable) and progestogen-only methods (oral, injectable, or implant).

3. Results

We identified 7860 articles (duplicates removed) in our initial search and review of abstracts led to further review of 116 full-text articles (Fig. 1). A total of 16 studies met inclusion criteria: 9 focused on medical abortion and 7 on surgical abortion (Tables 2 and 3) [16–31]. We did not identify any studies of hormonal contraception use following spontaneous or septic abortion that met our inclusion criteria. Six studies addressed timing of hormonal contraception initiation, and 11 studies compared hormonal contraception initiation with nonhormonal or no contraception. Nine studies reported on success of medical abortion after hormonal contraception initiation. Thirteen studies reported on adverse events and side effects.

3.1. Medical abortion

We identified 9 medical abortion studies that used a regimen of mifepristone 200 mg orally followed by a prostaglandin analogue 24 to 48 hours later (8 studies used misoprostol and 1 study used gemeprost) and included pregnancies <70 days gestation (Table 2) [19,20,22,24–28,31]. Six studies were RCTs [19,20,22,25–27] and 3 were prospective cohort studies [24,28,31]. Nine studies assessed medical abortion effectiveness and 6 evaluated bleeding outcomes. The quality of the studies was fair or poor.

3.1.1. Immediate vs delayed initiation of hormonal contraception

Five studies compared immediate vs delayed initiation of hormonal contraception following medical abortion [19,24–27]. All 5 studies reported abortion success outcomes [19,24–27] and 4 reported bleeding changes or bleeding-related method discontinuation [19,25–27]. One study assessed the initiation of depot medroxyprogesterone (DMPA) [27], 3 studies assessed the etonogestrel implant [24–26], and 1 study assessed combined oral contraception (COC) [19]. Immediate contraception initiation in all 5 studies was the day of mifepristone administration.

A fair-quality, noninferiority RCT assigned participants up to 75 days gestation to DMPA initiation at the time of mifepristone (n = 220) or after abortion completion (n = 226) [27]. The investigators defined abortion success as not needing surgery to complete abortion, assessed by urine pregnancy test (UPT) and/or ultrasound. They collected follow-up data within 1 month and at 4 and 7 months. The investigators found no significant differences between the groups in the proportion needing surgery to complete the abortion (risk difference 1.1%, 90% CI −2.8 to 4.9) or the proportion needing any additional treatment (risk difference −0.1%, 90% CI −5.2 to 4.9). Ongoing pregnancy before additional treatment, however, was significantly higher with immediate DMPA compared with delayed DMPA (3.6% vs 0.9%, risk difference 2.7%, 90% CI 0.4–5.6). Those in the immediate DMPA group were more likely to have ≥15 median days of bleeding compared to delayed DMPA group (p = 0.01) but no difference in self-reported bleeding heavier than menses (74% vs 78%, p = 0.27).

