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SUMMARY WITH CRITICAL APPRAISAL

Routine Pathology for Intrauterine Devices and Therapeutic Abortion: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Abbreviations

AGREE II	Appraisal of Guidelines for Research and Evaluation II
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
IUD	Intrauterine device
NAF	National Abortion Federation
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUADAS	Quality Assessment of Diagnostic Accuracy Studies
SOGC	Society of Obstetricians and Gynaecologists of Canada

Context and Policy Issues

When human tissue is removed as part of a medical procedure, the tissue may then be sent to a laboratory for examination and evaluation by a pathologist for documentation and reporting. There are costs to the healthcare system associated with processing tissues, preparing tissue for analysis, time spent examining tissue, and the time required to produce a written pathology reports.[1] The potentially low diagnostic or clinical value of some routine pathology tests has made it unclear if it is necessary to send all tissues removed during surgery or other procedures for examination by a pathologist.[1]

The intrauterine device (IUD) is one of the most common forms of contraception used worldwide and is a highly effective form of contraception.[2] There are different types of IUDs available in Canada (copper IUDs and hormone containing IUDs),[3] but all types of devices are inserted into the uterus until removal.[2] Fertility returns to normal after removal (discontinuation). Reasons for removing an IUD may include expiry of the device, the development of a contraindication to the device, adverse effects, or patient choice to have the IUD removed.[2] After removal, the IUD may be sent for routine pathology examination, but it unclear if there is value in this assessment.

In therapeutic abortion, the pathologic examination of products of conception has the main goal of documenting the chorionic villi and fetal tissue.[4] Pathologic examination may be performed to confirm a successful outcome of the procedure, or to confirm prenatal diagnosis related to the mother or the fetus for pregnancies that are terminated for these reasons.[4] However, in the absence of such complications, it is unclear if analysis of the products of conception by a pathologist provides additional benefit beyond an examination performed by the surgeon immediately following the procedure.

The purpose of this report is to review the evidence assessing the clinical utility and cost-effectiveness of performing routine pathology for removed IUDs and therapeutic abortions (i.e., those that were an elective termination of pregnancy and not in response to the physical health of the mother, clinical expectation of fetal abnormalities, or another complication such as infection, spontaneous abortion, missed abortion, or molar pregnancy). The evidence-based guidelines regarding routine pathology for IUDs or therapeutic abortions, where available, will also be reviewed.

Research Questions

1. What is the clinical utility of routine pathology for removed intrauterine devices?
2. What is the clinical utility of routine pathology for therapeutic abortions?
3. What is the cost-effectiveness of routine pathology for removed intrauterine devices?

4. What is the cost-effectiveness of routine pathology for therapeutic abortions?
5. What are the evidence-based guidelines regarding routine pathology for intrauterine devices or therapeutic abortions?

Key Findings

Evidence from one non-randomized study with several key limitations suggested that both surgeons and pathologists were poor at predicting abnormal outcomes following therapeutic abortion at less than six weeks gestation. The agreement between assessments performed by surgeons and pathologists was poor.

Evidence-based guidelines from the Society of Obstetricians and Gynaecololgists of Canada strongly recommend histopathological examination of products of conception when gestational trophoblastic neoplasia or ectopic pregnancy is suspected. However, this is a general recommendation; no recommendation was provided specific to therapeutic abortion unrelated to fetal abnormalities or medical concerns, which was the population of interest to this report. Guidelines from the National Abortion Federation state that additional pathological examination of evacuated uterine contents is not required.

