

Systematic Review

Efficacy, Safety, and Fertility Outcomes of Loop Electrosurgical Excision Procedure Versus Cold-Knife Conization for Cervical Intraepithelial Neoplasia: A Systematic Review and Meta-Analysis

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Abstract

Background: Loop electrosurgical excision procedure (LEEP) and cold-knife conization (CKC) are both used for cervical intraepithelial neoplasia (CIN), yet their comparative efficacy and reproductive safety remain unclear. **Methods:** We systematically searched PubMed, Embase, the Cochrane Central Register of Controlled Trials and Web of Science through March 2025 for randomized controlled trials (RCTs) comparing LEEP with CKC in histologically confirmed CIN. 7 RCTs enrolling 1007 women (LEEP, $n = 508$; CKC, $n = 499$) from six countries were included. Primary endpoints were residual disease, perioperative morbidity, and obstetric outcomes; secondary endpoints included recurrence and re-intervention. Risk of bias was assessed with Cochrane tools, and data were pooled using RevMan. **Results:** CKC was associated with a lower rate of residual disease than LEEP (relative risk [RR] = 1.55; 95% confidence interval [CI]: 1.04–2.31; $p = 0.03$). Conversely, LEEP was associated with numerically lower rates of preterm births (RR = 0.54; 95% CI: 0.23–1.28; $p = 0.16$) and premature rupture of membranes (RR = 0.57; 95% CI: 0.29–1.14; $p = 0.11$), although CIs crossed unity. Excision dimensions, positive margins, postoperative bleeding, cervical stenosis, infection, spontaneous abortion, and reoperation rates did not differ significantly between groups. Recurrence showed a nonsignificant trend toward being higher after LEEP (RR = 2.25; 95% CI: 0.87–5.78; $p = 0.09$). **Conclusions:** CKC demonstrated superiority in reducing residual disease, whereas LEEP showed a nonsignificant trend toward lower risks of premature birth and premature rupture of membranes. Perioperative morbidity was comparable between procedures. Treatment decisions should integrate pathologic accuracy, surgical feasibility, and fertility considerations. Long-term, rigorously designed trials incorporating quality-of-life endpoints are warranted to validate these findings. **Registration:** The study has been registered on <https://www.crd.york.ac.uk/PROSPERO/> (registration number: CRD420251009221; registration link: <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251009221>).

Keywords: cervical intraepithelial neoplasia (CIN); loop electrosurgical excision procedure (LEEP); cold-knife conization (CKC); systematic review; meta-analysis

1. Introduction

Cervical cancer is one of the most common malignancies and a leading cause of cancer-related mortality among women worldwide [1,2,3,4,5]. In 2018, approximately 569,000 new cases of cervical cancer were diagnosed globally, resulting in about 311,000 deaths [6,7,8,9]. By 2022, the number of new cervical cancer cases exceeded 660,000, with approximately 348,000 deaths reported worldwide [10,11,12]. However, the burden is more severe in low- and middle-income countries. It is estimated that, over the next 10–20 years, 11 million women in these regions will be diagnosed with cervical cancer. It is the second most common cancer among women and is the second leading cause of cancer-related deaths in women [6,13]. Cervical intraepithelial neoplasia (CIN) represents the premalignant phase in the progression toward invasive cervical carcinoma. Histologically, it is classified into three grades: CIN 1, CIN 2, and CIN 3 [14,15,16]. According to a laboratory survey conducted by the College of American Pathol-

ogists (CAP), over one million women are diagnosed with CIN 1 annually, with 500,000 found to have high-grade cervical precancerous lesions (CIN 2 and CIN 3) [17]. Evidence indicates that among patients diagnosed with CIN 3 at Auckland National Women's Hospital, New Zealand, between 1955 and 1976, untreated individuals exhibited a cumulative cervical cancer incidence rate of 31.3%–50.3% over a 30-year follow-up period. In contrast, patients receiving adequate treatment demonstrated a cumulative incidence rate of only 0.7% [18]. These data demonstrate that timely and appropriate therapeutic intervention plays a crucial role in reducing the risk of cervical cancer development [19,20]. Furthermore, in a 22-year follow-up study, patients with CIN who underwent excisional therapy exhibited an extremely low recurrence rate of only 1.1%, with no progression to invasive cervical cancer [21]. This further supports the efficacy and importance of evidence-based therapeutic interventions in the management of cervical precancerous lesions [22].



Currently, CIN treatment primarily involves excisional and ablation therapies [23,24,25,26]. Excisional methods include cold-knife conization (CKC) and the loop electrosurgical excision procedure (LEEP) [27,28,29]. CKC is a traditional surgical approach [30,31]. It employs a surgical knife for excision, yielding more complete tissue specimens but potentially causing greater bleeding and longer procedure times. LEEP, the most commonly used method, uses an electrode loop to excise lesions, offering shorter procedure times and less bleeding [32,33]. However, thermal damage may affect pathological assessment of specimen margins [34]. Furthermore, women diagnosed with CIN are typically of reproductive age, with an average age of approximately 30 years, and may include younger individuals, such as adolescents [32,35,36]. The impact of both methods on female fertility is a key clinical concern, particularly for patients with future childbearing desires. Currently, multiple comparative studies of LEEP and CKC for the treatment of CIN have been conducted, but their results are not entirely consistent. Some studies have shown comparable therapeutic efficacy between LEEP and CKC; however, LEEP demonstrates several advantages, such as shorter operative time, reduced bleeding, and simpler procedural execution [37,38,39,40,41]. Conversely, other research suggests CKC may yield lower positive margin rates and recurrence rates [42,43,44,45]. Furthermore, controversy persists regarding the effects of both methods on subsequent pregnancy outcomes, including preterm birth and premature rupture of membranes [46,47,48,49].