Two fair-quality RCTs and 1 poor-quality prospective cohort study assessed etonogestrel implants and none demonstrated a significant difference in abortion success rates, rates of surgery required to complete the abortion, or rates of additional treatment [24–26]. All 3 studies defined abortion success as not needing surgical evacuation. In a noninferiority RCT with a similar design as the DMPA trial, the etonogestrel implant insertion was on the same day as mifepristone (n = 236) or after the abortion (n = 240) [26]. The investigators assessed abortion success by UPT and/or ultrasound. The study included those who were eligible for an outpatient medical abortion, and approximately 14% to 18% of included
<table>
<thead>
<tr>
<th>Author, year, location, funding</th>
<th>Study design, follow-up, study quality</th>
<th>Population, abortion regimen</th>
<th>Intervention (I)</th>
<th>Comparison (C)</th>
<th>Outcomes and results</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raymond, 2016 [26] Mexico United States Anonymous donor</td>
<td>Noninferiority RCT Visit or phone f/u at 4 or 7 months, assessed with UPT and 80%-91% had US Fair quality</td>
<td>Women eligible for outpatient medical abortion (up to 75 days GA) and desired DMPA (n = 461) -GA of 64 d or greater: 12% Abortion: mifepristone 200mg PO, misoprostol 800μg buccal 1–2 days later</td>
<td>Immediate DMPA: on day of mifepristone (n = 225, n = 220 analyzed)</td>
<td>Delayed DMPA: once abortion completed &gt;6 days after mifepristone (n = 236, n = 226 analyzed)</td>
<td>Surgery Success Surgery to complete abortion (%): I: 14/220 (6.4%) C: 12/225 (5.3%) Difference (90% CI): 1.1 (–2.8, 4.9) Additional surgical or medical treatment (%): I: 25/225 (11.4%) C: 26/226 (11.5%) Difference (90% CI): –0.1 (–5.2, 4.9) Ongoing pregnancy (%): I: 8/220 (3.6%) C: 2/226 (0.9%) Difference (90% CI): 2.7 (0.4, 5.6) Bleeding: self-reported within 1, 4, and 7 months Median bleeding days: I: 0-7 – 21.8% 8-14 – 53.2% 15+ – 29.0% C: 0-7 – 26.1% 8-14 – 57.8% 15+ – 16.1% p = 0.01 Bleeding heavier than menses: I: 159/220 (74%) C: 171/226 (78.4%) p = 0.27</td>
<td>Adequate randomization and allocation concealment Low attrition (immediate: 2.2%, delayed: 4.2%); Masked record review by independent clinician blinded to group assignments for those who received extra treatment Adequate sample size powered to detect difference in medical abortion failure</td>
<td>Timing of DMPA administration in delayed group not described US assessment not reported as blinded</td>
</tr>
<tr>
<td>Raymond, 2016 [27] Mexico United States Anonymous donor</td>
<td>Non-inferiority RCT Visit or phone f/u at 4 or 7 months, assessed with UPT and 90-92% had US Fair quality</td>
<td>Women eligible for outpatient medical abortion and desired ENG implant (n = 476) -GA of 64 d or greater: 14-18% Abortion: mifepristone 200mg PO, misoprostol 800μg buccal 1-2 days later</td>
<td>Immediate ENG implant: inserted on day of mifepristone (n = 236, n = 229 analyzed)</td>
<td>Delayed ENG implant: inserted once abortion completed &gt;6 days after mifepristone (n = 240, n = 234 analyzed)</td>
<td>Surgery Success Surgery to complete abortion (%): I: 9/229 (3.9%) C: 9/234 (3.9%) Difference (90% CI): 0.08 (–3.06, 3.25) Additional surgical or medical treatment (%): I: 21/229 (9.2%) C: 26/234 (11.1%) Difference (90% CI): –1.94 (–6.68, 2.77) Ongoing pregnancy (%): I: 2/229 (0.9%) C: 2/234 (0.9%) Difference (90% CI): 0.02 (–1.8, 1.85) Bleeding: self-reported within 1, 4, and 7 months Median bleeding days: I: 12 C: 10 p = 0.03 Bleeding heavier than menses: I: 155/229 (68.3%) C: 158/234 (68.1%) p = 0.91</td>
<td>Adequate randomization and allocation concealment Low attrition (immediate: 3.0%, delayed: 2.5%); Masked record review by independent clinician blinded to group assignments for those who received extra treatment Adequate sample size powered to detect difference in medical abortion failure</td>
<td>Timing of implant insertion in delayed group not described US assessment not reported as blinded</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Author, year, location, funding</th>
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<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hogrent, 2016 [25]</td>