No evidence of the clinical utility of routine pathology for removed intrauterine devices, cost-effectiveness of routine pathology for therapeutic abortions or removed intrauterine devices, or evidence-based guidelines regarding routine pathology for intrauterine devices was identified.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were pathological examinations and abortions or intrauterine devices. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 1999 to August 8, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1, Q3, Q5: Patients of reproductive age who have had an IUD removed; Q2, Q4, Q5: Patients of reproductive age who have had a therapeutic abortion (i.e., elective termination of pregnancy; not in response to physical health of mother, clinical expectation of fetal abnormalities, infection, spontaneous abortion, missed abortion, or molar pregnancy)
Intervention	Q1, Q3, Q5: Routine laboratory pathology examination of removed IUD Q2, Q4, Q5: Routine laboratory pathology examination of products of conception (e.g., placental tissue, fetal tissue, maternal uterine lining) removed during therapeutic abortion
Comparator	Q1-4: Examination by clinician; no pathology examination Q5: Not applicable
Outcomes	Q1-2: Clinical effectiveness (i.e., identification of medical issue e.g., molar pregnancy, unusual infection, tumor, confirmation of pregnancy) Q3-4: Cost-effectiveness Q5: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, guidelines

IUD = intrauterine device.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 1999. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

Studies of diagnostic accuracy and clinical utility were evaluated using the QUADAS 2 instrument[5] and guidelines were assessed with the AGREE II instrument.[6] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 552 citations were identified in the literature search. Following screening of titles and abstracts, 530 citations were excluded and 22 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search for full text review. Of these 24 potentially relevant articles, 21 publications were excluded for various reasons, and three publications met the inclusion criteria and were included in this report. These comprised one non-randomized study and two evidence-based guidelines. Appendix 1 presents the PRISMA[7] flowchart of the study selection.

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

One non-randomized study was included that addressed the clinical utility of routine pathology examination of products of conception. In this study, a consecutive cohort of patients (n=1155) with pregnancies of less than six weeks gestation were recruited from three Planned Parenthood clinics (Appendix 2, Table 2).[8]

Two evidence-based guidelines were identified and included in the report, one from the National Abortion Federation (NAF)[9] and one from the Society of Obstetricians and Gynaecologists of Canada (SOGC) (Appendix 2, Table 3).[10] Both guidelines were developed based on systematic literature searches of multiple databases;[9,10] however, the NAF guideline was an update to a guideline produced the previous year (2017). The study designs selected for inclusion were not reported for the SOGC guideline, but the NAF guideline included study designs that were considered adequate to assess impact of intervention.[9] Studies that were considered to be of poor methodology were excluded (no further detail was provided on assessment).[9] The SOGC guideline rated the quality of evidence and strength of recommendations using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.[10] The NAF guidelines did not present the quality of evidence for their recommendations, but categorized statements as either standards, recommendations, and options which are hierarchical categories (with a standard being the strongest guidance for a point, followed by a recommendation, and then option).[9]

Country of Origin

The included non-randomized study that assessed the clinical utility of routine pathology examination of products of conception was located in the United States (Appendix 2, Table 2).[8]

One included guideline was Canadian[10] and the other included guideline was American (Appendix 2, Table 3).[9]

Patient Population

The patient population was not described in the included non-randomized study in terms of demographic or clinical characteristics.[8] However, all patients had no contraindications to outpatient surgical abortion and an intrauterine sac of less than six weeks gestation. Consecutive patients were enrolled from three Planned Parenthood clinics from January 1, 1998 to August 31, 2000 (Appendix 2, Table 2).

For the NAF guideline, the intended users of the guideline included facilities that provide abortion care and providers of abortion and the target population was women undergoing abortion.[9] Gynecologists, family physicians, nurses, midwives, residents, and other health care providers who currently or intend to provide and teach induced abortions were the intended users of the SOGC guideline, and the target population was women with an unintended or abnormal first or second trimester pregnancy (Appendix 2, Table 3).[10]

Interventions and Comparators

The interventions assessed in the non-randomized study were examination of fresh tissue aspirate by surgeon immediately following the procedure to identify the gestational sac, villi, and decidua, and microscopic examination of tissue aspirate by a pathologist at an external pathology laboratory. The comparator (“gold standard”) was considered to be verification of abortion outcome in clinic at a two-week follow-up appointment (Appendix 2, Table 2).[8]

The NAF guideline considered all aspects of abortion care, prior to, during, and following the procedure.[9] Similarly, the SOGC guideline considered all aspects of surgical induced abortion and second trimester medical abortion, including pre- and post-procedural care (Appendix 2, Table 3).[10] In both guidelines, the need for sending the products of conception for pathological analysis was specifically addressed as part of the larger guideline.