To date, randomized evidence comparing LEEP with CKC remains fragmented. We therefore conducted a systematic review and meta-analysis to synthesize available data on cure rates, adverse events, and subsequent reproductive outcomes. These findings provide clinicians with quantitative, high-certainty benchmarks to guide the selection between these two excisional strategies for CIN.

2. Materials and Methods

The review protocol was registered with International Prospective Register of Systematic Reviews (PROSPERO) on March 11, 2025 (CRD420251009221). All prespecified endpoints in the registered protocol were included in the final manuscript. No changes were made to the primary or secondary outcomes. The only modification was the addition of Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment, as suggested during peer review, to enhance evaluation of evidence quality.

2.1 Literature Search Strategy

This study conducted a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Comprehensive electronic searches were conducted across four major databases: PubMed, Embase, the

Cochrane Central Register of Controlled Trials, and Web of Science. The time window was set from the inception of each database to 31 March 2025. To ensure reproducibility, the search strategy was constructed in accordance with the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework. Eligible participants were defined as women with a confirmed diagnosis of CIN. The experimental intervention was defined as loop electrosurgical excision, whereas CKC was designated as the comparator. Outcomes of interest included specimen dimensions, margin involvement, residual disease, postoperative hemorrhage, cervical stenosis, recurrence, infection, need for secondary surgery, and obstetric outcomes such as spontaneous abortion, preterm birth, premature rupture of membranes, and cesarean delivery. Only randomized controlled trials (RCTs) were included. Detailed search strategies are presented in Table 1.

2.2 Inclusion and Exclusion Criteria

Inclusion Criteria: (1) RCTs; (2) studies comparing the efficacy of LEEP versus CKC for the treatment of CIN; (3) patients with histologically confirmed CIN; and (4) outcomes including at least one of the following: resection depth, resection diameter, positive margins, residual disease, postoperative bleeding, cervical stenosis, recurrence, infection, reoperation, spontaneous abortion, preterm delivery, premature rupture of membranes, and cesarean section.

Exclusion Criteria: studies were excluded if random allocation was absent from the study design. Duplicate reports of identical datasets were also removed. Studies in which critical numerical results were either incomplete or could not be retrieved after author contact were also omitted.

2.3 Literature Screening

EndNote software (version X9; Clarivate Analytics, Philadelphia, PA, USA) was used for bibliographic management throughout the study. Initially, two independent researchers screened the literature, excluding duplicates, non-RCTs, review articles, conference papers, protocols, and correspondence. Next, abstracts of the remaining studies were reviewed for eligibility against the inclusion and exclusion criteria. Finally, studies that passed abstract screening underwent full-text review by both researchers to determine final inclusion. Disagreements during screening or full-text assessment were resolved through discussion with a third researcher.

2.4 Data Extraction

The required numbers were independently extracted by two reviewers. Basic citation information, including first author, publication year, and sample size, was recorded, along with age distribution, lesion grade, and any additional demographic characteristics. Surgical details for LEEP or CKC were documented, and all reported

Table 1. Search strategies for electronic databases.