<td>Equivalence RCT</td>
<td>Women who had a medical abortion at ( \leq 63 ) days GA based on ultrasound and desired ENG implant (( n = 538 )) -Median GA: 46 days Abortion: mifepristone 200mg PO, misoprostol 800μg PV 1-2 days later, in Sweden additional misoprostol 400 μg if no bleeding by 3 hours</td>
<td>Immediate ENG implant; inserted on day of mifepristone (( n = 282 ), ( n = 277 ) ITT, ( n = 274 ) per protocol analyzed)</td>
<td>Delayed ENG implant; inserted 2-4 weeks after mifepristone (( n = 268 ), ( n = 261 ) ITT, ( n = 249 ) per protocol analyzed)</td>
<td>Abortion Success: Surgery to complete abortion (%): ITT: I: 16/277 (5.7%) C: 10/261 (3.8%) Difference (95% CI): 1.3 (-0.9, 4.1) Additional medical treatment needed (extra dose of misoprostol) (%): I: 19/277 (6.8%), 6 women also had surgery C: 9/261 (3.4%), 3 women also had surgery( \Delta = 0.083 ) Bleeding: No surgery to complete abortion (%):</td>
<td>Adequate randomization and allocation concealment</td>
<td>Reason for surgery not detailed, including reporting of ongoing pregnancy Reporting of additional misoprostol to those who did not bleed within 3 hours after mifepristone</td>
</tr>
<tr>
<td>Barros Pereira, 2015 [24]</td>
<td>Prospective cohort</td>
<td>Women who had a medical abortion at ( \leq 70 ) days GA and desired ENG implant (( n = 129, n = 119 ) analyzed) -GA results are not detailed Abortion: mifepristone 200mg PO, misoprostol 800μg PO 48h later</td>
<td>Immediate ENG implant; inserted on day of mifepristone (( n = 61, ) ( n = 57 ) analyzed)</td>
<td>Delayed ENG implant; clinic visit at 4 weeks (( n = 68, n = 62 ) analyzed)</td>
<td>Abortion Success</td>
<td>Adequate randomization and allocation concealment</td>
<td>Small sample size; not powered to detect difference for outcomes of interest No confounding assessment Some in delayed group used “other groups” (( n = 29 ))</td>
</tr>
<tr>
<td>Martin, 1998 [19]</td>
<td>RCT</td>
<td>Women who had a medical abortion at ( \leq 63 ) days GA in a hospital (( n = 40 )) -mean GA for all four groups: 48-49 days Abortion: mifepristone 200mg PO, 0.5 mg gemeprost pessary 48 hours later</td>
<td>Immediate COC (Group A): initiated after abortion success confirmed and prior to discharge from hospital (( n = 20, n = 19 ) analyzed)</td>
<td>Delayed COC (Group B): initiated on 1st day of next menses (( n = 20, n = 19 ) analyzed)</td>
<td>Abortion Success: Incomplete abortion requiring surgery (%): I: 0(1%)=0% C: 0 (0%) Bleeding Days of bleeding after abortion (median, range): I: 14 (9-45) C: 17 (6-34)</td>
<td>Adequate randomization Low loss to follow up (total of 2 women from the 80) Bleeding measured with daily bleeding diaries</td>
<td>Allocation concealment not detailed Outcome assessment (blinding and criteria used) not detailed No information on participation rates, COC adherence Large ranges of bleeding duration around median (continued on next page)</td>
</tr>
<tr>
<td>Study design, follow-up, study quality</td>
<td>Population, abortion regimen</td>
<td>Intervention (I)</td>
<td>Comparison (C)</td>
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</tr>
<tr>
<td>Lang, 2018 [31]</td>
<td>Retrospective cohort</td>
<td>Women who had a medical abortion at ≤ 63 days GA (n = 5122)</td>
<td>Hormonal method: initiated with misoprostol DMPA (n = 475)</td>
<td>Abortion Success</td>
<td>Database review for subsequent visit for abortion services, ongoing pregnancy or maternity care</td>
<td>Large study</td>
<td>Details of timing and duration of method not provided</td>
</tr>
<tr>
<td>Scotland</td>
<td>Low-sensitivity</td>
<td>GA 3-8 weeks: 18% Abortion: mifepristone 200 mg PO, misoprostol 800 mcg PV or SL 24-48 hours later in clinic</td>
<td>COC: 400μg POP, LNG implant, or EN implant initiated within 15 minutes of mifepristone (n = 511, n = 448 analyzed)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No financial disclosures</td>
<td>UPT at home at 2 weeks</td>
<td></td>
<td>No hormonal method/no: condoms, diaphragm, IUD, sterilization or no method (n = 1813)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fair quality</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Douthwaite, 2016 [28]</td>
<td>Retrospective cohort</td>
<td>Women who had a medical abortion at ≤ 63 days GA (n = 2482, n = 2204 analyzed)</td>