Outcomes

The outcomes assessed in the non-randomized study were the sensitivity, specificity, positive predictive value, and negative predictive value of the interventions for an abnormal outcome of abortion. An abnormal outcome was defined as any outcome other than complete abortion, examples of which include failed attempted abortion, incomplete abortion, or ectopic pregnancy. Outcomes were compared for assessment of the tissue aspirate by a surgeon immediately following the procedure and assessment by a pathologist at a laboratory relative to the gold standard, which was considered to be confirmation of abortion outcome in clinic two weeks later (Appendix 2, Table 2).

No outcomes were specified for either of the included guidelines.[9,10]

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Primary Clinical Studies

The included non-randomized study[8] recruited a consecutive sample of patients and had minimal exclusion criteria; however, only women with intrauterine sacs of less than six weeks were included. Thus, the results would not be applicable to with intrauterine sacs of more than six weeks. Of note, depending on the province or territory, therapeutic abortion may be provided from up to 12 weeks to up to 24 weeks gestation.[11]

The reference standard applied in the study (verification in clinic two weeks later) was likely to correctly classify patients, but was missing for 41% of patients, leading to their exclusion from the analysis. The exclusion of 41% of patients from the analysis has the potential to bias the estimates of diagnostic accuracy (relative to what may have been obtained from the full study population if data were available) and may limit the generalizability of the results to the entire population. The time between assessment of the products of conception by the surgeon and the pathologists was not reported. It is not clear if a time delay would influence the interpretation of outcomes by the pathologists, leading to different results for this group. The tests were interpreted with knowledge of the reference standard. It is not clear, however, if this would be a source of bias given the outcome, which is objective in nature (Appendix 3, Table 4).

The two included guidelines[9,10] reported limited details on the methodology used in their development. As such, the two guidelines failed to meet the majority of the checklist criteria for the AGREE II instrument. While the purpose and scope of the guidelines was clear, it was not clear if the views and preferences of the target population (patients, public, etc.) have been sought or guideline development group included individuals from all relevant professional groups. Both guidelines identified the relevant literature from systematic database searches, but the process for screening and selecting literature was not reported. The SOGC guideline used the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach to summarize the strengths and limitations of the body

of evidence.[10] The approach used in the NAF guideline was not reported.[9] The methods for formulating the recommendations were not described for either guideline (Appendix 3, Table 5).

Summary of Findings

Clinical Utility of Routine Pathology for Removed Intrauterine Devices

No relevant evidence regarding the routine pathology for removed IUDs was identified; therefore, no summary can be provided.

Clinical Utility of Routine Pathology for Therapeutic Abortions

Appendix 4 Table 6 presents a table of the main study findings and authors' conclusions. One non-randomized study compared the results of assessment of the products of conception by a surgeon and a pathologist, relative to a reference standard of in clinic follow-up two weeks after the procedure. Of a total of 1155 early abortions performed during the study period, 676 cases had complete outcome data and were used for the final analysis. For surgeon assessment, sensitivity for detecting an abnormal outcome was 22% (95% CI, 8% to 44%) with a specificity of 90% (95% CI, 88% to 93%). For pathologists, the sensitivity was 57% (95% CI, 35% to 76%) and the specificity was 88% (95% CI, 85% to 91%). Overall, tissue analyses by the surgeons and pathologists agreed in 83% of cases (kappa coefficient 0.16, P = 0.00). The authors concluded that both surgeons and pathologists did poorly at predicting abnormal outcomes following therapeutic abortion and that routine pathology examination did not confer an important benefit.