	PubMed
#1	Squamous Intraepithelial Lesions [MeSH Terms]
#2	((((((((((Squamous Intraepithelial Lesions[Title/Abstract]) OR (high-grade squamous intraepithelial lesions[Title/Abstract])) OR (high-grade squamous intraepithelial lesion[Title/Abstract])) OR (High-Grade Squamous Intraepithelial Lesions[Title/Abstract])) OR (High-Grade Squamous Intraepithelial Lesion[Title/Abstract])) OR (High Grade Squamous Intraepithelial Lesions[Title/Abstract])) OR (High Grade Squamous Intraepithelial Lesion[Title/Abstract])) OR (high-grade cervical intraepithelial neoplasia[Title/Abstract])) OR (HSIL[Title/Abstract])) OR (CIN2[Title/Abstract])) OR (CIN3[Title/Abstract])) OR (CIN[Title/Abstract]))
#3	#1 OR #2
#4	((((((((((loop electrosurgical excision procedure[Title/Abstract]) OR (LEEP[Title/Abstract])) OR (high frequency radiosurgical knife[Title/Abstract])) OR (cold knife conization[Title/Abstract])) OR (CKC[Title/Abstract])) OR (cold knife[Title/Abstract])) OR (electric knife[Title/Abstract])) OR (conical cervical resection[Title/Abstract])) OR (cervical cone excision[Title/Abstract])) OR (excisional cone cervix[Title/Abstract])) OR (cervical conization[Title/Abstract]))
#5	#3 AND #4
	EMBASE
#1	'squamous intraepithelial lesions':ab,ti OR 'high-grade squamous intraepithelial lesions':ab,ti OR 'high-grade squamous intraepithelial lesion':ab,ti OR 'high grade squamous intraepithelial lesions':ab,ti OR 'high grade squamous intraepithelial lesion':ab,ti OR 'high-grade cervical intraepithelial neoplasia':ab,ti OR hsil:ab,ti OR cin2:ab,ti OR cin3:ab,ti OR cin:ab,ti
#2	'loop electrosurgical excision procedure': ab, ti OR leep: ab, ti OR 'high frequency radiosurgical knife': ab, ti OR 'cold knife conization': ab, ti OR ckc: ab, ti OR 'cold knife': ab, ti OR 'electric knife': ab, ti OR 'conical cervical resection': ab, ti OR 'excisional cone cervix': ab, ti OR 'cervical conization': ab, ti
#3	#1 AND #2
	Web of Science
#1	((((((((((AB=(Squamous Intraepithelial Lesions)) OR AB=(high-grade squamous intraepithelial lesions)) OR AB=(high-grade squamous intraepithelial lesion)) OR AB=(High-Grade Squamous Intraepithelial Lesions)) OR AB=(High-Grade Squamous Intraepithelial Lesion)) OR AB=(High Grade Squamous Intraepithelial Lesions)) OR AB=(High Grade Squamous Intraepithelial Lesion)) OR AB=(high-grade cervical intraepithelial neoplasia)) OR AB=(HSIL)) OR AB=(CIN2)) OR AB=(CIN3)) OR AB=(CIN))
#2	((((((((((AB=(loop electrosurgical excision procedure)) OR AB=(LEEP)) OR AB=(high frequency radiosurgical knife)) OR AB=(cold knife conization)) OR AB=(CKC)) OR AB=(cold knife)) OR AB=(electric knife)) OR AB=(conical cervical resection)) OR AB=(cervical cone excision)) OR AB=(excisional cone cervix)) OR AB=(cervical conization))
#3	#1 AND #2
	Cochrane
#1	(Squamous Intraepithelial Lesions): ti, ab,kw OR (high-grade squamous intraepithelial lesions): ti, ab,kw OR (high-grade squamous intraepithelial lesion): ti, ab,kw OR (High-Grade Squamous Intraepithelial Lesions): ti, ab,kw OR (High-Grade Squamous Intraepithelial Lesion): ti, ab,kw
#2	(High Grade Squamous Intraepithelial Lesions):ti,ab,kw OR (High Grade Squamous Intraepithelial Lesion):ti,ab,kw OR (high-grade cervical intraepithelial neoplasia):ti,ab,kw OR (HSIL):ti,ab,kw OR (CIN2):ti,ab,kw
#3	(CIN3):ti,ab,kw OR (CIN):ti,ab,kw
#4	#1 OR #2 OR #3
#5	(loop electrosurgical excision procedure):ti,ab,kw OR (LEEP):ti,ab,kw OR (high frequency radiosurgical knife):ti,ab,kw OR (cold knife conization):ti,ab,kw OR (CKC):ti,ab,kw
#6	(cold knife): ti, ab,kw OR (electric knife): ti, ab,kw OR (conical cervical resection): ti, ab,kw OR (cervical cone excision): ti, ab,kw OR (excisional cone cervix): ti, ab,kw
#7	(cervical conization): ti, ab,kw
#8	#5 OR #6 OR #7
#9	#4 AND #8

CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesions; LEEP, loop electrosurgical excision procedure; CKC, cold-knife conization.

data on operative time, blood loss, specimen dimensions, margin status, recurrence, bleeding or infection episodes, and obstetric outcomes such as preterm delivery or rupture of membranes, were collected.

2.5 Risk of Bias Assessment for Individual Studies

Two reviewers working independently assessed the methodological quality of each trial with the Cochrane risk-of-bias tool (Cochrane Handbook, version 5.1.0). Seven predefined domains were evaluated: sequence generation, allocation concealment, blinding of caregivers, blinding of outcome assessors, completeness of follow-up, selective outcome reporting, and any additional potential sources of bias. After the initial assessment, studies were classified into three summary categories: low risk (≤ 2 domains rated as high risk), moderate risk (3–4 high-risk domains), or high risk (≥ 5 high-risk domains). Whenever published reports lacked sufficient detail, corresponding authors were contacted via email to obtain missing information or to clarify ambiguous descriptions.

2.6 Statistical Analysis

For dichotomous variables (e.g., positive margin rate, recurrence rate, complication incidence), the relative risk (RR) and 95% confidence interval (CI) were calculated. For continuous variables (e.g., resection depth, diameter), standardized mean differences (SMDs) and its 95% CI were calculated. Heterogeneity was assessed using the I^2 statistic. When the I^2 statistic exceeded 50 %, substantial heterogeneity was considered present, and a random-effects model was applied. Conversely, values at or below this threshold led us to adopt a fixed-effects approach [50]. $p < 0.05$ was considered statistically significant. For continuous variables measured using a uniform unit across studies (e.g., resection depth in millimeters), the mean difference (MD) was initially considered for analysis. However, given the significant heterogeneity in measurement methods and reporting standards across the nearly three decades of the included RCTs (from 1994 to 2020), SMD was selected to ensure statistical robustness. SMD provides comparable effect size estimates despite variations in absolute values due to differences in surgical equipment, techniques, as well as measurement protocols.