<td>POC: Net-EN, DMPA, LNG implant, or EN implant initiated within 15 minutes of mifepristone (n = 511, n = 448 analyzed)</td>
<td>Abortion Success</td>
<td>Rate of complete uterine evacuation without additional interventions</td>
<td>Large sample size</td>
<td>Record review</td>
</tr>
<tr>
<td>Mexico City</td>
<td>Phone f/u at 8 and 30 days with UPT at 30 days or visit f/u at 3 weeks with UPT/US</td>
<td>GA 7-9 weeks: 30% Abortion: mifepristone 200mg PO, misoprostol 800mcg buccal 24-48 hours later</td>
<td>None: no method initiated (n = 1971, n = 1756 analyzed)</td>
<td></td>
<td></td>
<td>Groups differed by type of follow-up and parity – no confounding assessment</td>
<td></td>
</tr>
<tr>
<td>Marie Stopes International</td>
<td>Poor quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Small sample size of POC users, other than DMPA users, could not be analyzed separately</td>
<td></td>
</tr>
<tr>
<td>Tang, 2002 [22]</td>
<td>RCT</td>
<td>Women with menstrual delay ≤ 35 days presenting for medical abortion, GA confirmed with US</td>
<td>COC (30μg EE/0.15mg LNG): initiated 1 day after misoprostol x 21 days (n = 50)</td>
<td>Abortion Success</td>
<td>No emergency/ elective surgery in the interval up to first menses</td>
<td>Adequate sample powered to detect difference in blood loss of 65mL</td>
<td>Allocation not defined</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>Visits at day 15 (exam, US, Hgb), day 43 (exam), day 67 if persistent bleeding or no menses</td>
<td>Mean menstrual delay: 17 days Abortion: mifepristone 200mg PO, misoprostol 400ug miso PV in hospital 48h later</td>
<td>Placebo: initiated after misoprostol x 21 days (n = 50)</td>
<td></td>
<td></td>
<td>Methods for blinding not reported</td>
<td></td>
</tr>
<tr>
<td>Shanghai WHO HRP</td>
<td>Fair quality</td>
<td></td>
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<tr>
<th>Author, year, location, funding</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Tang, 1999 [20] Hong Kong Shanghai WHO HRP</td>
<td>RCT</td>
<td>Women with menstrual delay ≤ 21 days presenting for medical abortion, GA confirmed with exam +/- US</td>
<td>COC (30μg EE/0.15mg LNG); initiated 1 day after misoprostol x 21 days (n = 100)</td>
<td>Placebo; initiated after misoprostol x 21 days (n = 100)</td>
<td>Abortion Success No emergency/elective surgery in the interval up to first menses <strong>No need for surgery (% 95% CI):</strong> COC: 98% (93.0, 99.8) Placebo: 99% (94.6, 100.0) NS (p-value not reported) Bleeding: Hgb testing and bleeding diaries <strong>Hgb level, g/L (mean, SD):</strong> Day 1 122.1 (9.8) Day 15 116.8 (10.4p &lt; 0.001 Placebo: Day 1 123.5 (10.0) Day 15 123.1 (0.9) NS (p-value not reported) <strong>Median bleeding days (median, range):</strong> COC: 17 (5-57) Placebo: 16 (6-55) No significance testing reported <strong>Bleeding more than menses (%):</strong> COC: 53% Placebo: 59% No significance testing reported <strong>Bleeding Days of bleeding after abortion (median, range):</strong> COC: 14 (9-45) Placebo: 15 (7-35) <strong>Days of heavy bleeding after abortion (median, range):</strong> COC: 4 (1-10) Placebo: 4 (0-8)</td>
<td>Adequate randomization Multiple methods to assess blood loss including objective Hgb measurements Well defined outcomes Low attrition (varied by outcome but highest is 12%)</td>
<td>Allocation not described Methods for blinding not described No significance testing reported for several outcomes</td>
</tr>
<tr>
<td>Martin, 1998 [19] Scotland</td>
<td>RCT, indirect comparison F/u at 2 and 6 weeks Poor quality</td>
<td>Women who had a medical abortion at ≤ 63 days GA in hospital (n = 80) -mean GA for all four groups: 48-49 days</td>
<td>COC (Group A); initiated after abortion completion confirmed and prior to discharge from hospital (n = 20, n = 19 analyzed)</td>
<td>Placebo (Group D); injection was given after abortion complete confirmed and prior to discharge from hospital (n = 20, n = 20 analyzed)</td>
<td><strong>Low loss to follow up (total of 2 women from the 80)</strong> Bleeding measured through daily diaries</td>
<td>Low loss to follow up (total of 2 women from the 80) Bleeding measured through daily diaries</td>
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</tbody>
</table>