Cost-effectiveness of Routine Pathology for Removed Intrauterine Devices

No relevant evidence regarding the cost-effectiveness of routine pathology for removed IUDs was identified; therefore, no summary can be provided.

Cost-effectiveness of Routine Pathology for Removed Therapeutic Abortions

No relevant evidence regarding the cost-effectiveness of routine pathology for therapeutic abortions was identified; therefore, no summary can be provided.

Guidelines Regarding Routine Pathology for Removed Intrauterine Devices

No relevant guidelines regarding routine pathology for removed IUDs was identified; therefore, no summary can be provided.

Guidelines Regarding Routine Pathology for Therapeutic Abortions

Appendix 4 Table 7 presents a table of the main guideline recommendations. The NAF guidelines state that termination of pregnancy must be confirmed prior to a patient leaving the facility. They recommend that in "first-trimester terminations, flotation of tissue should be used to identify products of conception, including gestational sac" (p.52). Tissue flotation is performed at the facility by the abortion provider (e.g., surgeon). The NAF guidelines also include the statement that "sending the evacuated uterine contents for additional pathological examination is not required" (p.52) as an option. An 'option' means that the individual provider should have flexibility to make the decision.[9]

The SOGC guidelines state that “routine gross examination of the uterine contents should be performed immediately after induced abortion” and that “histopathological examination of products of conception must be performed when gestational trophoblastic neoplasia or ectopic pregnancy is suspected.” (p.753)[10] Both were strong recommendations based on very low level of evidence. Thus, routine pathology for therapeutic abortions does not appear to be a guideline recommendation by the SOGC.

Limitations

The literature of the clinical utility of routine pathology for therapeutic abortion was sparse, consisting of one study that was published in 2002.[8] Further, the data were generated from three clinics. It is not clear if similar results would be observed with more recent data or with data from other clinics. Further, this study was limited by the amount of missing outcome data, which could bias the estimates of diagnostic accuracy (relative to an estimate that was obtained from the full study population if available) and may limit the generalizability of the results to the entire population originally enrolled in the trial. Further, a study inclusion criteria was less than six weeks gestation. It is not clear if the results would be applicable to therapeutic abortions performed after six weeks gestation, and all Canadian provinces and territories offer abortion services beyond six weeks.[11]

Two guidelines were identified, both of which were from North America, and one of which was from Canada.[9,10] Thus, the guidelines would be expected to be generalizable to the Canadian context. The evidence base from which the guidelines were developed was limited[9,10] and the level of evidence was considered very low by the SOGC.

No evidence of the clinical utility of routine pathology for removed intrauterine devices was identified, or evidence of cost-effectiveness of routine pathology for therapeutic abortion or removed IUDs. No guidelines regarding removed IUDs were identified.

Conclusions and Implications for Decision or Policy Making

Based on one non-randomized study, both surgeons and pathologists were poor at identifying abnormal outcomes following therapeutic abortion at less than six weeks gestation. The agreement between surgeons and pathologists was also poor. However, the ability to draw firm conclusions about the clinical utility of routine pathology for therapeutic abortion is limited by the sparse evidence base and the amount of missing data and lack of generalizability beyond six weeks gestation of the one included study. The two identified evidence-based guidelines do not state that routine pathology is required for elective therapeutic abortion. However, the SOGC strongly recommends histopathological examination of products of conception when gestational trophoblastic neoplasia or ectopic pregnancy is suspected.

No conclusions can be made regarding the clinical utility of routine pathology for removed intrauterine devices or cost-effectiveness of routine pathology for therapeutic abortion or removed intrauterine devices, due to the lack of literature identified for these questions. No guidelines regarding routine pathology for removed intrauterine devices were identified. As such, no conclusion can be made.