2.7 Outcome Definitions and Standardization

To address potential heterogeneity in outcome definitions across studies, standardized definitions during data extraction were applied. Residual disease was defined as histologically confirmed CIN of any grade or invasive cancer identified in specimens obtained from subsequent surgical procedures (re-conization or hysterectomy) performed within 6 months following the initial conization. Recurrence was defined as histologically confirmed CIN grade 2 or higher, or invasive cancer, detected at least 6 months after a documented disease-free interval, and characterized

by negative surgical margins on the initial conization and at least one negative follow-up test. Positive margins were defined as the presence of CIN grades 2–3 at the inked surgical margin on permanent section histopathology; studies utilizing frozen section analysis were excluded from margin-related meta-analyses. Preterm birth was defined as delivery prior to 37 weeks of gestation, and premature rupture of membranes was defined as membrane rupture occurring before labor onset at < 37 weeks of gestation.

2.8 GRADE Assessment

The certainty of evidence for each outcome was assessed using the GRADE framework, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

3. Results

3.1 Overview of Search Results

Using the predefined search strategy, electronic database searches initially yielded 4242 records. Following the removal of 1795 duplicates, two independent reviewers (LP and XH) screened the titles and abstracts of the remaining 2447 references, excluding 2381 records deemed irrelevant. Ultimately, 66 full-text articles were retrieved for eligibility assessment. Of these, 59 were subsequently excluded for the following reasons: 1 with incomplete data, 29 reviews, conference abstracts, or case reports, 3 involving pregnant women, 24 single-arm studies, 1 clinical practice guideline and 1 Long-term follow-up of the same RCT. 7 RCTs met the inclusion criteria and were included in the final analysis. The study selection process is illustrated in Fig. 1.

3.2 Overview of Included Studies

A total of 7 RCTs [34,37,38,42,43,46,51,52] were included. Mathevet et al. (1994) [42] and Mathevet et al. (2003) [52] described the same randomized cohort: reference 42 reported baseline and short-term perioperative findings, and reference 52 provided long term obstetric follow-up for participants from this trial; reference 52 was not counted as an independent randomized controlled trial. The combined study population comprised 1007 participants (LEEP = 508; CKC = 499) from six countries, China ($n = 2$), Canada ($n = 1$), Austria ($n = 1$), the United States ($n = 1$), France ($n = 1$), and Slovenia ($n = 1$). Follow-up durations ranged from 3 to 65 months, with the 65-month follow-up obtained from reference [52]. The experimental group underwent LEEP, while the control group received CKC. Outcome measures included resection depth, resection diameter, positive margins, residual disease, postoperative bleeding, cervical stenosis, recurrence, infection, reoperation, spontaneous abortion, preterm birth, premature rupture of membranes, and cesarean section. Detailed characteristics of the included studies are summarized in Table 2 (Ref. [34,37,38,42,43,46,51,52]).

Table 2. Detailed characteristics of included studies.

Study	Country	Population	Age	Total	Research design	Long-term follow-up time	Inclusion criteria	Exclusion criteria	Outcome
Girardi F et al. (1994) [51]	Austria	CIN 1–3	LEEP: 31 CKC: 30	LEEP: 38 CKC: 52	RCT	10 months	Patients must have CIN confirmed by biopsy pathology, including CIN 3 (severe dysplasia or carcinoma <i>in situ</i>) and persistent CIN 1 or CIN 2 (mild or moderate dysplasia). Patients were scheduled to undergo conization for both diagnostic and treatment.	Patients with suspicious cytological findings alone, but not confirmed by biopsy pathology, were excluded. Patients with lesions limited to the cervical canal (no ectocervical lesions) were excluded, as such lesions may not be suitable for loop electrosurgical (LEEP).	Positive resection margin Disease residue Postoperative bleeding Disease recurrence Spontaneous abortion
Mathevet P et al. (1994) [42,52]	Canada	CIN 1–3	LEEP: 33.5 CKC: 34.1	LEEP: 36 CKC: 37	RCT	6 months	The patient presented cervical cytology results of high-grade squamous intraepithelial lesion (HSIL). Cervical biopsy showed either CIN 1–2 (CIN grade 1 or 2) with no squamocolumnar junction visible, or CIN3 (CIN grade 3).	NA	Positive resection margin Disease residue Postoperative bleeding Cervical stenosis Disease recurrence Spontaneous abortion Premature delivery Premature rupture of membranes Cesarean section
Duggan BD et al. (1999) [38]	US	CIN 1–3	LEEP: NA CKC: NA	LEEP: 91 CKC: 89	RCT	12 months	Age ≥18 years, non-pregnant, with one of the following indications: unsatisfactory colposcopy and cervical biopsy showing CIN; cervical tube scratch specimen positive; cervical invasive carcinoma is suspected but not confirmed by biopsy; Pap smear results are inconsistent with cervical biopsy results; Cervical biopsy revealed microscopic invasion or adenocarcinoma <i>in situ</i> .	Active cervical inflammation or infection, cervical anatomy unsuitable for LEEP, suspected invasive cancer, surgical contraindications, satisfactory colposcopy with negative cervical scrub, previous cryotherapy, laser or conization, HIV infection, history of cervical cancer, or pelvic radiotherapy.	Positive resection margin Disease residue Cervical stenosis Disease recurrence Infection Second operation

Table 2. Continued.