**AE, adverse events; CI, confidence interval; COC, combined oral contraception; DMPPA, depot medroxyprogesterone acetate; EE, ethinyl estradiol; LNG, levonorgestrel; Net-EN, norethisterone enanthate; NR, not reported; NS, not significant; PO, oral route; POC, progestogen-only contraception; POP, progestogen-only pill; PV, vaginal route; RCT, randomized controlled trial; SE, side effects; SD, standard deviation; SL, sublingual route; UPT, urine pregnancy test; US, ultrasound; WHO, World Health Organization.**

*Quality rating based on the US Preventive Services Task Force (USPSTF) grading criteria [12,13].*
<table>
<thead>
<tr>
<th>Author, year, location, funding</th>
<th>Study design, follow-up, study quality*</th>
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<tr>
<td>Steinauer, 2014 [23] United States</td>
<td>RCT Phone f/u at 2 and 6 months Poor quality</td>
<td>Women who had a surgical abortion (1st and 2nd trimester) Median weeks GA at time of abortion: Immediate: 15.9 wks delayed: 15.6 wks (n = 298, n = 212 analyzed at 2 month)</td>
<td>Immediate contraceptive patch: observed initiation in clinic after abortion (n = 154, n = 108 analyzed at 2 month)</td>
<td>Delayed contraceptive patch: initiated on first Sunday after abortion (n = 144, n = 104 analyzed at 2 month)</td>
<td>Bleeding</td>
<td>Pattern Changes</td>
<td>Adequate randomization and allocation concealment Blinded outcome assessment by research assistant conducting follow-up Acceptable attrition (immediate: 29.9%, delayed: 27.8%)</td>
</tr>
<tr>
<td>Hou, 2017 [30] China Shanghai Population and Family Planning Commission Of PR China</td>
<td>Prospective cohort Phone f/u at 1, 3, and 6 months Poor quality</td>
<td>Women who had a vacuum aspiration at 42-70 days GA (n = 705)</td>
<td>COC (EE/ desogestrel): initiated immediately after abortion (n = 230)</td>
<td>Non-hormonal: no COC x 21 days after abortion, recommended condom use (n = 414)</td>
<td>Bleeding</td>
<td>Pattern Changes</td>
<td>Day of COC initiation was not detailed nor confirmed Non-comparable groups (COC users were younger and had a higher education level; IUD users were older) Self-report of bleeding duration</td>
</tr>
<tr>
<td>Wang, 2017 [29] China Source of funding NR</td>
<td>Prospective cohort Clinic f/u on day 21 following abortion Poor quality</td>
<td>Women who had a surgical abortion, GA was not clearly stated (n = 726)</td>
<td>COC (30μg EE/3 mg desogestrel): initiated immediately after abortion x 21 days (n = 312)</td>
<td>Non-hormonal: no COC x 21 days after abortion, recommended condom use (n = 414)</td>
<td>Bleeding</td>
<td>Pattern Changes</td>
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</tr>
<tr>
<td>Orsayli, 2001 [21] Turkey Population Council Nobel Co.</td>
<td>Prospective cohort Clinic f/u at 2 weeks, 6 weeks, 6 and 12 months (Hct at 6 weeks, 6 and 12 months) Menstrual diaries collected at 2 and 6 weeks Poor quality</td>
<td>Women who had a surgical abortion at ≤ 10 weeks GA by vacuum or electric aspiration (n = 150) Mean GA age implant: 54.2 days Nonhormonal: 49.4 days</td>
<td>LNG implant: inserted immediately after abortion (n = 50)</td>
<td>Non-hormonal/none: withdrawal method or no method (n = 50)</td>
<td>Bleeding Pattern Changes</td>
<td>Groups similar at baseline by education, pregnancy and abortion history, and use of recent contraception, experience with IUDs or condoms, and BP; Hct and GA Long follow up time Well defined outcomes</td>
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<th>Author, year, location, funding</th>
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<tr>
<td>Querido, 1985 [18] Netherlands Organon Schering</td>
<td>Multi-site prospective cohort Clinic f/u at 6 weeks Poor quality</td>
<td>Women who had a surgical abortion, GA was not clearly stated ( n = 423 )</td>
<td>OC: initiated after abortion, unclear timing ( n = 123 )</td>
<td>Non-hormonal: Cu-IUD inserted immediately after abortion ( n = 300 )</td>
<td>Bleeding Pattern Changes <strong>Bleeding days after abortion</strong> (%): 1-7 days of bleeding: OC: 56.6% Cu-IUD: 29.7% &gt;14 days of bleeding: OC: 9.8% Cu-IUD: 19.9% ( p &lt; 0.0001 )</td>
<td>OC group was overrepresented with younger, unmarried, nulliparous, without prior abortion</td>
<td>OC type not specified OC initiation not detailed Groups differed demographically Range of follow-up times (range of less to more than 6 weeks) Unclear randomization of OC group Small study size with no power calculations Assignment of contraception type not described Groups only described and compared by assignment not insertions at baseline Attrition not reported No confounding assessment Groups not assessed at baseline or by outcome for potential confounders Outcome ascertainment not described No significance testing to detect outcome differences Unclear what GA included in study Only outcome is a self-reported outcome with potential for recall bias</td>
</tr>
<tr>
<td>Kurunmaki, 1983 [17] Finland International Development Research Center of Canada, Ford Foundation, Rockefeller Foundation</td>
<td>Prospective cohort Clinic f/u at 3, 6, 12 months (measured Hgb, BP, weight; daily bleeding records) Poor quality</td>
<td>Women who had a surgical abortion in the first trimester ( n = 68 )</td>
<td>LNG implant: inserted immediately after abortion ( n = 38 ) assigned, ( n = 36 ) inserted</td>
<td>Non-hormonal: Cu-IUD inserted immediately after abortion ( n = 30 ) assigned, ( n = 23 ) inserted</td>
<td>Bleeding Pattern Changes <strong>Bleeding days after abortion</strong> (mean, SD): Implant: 15.1 ± 6.9 Cu-IUD: 14.3 ± 6.9p = NS</td>
<td>Measured bleeding by both objective and subjective measures Outcomes clearly defined</td>
<td></td>
</tr>
<tr>
<td>Peterson, 1974 [16] United States Wyeth Labs</td>
<td>Prospective cohort Clinic f/u at 6 weeks or form filled out by non-study physician at 6 weeks and mailed to clinic Poor quality</td>
<td>Women who had a surgical abortion, GA was not clearly stated ( n = 978, n = 823 ) analyzed</td>
<td>CDC: initiated on day of abortion ( n = 479 ) analyzed</td>
<td>Non-hormonal/none: diaphragms, condoms, no method ( n = 198 ) analyzed</td>
<td>Bleeding Pattern Changes <strong>Stopped bleeding by day 7</strong> (%): CDC: 58% Control: 59% <strong>Stopped bleeding by day 14</strong> (%): CDC: 86% Control: 90% <strong>Stopped bleeding by day 21</strong> (%): CDC: 94% Control: 96% <strong>Stopped bleeding by day 28</strong> (%): CDC: 97% Control: 98%</td>
<td>Two control groups using non-hormonal contraceptives Acceptable attrition (overall 15.8%)</td>
<td></td>
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</table>