References

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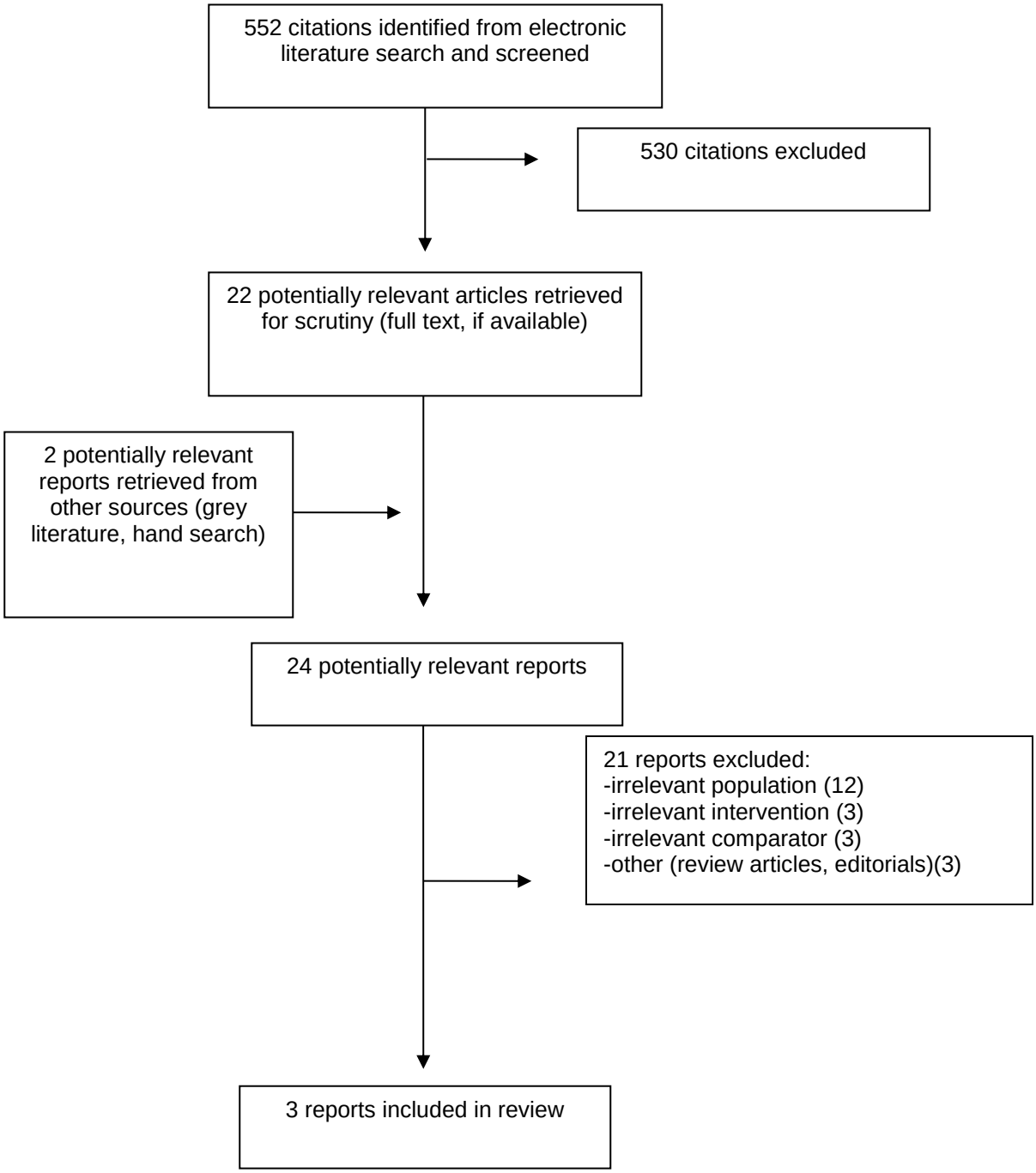
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Non-randomized studies				
Paul, 2002[8] United States	Single cohort of patients who underwent early therapeutic abortion (less than six weeks gestation) at three Planned Parenthood clinics in the United States from January 1, 1998 to August 31, 2000.	1155 early abortions performed with vacuum aspiration, 679 (59%) of which had data available for analysis.	Surgeon - Examination of fresh tissue aspirate by surgeon immediately following the procedure to identify the gestational sac, villi, and decidua. Pathologist - Microscopic examination of tissue aspirate by a pathologist at an external pathology laboratory. Gold standard – verification of abortion outcome in clinic at a two-week follow-up appointment.	Abnormal outcome (defined as any outcome other than complete abortion examples of which include failed attempted abortion, incomplete abortion, or ectopic pregnancy). Sensitivities, specificities, and positive and negative predictive values of the surgeons' and the pathologists' tissue examinations were calculated.