Study	Country	Population	Age	Total	Research design	Long-term follow-up time	Inclusion criteria	Exclusion criteria	Outcome
Giacalone PL et al. (1999) [43]	France	CIN 2–3	LEEP: 34.3 ± 6.1 CKC: 36.5 ± 9.5	LEEP: 28 CKC: 38	RCT	3 months	Histologically confirmed grade 3 CIN or grade 2 CIN with no squamocolumn junction.	With persistent abnormal histology or recurrent disease after previous treatment.	Depth Diameter Positive resection margin Disease residue Postoperative bleeding Cervical stenosis
Takac I and Gorisek B (1999) [37]	Slovenia	CIN 1–3	LEEP: 33 ± 7 CKC: 32 ± 9	LEEP: 120 CKC: 120	RCT	3 months	Patients with abnormal cervical cytology and colposcopy. Patients with histologically confirmed CIN 2 or CIN 3, persistent CIN 1, or with inconsistencies between cytology and histology.	NA	Positive resection margin Disease residue Postoperative bleeding Disease recurrence Infection Second operation
Liu Y et al. (2014) [46]	China	CIN 2–3	LEEP: 27.3 ± 7.6 CKC: 28.6 ± 6.8	LEEP: 124 CKC: 120	RCT	All patients treated with LEEP or CKC underwent regular clinical examinations after surgery until delivery.	Be younger than 39 years of age and plan to conceive naturally within the next 3 years; Previous cytological examination; Histologically confirmed CIN-III.	A history of repeated cervical excision or ablation; known major risk factors for preterm birth, including previous preterm birth and multiple pregnancies; a major medical condition (such as cardiovascular disease, diabetes or high blood pressure); alcohol, smoking, or drug abuse history.	Spontaneous abortion Premature delivery Premature rupture of membranes Cesarean section
Cai L et al. (2020) [34]	China	HSIL	LEEP: 46.66 CKC: 48.95	LEEP: 71 CKC: 43	RCT	3 months	HSIL was confirmed pathologically by colposcopy and cervical biopsy.	Pregnant women or those who have been pregnant in the past 6 months. Previous history of surgery, curettage or abortion. People with cancer, HIV/AIDS, or autoimmune diseases.	Depth Diameter Infection

Note: CIN, cervical intraepithelial neoplasia; CKC, cold knife conization; HSIL, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial lesions; LEEP, loop electrosurgical excision procedure; HIV/AIDS, human immunodeficiency virus/acquired immunodeficiency syndrome; NA, unavailable; RCT, randomized controlled trial. Mathevet et al., 2003 [52] reports long-term obstetric follow-up of this identical RCT cohort and is not an independent trial. Obstetric outcomes, disease recurrence and cervical stenosis were extracted from reference [52], whereas perioperative data were obtained from reference [42].

3.3 Risk of Bias in Included Studies

Fig. 2 represents the risk of bias (ROB) assessments of the included studies. All 7 studies employed appropriate randomization methods, including random number tables or computer-generated randomization. Regarding allocation concealment, 1 study explicitly reported using sequentially numbered sealed envelopes to conceal group allocation, an approach that prevents selection bias by preventing prediction of group assignment. The remaining 6 studies employed randomization methods but did not clearly specify measures for concealing allocation, such as using a centralized randomization system or sealed envelopes. Therefore, the concealment status of the random allocation scheme could not be determined, leaving the risk of bias unclear. Due to the nature of the surgical procedures (CKC versus LEEP), blinding of the intervention provider (surgeon) was not feasible, thus resulting in a higher risk of bias. In 3 studies, pathologists analyzing the conization specimens were unaware of the specific surgical technique performed on the patient (i.e., blinding of outcome assessors). 4 studies did not mention whether outcome assessors (e.g., surgeons, assistants, pathologists) were blinded to patient group assignment, potentially leading to measurement bias. Therefore, the risk of bias was deemed unclear. Regarding selective reporting, 6 studies detailed primary outcomes (e.g., cone biopsy specimen size, margin status, thermal injury severity, colposcopy findings, treatment success rates) and performed statistical analyses on these outcomes. No evidence of selective reporting was identified in these 6 studies, indicating a low risk of bias. 1 study did not explicitly state whether all predefined outcomes were reported or whether a predefined protocol was followed. Therefore, the possibility of selective reporting in this study could not be determined, resulting in an unclear risk of bias. The literature provided detailed descriptions of subject selection, surgical technique implementation, and postoperative follow-up. No other obvious sources of bias were identified, and all patients met strict inclusion criteria. Given the rigorous study design and implementation, the risk of other bias was assessed as low.