BP, blood pressure; COC, combined oral contraception; Cu, copper; EE, ethinyl estradiol; F/U, follow-up; GA, gestational age; Hct, hematocrit; Hgb, hemoglobin; IUD, intrauterine device; LNG, levonorgestrel; LTFU, lost to follow up; NR, not reported; NS, not significant; OC, oral contraception; RCT, randomized controlled trial.

*Quality rating based on the US Preventive Services Task Force (USPSTF) grading criteria [12,13].
participants had a gestational age greater than 64 days. There were no differences between the immediate and delayed initiation groups in the proportion needing surgery to complete abortion (risk difference 0.08%, 90% CI −3.1 to 3.3), the proportion needing any additional treatment (risk difference −1.9%, 90% CI −6.7 to 2.8), or the proportion of ongoing pregnancies (risk difference 0.02%, 90% CI −1.8 to 1.9). Those in the immediate etonogestrel implant group had a median of 12 days of bleeding after the abortion compared with 10 days for the delayed implant group (p = 0.03) but no difference in self-reported bleeding heavier than menses (68% vs 68%, p = 0.91). A second RCT compared 277 participants at ≤63 days gestational age who had an etonogestrel implant inserted within 1 hour of mifepristone with 261 participants with insertion at 2 to 4 weeks after mifepristone [25]. There was equivalence in the need for surgery to complete the abortion (risk difference 1.8%, 95% CI 0.4–4.1) and similar implant discontinuation rates due to bleeding at three and six months in the immediate and delayed initiation groups (3 months: 2.2% vs 2.1%; 6 months: 4.3% vs 5.9%, no significance testing reported) [25]. A pooled analysis from these 2 RCTs [25,26] indicated no significant increased risk of requiring surgery to complete the abortion (OR 1.29, 95% CI 0.71–2.36, n = 1014, \( P^2 = 0\)) or requiring additional medical treatment (OR 1.08, CI 0.60–1.92, n = 1014, \( P^2 = 66\%\)) with immediate insertion compared to delayed insertion (Figs. 2 and 3). Finally, a prospective cohort study of women ≤70 days compared immediate etonogestrel implant (n = 68) with etonogestrel implant insertion at a 4-week follow-up visit (n = 68) [24]. At the 2-week visit, assessment of abortion success by transvaginal ultrasound showed no difference between the immediate and delayed initiation groups (96.5% vs 98.4%, p = 0.47). One poor-quality RCT assessed COC initiation after medical abortion by randomizing participants at ≤63 days gestational age into immediate COC initiation after abortion success confirmed (n = 20) vs initiation on the first day of next menses (n = 20) [19]. The study defined abortion success as need for surgical evacuation due to retained products of conception (POC) and assessed at 2 and 6 weeks postabortion. There were no cases of incomplete abortion in either group and no differences in bleeding duration between the groups.

### 3.1.2. Hormonal contraception vs nonhormonal or no contraception

Five studies compared hormonal contraception vs nonhormonal or no contraception following a medical abortion [19,20,22,28,31]. Four studies reported abortion success outcomes, which all found no significant difference in abortion success rates [20,28,31]. Three studies reported on bleeding changes [19,20,22]. Three studies assessed the initiation of COC [19,20,22] and 2 studies assessed the initiation of multiple methods: DMPA, COC, progestogen-only pill (POP), and progestogen-only implant [28,31].

Two fair-quality RCTs randomized participants to either COCs or placebo and compared rates of abortion success, defined as no need for curettage prior to first menses [20,22]. Follow-up in both trials was at days 15 and 43 after misoprostol. The first RCT enrolled 100 participants with menstrual delay ≤21 days in each group, and there were similar rates of abortion success among COC users (98%, 95% CI 93.0–99.8) and placebo (99%, 95% CI 94.6–100.0) [20]. The second RCT enrolled 50 participants with menstrual delay ≤35 days in each group, and the abortion success rate among COC users (98%) was not different from those taking placebo (92%; CI and p value not reported) [22]. In both studies, participants recorded all bleeding and other side effects in diaries and had hemoglobin measurements at days 1 and 15 following mifepristone. The RCT that assessed median blood loss extracted from sanitary pads reported no difference between groups (COC: 69.9 mL, range [4.4–429.6]; placebo: 72.8 mL, range [5.2–855.0]; no p values reported) [22]. For self-reported outcomes, neither study reported a difference in median duration of bleeding, and 1 study did not find a difference in bleeding described as heavier than normal menses. We performed a pooled analysis of data from these 2 RCTs [20,22] and found no significantly different rate of abortion success, defined as no need for curettage prior to first menses, among the group that initiated COC compared with placebo (OR 1.67, 95%
CI 0.41–6.83, n = 300, $I^2 = 40\%$; Fig. 4). A third poor-quality RCT compared side effects of COC initiation to placebo using a daily bleeding diary for 6 weeks [19]. The bleeding duration and median heavy bleeding days was similar between the 2 groups.

A fair-quality retrospective cohort study included 5122 people at $\leq 63$ days who either initiated a hormonal method (DMPA, COC, POP, or implant) at the time of misoprostol or had no hormonal method. The 2-week follow-up involved a home low-sensitivity UPT [31]. For all 4 methods, there were no differences in continuing pregnancy rates compared with no hormonal method. A second poor-quality retrospective cohort study compared 511 people at $\leq 63$ days receiving a progestogen-only method (injectables or implants) to 1971 people receiving no contraception [28]. Follow-up was by phone or at a 3-week clinic visit. The study defined abortion success as complete uterine evacuation without need for additional intervention. Among the progestogen-only subgroups (DMPA and all other progestogen-only methods) and the no contraception group, there was no difference in the abortion success rates (overall progestogen-only: 87.9%, DMPA: 85%, all other progestogen-only: 89.2%, no contraception: 85.7%, $p = 0.56$).