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
National Abortion Federation, 2018[9]						
Intended users: facilities that provide abortion care and providers of abortion. Target population: women undergoing abortion.	Abortion including abortions, including uterine aspiration, dilation and evacuation, and medical induction	A variety of outcomes related to abortion including pathological assessment of products of conceptions.	Limited detail provided but process based on based on the methodology described by in '*A Manual for Assessing Health Practices and Designing Practice Policies: The Explicit Approach'*. Update to their 2017 CPGs. Performed systematic literature searches of multiple databases to identify any new literature (no search range was provided). Seven new studies were selected for inclusion in the 2018 CPGs as "they changed one or more statements or substantially improved the level of evidence supporting a current statement."	Statements were categorized as standards, recommendations, or option according to their intended level of flexibility in application 1) Standards: intended to be applied in virtually all cases. Deviations will be rare and difficult to justify. 2) Recommendations: steering in nature. They do not have the force of standards, but when not adhered to, there should be documented, rational clinical justification. They allow some latitude in clinical management. 3) Options: neutral with respect to a treatment choice. They merely note that different interventions are available and that different people make different choices. They may contribute to the educational process, and they require no justification.	Changes to each policy statement were drafted by NAF's Medical Director and Associate Medical Director based on the included papers. No further details on development and evaluation were provided.	Newly identified and selected papers were reviewed by the NAF Clinical Policy Committee and changes to each policy statement were edited and approved by the entire committee. No further details on validation were provided.

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
Society of Obstetricians and Gynaecologists of Canada, 2018[10]						
Intended users: Gynecologists, family physicians, nurses, midwives, residents, and other health care providers who currently or intend to provide and/or teach induced abortions. Target population: Women with an unintended or abnormal first or second trimester pregnancy.	Surgical induced abortion and second trimester medical abortion, including pre- and post-procedural care.	Safety, efficacy, and costs.	Evidence identified from database search (multiple databases, but no search of the grey literature was performed). No details of evidence selection or synthesis were provided.	Quality of evidence was assessed using the GRADE methodology framework. Strength of Recommendation: Strong - Highly confident of the balance between desirable and undesirable consequences (i.e., desirable consequences outweigh the undesirable consequences, or undesirable consequences outweigh the desirable consequences). Weak - Less confident of the balance between desirable and undesirable consequences. Level of Evidence: High - Very confident that the true effect lies close to that of the estimate of the effect.	No details regarding development of recommendations and evaluation were provided.	No details were provided regarding guideline validation.

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
				Moderate - Moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low - Confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. Very low - Very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.		

CPG = Clinical practice guideline; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; NAF = National Abortion Federation.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Clinical Studies using QUADAS 2[5]

Strengths	Limitations
Paul 2002[8]	
A consecutive sample of patients who had early surgical abortion during the study period was enrolled into the study. There were no exclusion criteria. All patients who had early surgical abortion during the study period were eligible to participate. The reference standard (in person confirmation of abortion) was likely to correctly classify the target condition.	Only women with an intrauterine sac of less than six weeks were included. The 'gold standard' was verification of abortion at in person follow-up two weeks later. Of the 1155 patients that comprised the consecutive sample, 679 were verified with in person follow-up (59%). Thus 41% of patients were not assessed. The time between assessment of the products of conception by the surgeon and the pathologists was not stated. It is not clear if a time delay would influence the interpretation of outcomes by the pathologists. The tests were interpreted with knowledge of the reference standard.