3.4 Statistical Results

3.4.1 Surgical Technical Parameters

Meta-analysis revealed no significant differences between LEEP and CKC in resection depth (SMD = -0.53 , 95% CI: -1.81 – 0.75 , $p = 0.42$, $I^2 = 94\%$) [34,43] (Fig. 3) or resection diameter (SMD = 0.36 , 95% CI: -0.11 – 0.82 , $p = 0.13$, $I^2 = 55\%$) [34,43] (Fig. 4). Positive margin rates were also comparable between groups (RR = 1.12 , 95% CI: 0.75 – 1.66 , $p = 0.58$, $I^2 = 20\%$) [37,38,42,43,51] (Fig. 5). Notably, substantial statistical heterogeneity was observed for resection depth ($I^2 = 94\%$) and moderate heterogeneity for resection diameter ($I^2 = 55\%$). We acknowledge that, given the limited number of included studies ($n = 7$ RCTs), robust subgroup analyses or meta-regression could not be

performed to explore sources of heterogeneity. This limitation may affect the interpretation of findings regarding surgical technical parameters. Based on qualitative assessment of the included studies, several potential sources of heterogeneity were identified: (1) variations in measurement methodologies: Girardi et al. (1994) [51] reported histologically measured specimen depth (CKC 15.8 mm versus LEEP 9.2 mm), whereas Giacalone et al. (1999) [43] measured surgical specimen height (CKC 18.9 mm versus LEEP 12.8 mm), and Mathevet et al. (1994) [42] employed volume calculations (CKC 1.91 cm^3 versus LEEP 0.96 cm^3); (2) differences in LEEP technical parameters: variations in power settings across studies (Mathevet et al. (1994) [42]: 30–50 W; Cai et al. (2020) [34]: 25–30 W), and electrode ring dimensions (height 10–20 mm, width 15–20 mm); and (3) Variability in pathological assessment criteria: standards for evaluating thermal injury margins differed among studies, potentially affecting measurable tissue determination. Despite substantial statistical heterogeneity, the two studies included for resection depth showed opposite directions of effect: Giacalone et al. [43] reported a smaller resection depth in the LEEP group, while Cai et al. [34] found comparable resection depth between LEEP and CKC. This inconsistency partly accounts for the extreme high heterogeneity. We explicitly acknowledge that uncertainty regarding heterogeneity sources, coupled with the small sample size, represents a significant limitation that may compromise the precision and generalizability of our findings concerning surgical technical parameters.

3.4.2 Oncological and Operative Outcomes

Meta-analysis demonstrated that residual disease rates were significantly higher following LEEP compared to CKC (RR = 1.55 , 95% CI: 1.04 – 2.31 , $p = 0.03$, $I^2 = 0\%$) [37,38,42,43,51] (Fig. 6), suggesting that LEEP may be less effective in eradicating residual disease. No significant between-group differences were observed for operative complications, including postoperative bleeding (RR = 0.96 , 95% CI: 0.48 – 1.93 , $p = 0.92$, $I^2 = 0\%$) [37,42,43,51] (Fig. 7), cervical stenosis (cervical stenosis (RR = 0.74 , 95% CI: 0.10 – 5.41 , $p = 0.77$, $I^2 = 54\%$)) [38,43,52] (Fig. 8), infection (RR = 1.04 , 95% CI: 0.65 – 1.65 , $p = 0.88$, $I^2 = 0\%$) [34,37,38] (Fig. 9), or reoperation requirements (RR = 1.28 , 95% CI: 0.69 – 2.39 , $p = 0.43$, $I^2 = 0\%$) [37,38] (Fig. 10). Disease recurrence showed a nonsignificant trend toward increased risk with LEEP (RR = 2.25 , 95% CI: 0.87 – 5.78 , $p = 0.09$, $I^2 = 0\%$) [37,38,51,52] (Fig. 11).

3.4.3 Obstetric Outcomes

3 studies [46,51,52] evaluated adverse pregnancy outcomes following LEEP versus CKC for CIN. Meta-analysis revealed no significant difference in spontaneous abortion risk between groups (RR = 1.09 , 95% CI: 0.59 – 2.03 , $p = 0.79$, $I^2 = 0\%$) (Fig. 12). The LEEP group demonstrated lower risks of preterm birth (RR = 0.54 , 95% CI: 0.23 – 1.28 ,