3.2. Surgical abortion

We identified seven surgical abortion studies: one RCT [23] and 6 cohort studies [16–18,21,29,30] (Table 3). Gestational ages included both first and second trimester pregnancies. All 7 studies reported bleeding outcomes [16–18,21,29,30], and 2 reported bleeding-related method discontinuation rates [17,18]. We did not identify any studies that assessed other adverse events. The quality of the studies was fair or poor.

3.2.1. Immediate vs delayed initiation of hormonal contraception

One poor-quality RCT compared immediate vs delayed initiation of the contraceptive patch following a surgical abortion and assessed bleeding outcomes [23]. Participants (n = 298) underwent a first- or second-trimester surgical abortion and initiated a contraceptive patch immediately in clinic (n = 154) or on the following first Sunday (n = 144). The self-reported median days of bleeding was 5 in both groups ($p = 0.94$).

3.2.2. Hormonal contraception vs nonhormonal or no contraception

Six prospective cohort studies compared hormonal contraception versus nonhormonal or no contraception following surgical abortion and assessed bleeding days, comparison to menstrual flow, and hematocrit change [16–18,21,29,30]. Three studies assessed COC initiation [16,29,30], 1 study assessed the initiation of oral contraception (OC) [18], and 2 studies the initiation of levonorgestrel implant [17,21].

Three poor-quality studies assessed bleeding duration among COC users compared with nonhormonal/no contraception users, of which 2 studies found significantly shorter durations for COC users [16,29,30]. The earliest study included 823 people who had a surgical abortion at unspecified gestational ages with a 6-week follow-up clinic visit. The investigators assessed self-reported bleeding cessation following the abortion among those who initiated COC on the day of the surgical abortion (n = 479) compared with participants using diaphragm, condom, or no contraception (n = 198). Over the first 28 days, COC users and nonusers had similar proportions who had stopped bleeding (no significance testing reported). A second cohort study included 705 people who had a surgical abortion at 6 to 10 weeks gestation and initiated COC (n = 230), Cu-IUD (n = 240), or condoms (n = 235) on the day of the surgical abortion [30]. The COC group exhibited shorter duration of bleeding (COC: 5 days [2–7], Cu-IUD: 7 days [2–10], condom: 5.5 days [3–8]; $p = 0.041$) on telephone follow-up at 1, 3, and 6 months. The third study assessed 726 people after surgical abortion at unspecified gestation and compared COC users (n = 312) with condom users (n = 414) for 21 days after the abortion [29]. Almost 92% of COC users had bleeding duration <7 days, and only 1.3% of COC users had bleeding for more than 15 days compared with 6.5% of condom users ($p < 0.01$). COC users reported lower proportions of more than usual menstrual volume compared with condom users (4.2% vs 5.8%, $p < 0.01$).

One poor-quality study assessed bleeding patterns of OC users compared with Cu-IUD users [18]. In this multisite cohort study, 423 people had a surgical abortion at unspecified gestation and immediately initiated OC (n = 123) or Cu-IUD (n = 300). Follow-up at a 6-week clinic visit demonstrated differences in duration of bleeding. The majority of OC users experienced 1 to 7 days of bleeding (57%) while 40% of Cu-IUD users had >7 days of bleeding ($p < 0.0001$).

Two poor-quality studies assessed bleeding patterns of levonorgestrel implant users compared with nonhormonal or nonusers [17,21]. One study of 150 people who had a surgical abortion at $\leq 10$ weeks gestation assessed hematocrit levels among levonorgestrel implant users (n = 50) and participants using withdrawal or no contraception [21]. Follow-up visits were at 2 weeks, 6 weeks, 6 months, and 12 months. Between levonorgestrel implant users and comparison group, there was no difference in change from baseline to 6 weeks (levonorgestrel implant: 1.0 ± 3.8, control: 1.7 ± 4.3; not significant). This study assessed mean bleeding days as well as a second study which included 62 people who initiated either levonorgestrel implant or Cu-IUD immediately after a first-trimester surgical abortion [17,21]. In the first study, levonorgestrel implant users reported more mean bleeding days at 2 weeks than the comparison group (levonorgestrel implant: 5.0 ± 3.2, control: 4.4 ± 4.5; $p < 0.05$) [21]. However, in both studies, there was no difference in mean bleeding days at 4
to 6 weeks when comparing levonorgestrel implant users to nonhormonal/nonusers [21] or to Cu-IUD users [17].