Table 5: Strengths and Limitations of Guidelines using AGREE II[6]

Item	Guideline	
	National Abortion Federation, 2018[9]	Society of Obstetricians and Gynaecologists of Canada, 2018[10]
Domain 1: Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Yes
Domain 2: Stakeholder Involvement		
4. The guideline development group includes individuals from all relevant professional groups.	Unclear – limited detail provided.	Unclear – limited detail provided.

Table 5: Strengths and Limitations of Guidelines using AGREE II[6]

Item	Guideline	
	National Abortion Federation, 2018[9]	Society of Obstetricians and Gynaecologists of Canada, 2018[10]
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Unclear – limited detail provided.	Unclear – limited detail provided.
6. The target users of the guideline are clearly defined.	Yes – providers of abortion	Yes – Gynecologists, family physicians, nurses, midwives, residents, and other providers of abortion
Domain 3: Rigour of Development		
7. Systematic methods were used to search for evidence.	Yes – Databases described.	Yes – Databases described.
8. The criteria for selecting the evidence are clearly described.	Yes – Inclusion and exclusion criteria stated.	Yes – Inclusion and exclusion criteria stated.
9. The strengths and limitations of the body of evidence are clearly described.	No – Limited to no detail provided.	Yes – Used GRADE methodology
10. The methods for formulating the recommendations are clearly described.	No – Limited to no detail provided.	No – Limited to no detail provided.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Unclear – Limited to no detail provided.	Unclear – Limited to no detail provided.
12. There is an explicit link between the recommendations and the supporting evidence.	Yes – The evidence for each recommendation is provided in each section.	Yes – The evidence for each recommendation is reviewed and linked.
13. The guideline has been externally reviewed by experts prior to its publication.	Unclear – Limited to no detail provided.	Unclear – Limited to no detail provided.
14. A procedure for updating the guideline is provided.	No – Limited to no detail provided.	No – Limited to no detail provided.
Domain 4: Clarity of Presentation		
15. The recommendations are specific and unambiguous.	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes – The options for management are clear based on the rankings of the levels of evidence.	Unclear
17. Key recommendations are easily identifiable.	Yes – Clear presentation of recommendations.	Yes – All presented at the beginning of the document.

Table 5: Strengths and Limitations of Guidelines using AGREE II[6]

Item	Guideline	
	National Abortion Federation, 2018[9]	Society of Obstetricians and Gynaecologists of Canada, 2018[10]
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	No	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	No
20. The potential resource implications of applying the recommendations have been considered.	No	No
21. The guideline presents monitoring and/or auditing criteria.	No	No
Domain 6: Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	Unclear	Unclear
23. Competing interests of guideline development group members have been recorded and addressed.	Unclear – no declaration of conflict of interest.	Unclear – no declaration of conflict of interest.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Paul 2002[8]	
Pathologists' Tissue Examinations for Detecting Abnormal Abortion Outcomes (n = 676)[a] Sensitivity: 5/23 = 22% (95% CI, 8% to 44%) Specificity: 590/653 = 90% (95% CI, 88% to 93%) Positive predictive value: 5/68 = 7% (95% CI, 3% to 17%) Negative predictive value: 590/608 = 97% (95% CI, 95% to 98%) **Surgeons' Tissue Examinations for Detecting Abnormal Abortion Outcomes (n = 676)[a]** Sensitivity: 13/23 = 57% (95% CI, 35% to 76%) Specificity: 576/653 = 88% (95% CI, 85% to 91%) Positive predictive value: 13/90 = 14% (95% CI, 8% to 24%) Negative predictive value: 576/586 = 98% (95% CI, 97% to 99%) Overall, tissue analyses by the surgeons and pathologists agreed in 558 (83%) cases (kappa coefficient 0.16, P = 0.00).	*"In summary, routine pathology examination after early surgical abortion conferred no important benefit. Although the surgeons' tissue inspections were poor at predicting abnormal outcomes, the pathologists did no better. Our results challenge the rationale for regulations in Massachusetts and elsewhere, which mandate routine pathologic analysis of abortion specimens at added cost to providers. Directing resources toward improving the ability of physicians to detect abnormal outcomes at the time of the abortion procedure would do more to benefit women's health."* P.570