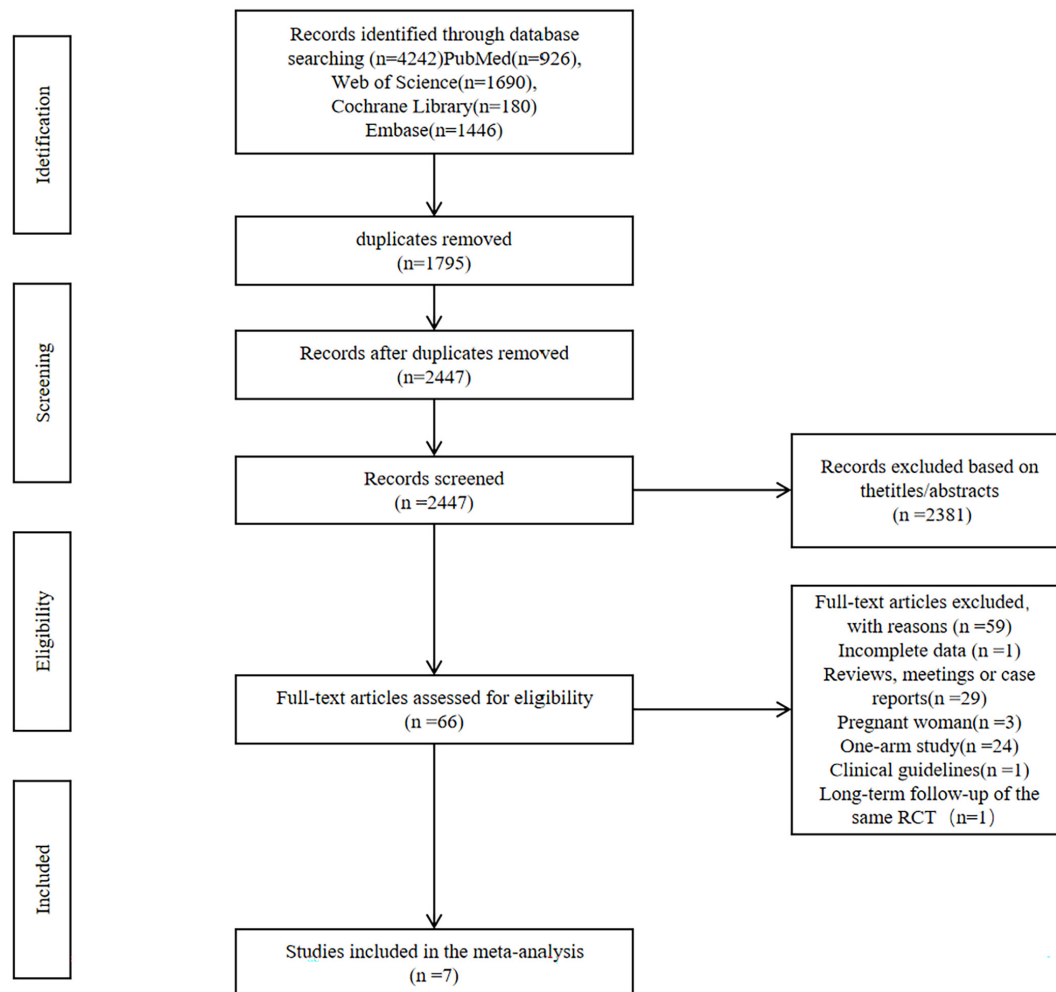


Fig. 1. PRISMA flow diagram of included and excluded studies. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

$p = 0.16$, $I^2 = 26\%$) [46,52] (Fig. 13) and premature rupture of membranes (RR = 0.57, 95% CI: 0.29–1.14, $p = 0.11$, $I^2 = 18\%$) [46,52] (Fig. 14), though neither finding achieved statistical significance. Conversely, the LEEP group exhibited nonsignificant higher cesarean section rate (RR = 1.36, 95% CI: 0.81–2.28, $p = 0.25$, $I^2 = 0\%$) [46,52] (Fig. 15). These results suggest comparable pregnancy outcomes between the two procedures, with LEEP potentially offering advantages in reducing preterm birth and premature rupture of membranes; however, further investigation is warranted to confirm these observations. It is worth noting that the analysis of pregnancy outcomes was based on only 3 studies (Mathevet et al. (2003) [52], Liu et al. (2014) [46] and partial data from Girardi F, et al (1994) [51]) with a relatively small total sample size. Therefore, potential benefits of LEEP in reducing risks of preterm birth and premature rupture of membranes should be interpreted cautiously as preliminary trends rather than definitive conclusions.

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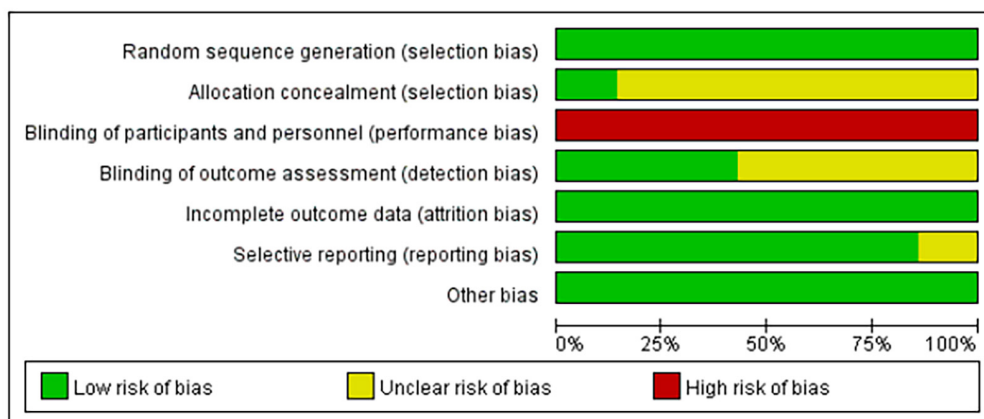
[52], Liu et al. (2014) [46] and partial data from Duggan et al. (1999) [38]) with a relatively small total sample size. Therefore, potential benefits of LEEP in reducing risks of preterm birth and premature rupture of membranes should be interpreted cautiously as preliminary trends rather than definitive conclusions.