4. Discussion

We assessed the effect of non-IUD hormonal contraception initiation on medical abortion effectiveness and the safety of non-IUD hormonal contraceptive methods following abortion. We evaluated the effect of hormonal contraception initiation as well as its timing. We found no studies that met our inclusion criteria for spontaneous or septic abortion nor did we find studies reporting on adverse outcomes of thrombosis and infection. Following a first trimester medical abortion, we found that hormonal contraception initiation (hormonal method vs nonhormonal/no method) and the timing of initiation (immediate vs delayed) generally had little effect on abortion effectiveness or bleeding outcomes. However, evidence was very limited, and estimation of effects was imprecise. One study did report an increase in ongoing pregnancy rate with immediate vs delayed DMPA initiation. Following a surgical abortion, there was mostly no difference in self-reported bleeding outcomes, but there was some variation depending on the method initiated.

We were particularly interested in the timing of systemic hormonal contraception initiation and medical abortion effectiveness given concerns of progesterone-containing methods interfering with mifepristone. Three studies of etonorgestrel implants, including 2 RCTs, found no difference in medical abortion success with immediate vs delayed insertion, which was reiterated by meta-analysis [24–26]. However, the overall confidence intervals are wide implying inadequate power to make definitive conclusions that success is not altered by implant use. One study of DMPA showed no increase in risk of surgery after medical abortion with a slight, statistically significant increase in ongoing pregnancy with immediate vs delayed DMPA use [27]. This difference may be due to the increased potency of DMPA compared to other progesterone-containing methods, where animal model studies have shown medroxyprogesterone exhibiting a higher concentration to produce half the maximal response [32]. Another plausible explanation is the pharmacologic profile of DMPA where serum MPA concentrations steadily peak to effective concentrations within the first 24 hours of injection and are at high levels the first 30 days [33,34]. In addition, the DMPA study reported on equivalent DMPA utilization rates at 6-month follow-up, thus implying no long-term benefit to immediate DMPA initiation [27]. Nevertheless, immediate initiation of most systemic hormonal methods can be an option and those who opt for immediate DMPA initiation should be informed of the slight increased risk of ongoing pregnancy.

When assessing the 2 studies that compared systemic hormonal contraception initiation to nonhormonal contraception following medication abortion, there was limited evidence to draw conclusions. Results were inconsistent; one study reported slightly fewer women with abortion success in the COC group, but differences were not statistically significant and event rates were very low. A pooled analysis of the 2 trials was similarly imprecise, with wide confidence intervals around the estimated effect. We require larger studies to evaluate whether there is no difference in success rates with COC initiation.

The safety concern with initiating hormonal contraception after abortion revolve around the theoretical concerns of the increased risk of thromboembolism after pregnancy [35] and with combined hormonal contraception use [36–38]. We did not identify any data that addressed this outcome. In addition, we identified no safety concerns in terms of bleeding following systemic hormonal contraception initiation after medical or surgical abortion. In terms of method discontinuation, bleeding was a main reason for implant removal in immediate and delayed groups at 3- and 6-month follow-up [25], which is consistent with other studies that found bleeding changes was a main reason for implant discontinuation [39,40].

Our study has several weaknesses. We were only able to pool results from four RCTs for 2 contraceptive methods. All included studies were of poor or fair quality. Primary reasons for these low-quality ratings were lack of blinding in abortion success assessment, mixed clinical and self-reporting of bleeding assessment. Currently, there are no standardized measurements for abortion success or postabortion bleeding. Efforts in standardizing abortion outcomes have been published (MARE guidelines, PAIRS framework STAR project) and immediate implementation by researchers will be critical in strengthening study designs and outcomes [41–43]. In particular, continued pregnancy as a reason for additional treatment is an important indicator of whether an abortion was successful, which not all studies reported. Further research is needed to confirm the risk of ongoing pregnancy with immediate DMPA initiation after medical abortion. All included studies were conducted in high-income or upper-middle-income settings. Future studies should explore hormonal contraception initiation in low-income and lower-middle income settings, where follow-up of adverse outcomes, including abortion failure, may be more challenging. Additional research gaps identified include the need for further investigation of hormonal contraception initiation prior to surgical abortion (e.g., at preprocedure visit or with osmotic dilator insertion) including the benefits of immediate initiation and hormonal contraception initiation with abortion at later gestational ages. The included studies focused on early medical abortions up to 70 days gestation and surgical abortions in the first-trimester or at unspecified gestational ages. We need robust data for medical and surgical abortion beyond 70 days and late second trimester gestation. Different safety concerns may arise with abortions at later gestations, such as risk of thromboembolism.

Initiating non-IUD hormonal contraceptive methods immediately after a medical or surgical abortion and as early as the same day as the first pill of the medical abortion did not result in appreciably different abortion success rates or more adverse bleeding and side effects compared to delayed initiation. While there was no increase in incomplete abortions requiring surgical intervention, there is evidence of slightly higher ongoing pregnancy rates with immediate DMPA use on day of mifepristone administration for medical abortion. Further research on immediate contraception provision after second trimester abortion is important to better inform practices, protocols and patient counseling. Individuals should be informed of potential risks and benefits and engaged in shared decision-making with their providers during contraceptive counseling and provision, which should be a routine component of abortion care for those who desire it.

Declaration of competing interest

None.

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Supplementary materials

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References

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