[a] Abnormal outcomes included any outcome other than complete abortion (i.e., failed attempted abortion, incomplete abortion, or ectopic pregnancy). The subset of procedures performed during the study period with complete outcome data was used for analysis (676/1155 = 41%).

CI = Confidence interval.

Table 7: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
National Abortion Federation, 2018[9]	
"13. EVALUATION OF EVACUATED UTERINE CONTENTS *Policy Statement: Identification of appropriate products of conception (POC) following evacuation abortion procedures confirms termination of an intrauterine pregnancy.* *Standard 13.1. Termination of pregnancy must be confirmed prior to the patient leaving the facility or further evaluation must be initiated.* *Recommendation 13.1.1. Evacuated uterine contents should be examined before the patient leaves the facility.* *Recommendation 13.1.2. In first-trimester terminations, flotation of tissue should be used to identify products of conception, including gestational sac.* *Option 13.1.2.1. Backlighting of tissue may be useful.* *Option 13.1.2.2. Sending the evacuated uterine contents for additional pathological examination is not required."* P.52	The lack of requirement for sending the evacuated uterine contents for additional pathological examination was considered an "option" meaning that the statement is neutral with respect to a treatment choice and is a note that different interventions are available and that different practitioners may make different choices.
Society of Obstetricians and Gynaecologists of Canada, 2018[10]	
"Routine gross examination of the uterine contents should be performed immediately after induced abortion. *Histopathological examination of products of conception must be performed when gestational trophoblastic neoplasia or ectopic pregnancy is suspected." P. 753*	Strong recommendation. Level of evidence: Very low. Strong recommendation. Level of evidence: Very low

Appendix 5: Additional References of Potential Interest

Guidelines with Unclear Methodology

BC's Agency for Pathology and Laboratory Medicine. Specimens not required for submission to pathology for examination. Vancouver (BC): Provincial Health Services Authority; 2017 (reviewed 2019): http://www.bccss.org/bcaplm-site/Documents/Working%20Groups/AP/Specimens%20Not%20Required%20for%20Submission%20to%20Pathology%20for%20Examination.pdf. Accessed 2019 Sep 9.

Laboratory Service, Interior Health. Tissues exempt from pathological examination policy. Kelowna (BC): Interior Health Authority; 2018: https://www.interiorhealth.ca/sites/Partners/LabServices/DeptSpecific/AnatomicalPathology/Documents/AP%20Exempt%20Tissues.pdf. Accessed 2019 Sep 9.

Department of Pathology and Laboratory Medicine. Specimens exempt from all gross &/or microscopic review; Saskatchewan Health Authority. Saskatoon (SK); 2018: https://www.saskatoonhealthregion.ca/locations_services/Services/Pathology-Laboratory-Med/healthpractitioners/Documents/Policy%20and%20Procedure/ANATOMIC%20PATHOLOGY%20SPECIMENS%20EXEMPT%20FROM%20ALL%20GROSS%20OR%20MICROSCOPIC%20REVIEW.pdf. Accessed 2019 Sep 9.

Yap SJ, Watts JC, Faithfull TJ, Wong SZ, Wylde KL, McGurgan PM. Is tissue an issue? Current practice and opinion in Western Australia for routine histopathology on products of conception. *Aust N Z J Obstet Gynaecol*. 2014 Oct;54(5):493-496. PubMed: PM25287569