3.5 Publication Bias

Results for 13 outcome measures, including excision depth, excision diameter, positive margins, and residual disease, are presented in Fig. 16. Funnel plot symmetry was formally assessed to evaluate the potential for selective bias. An approximately symmetrical distribution was observed on both sides of the pooled effect estimate, suggesting no significant publication bias. However, due to the limited number of studies included for most outcomes (typically 2–5 studies), the statistical power for Egger's and Begg's tests was insufficient, and the results should be interpreted with caution. For example, the Egger's test for residual disease yielded $p = 0.42$, while Begg's test yielded

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cai LI 2020	+	?	-	+	+	+	+
Duggan BD 1999	+	?	-	?	+	+	+
Giocalone PL 1999	+	+	-	+	+	+	+
Girardi, F 1994	+	?	-	?	+	?	+
Liu Y 2014	+	?	-	?	+	+	+
Mathevet P 1994	+	?	-	+	+	+	+
Takac I 1999	+	?	-	?	+	+	+

(A)



(B)

Fig. 2. Quality assessment. (A) Traffic_light diagram of the RCTs. (B) Summary of bias risk assessment for RCTs.

$p = 1.00$; however, interpretation is limited by the inclusion of only 5 studies. Therefore, interpretation was primarily based on visual inspection of the funnel plot (Fig. 16), which demonstrated a generally symmetrical distribution.

3.6 GRADE Assessment

4. Discussion

4.1 Primary Findings

This systematic review and meta-analysis comprehensively evaluated the efficacy, safety, and fertility out-

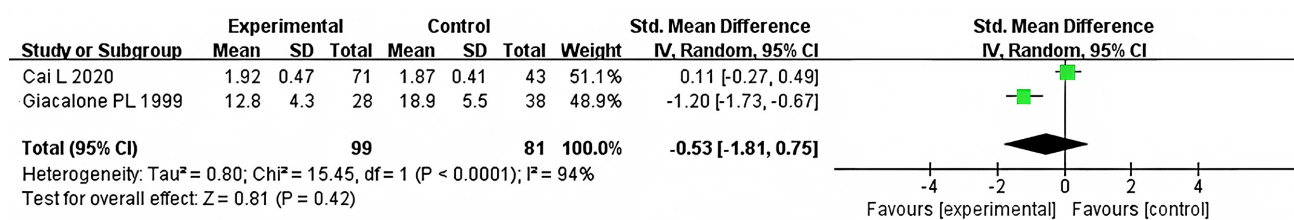


Fig. 3. Forest plot of resection depth.

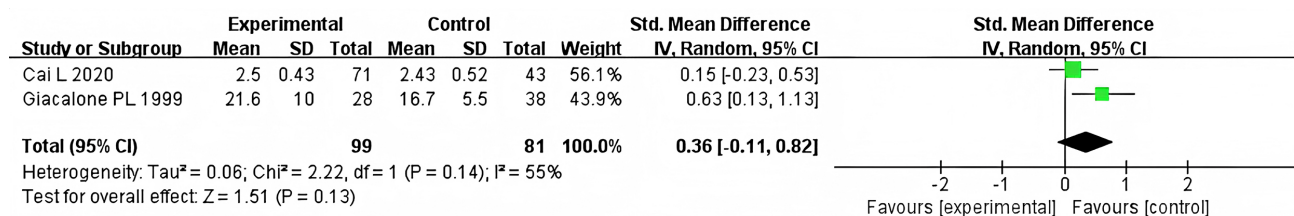


Fig. 4. Forest plot of resected tissue diameter.

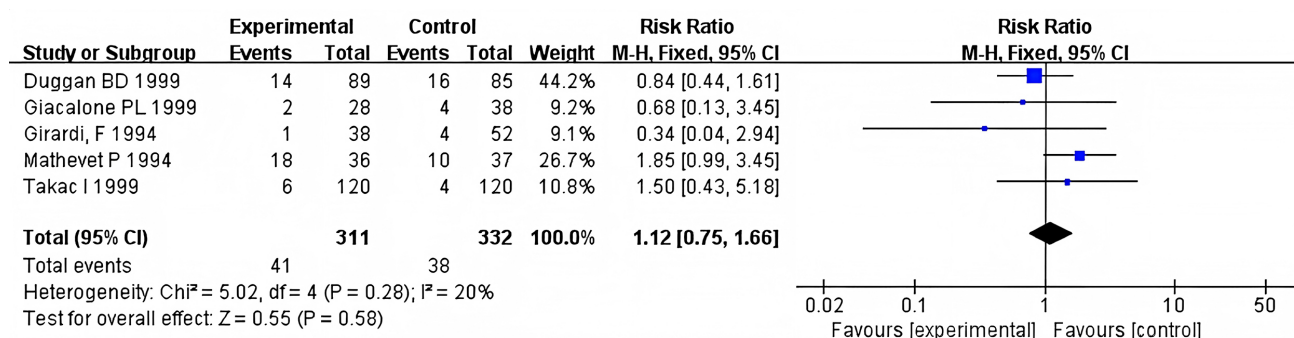


Fig. 5. Forest plot of positive resection margins.

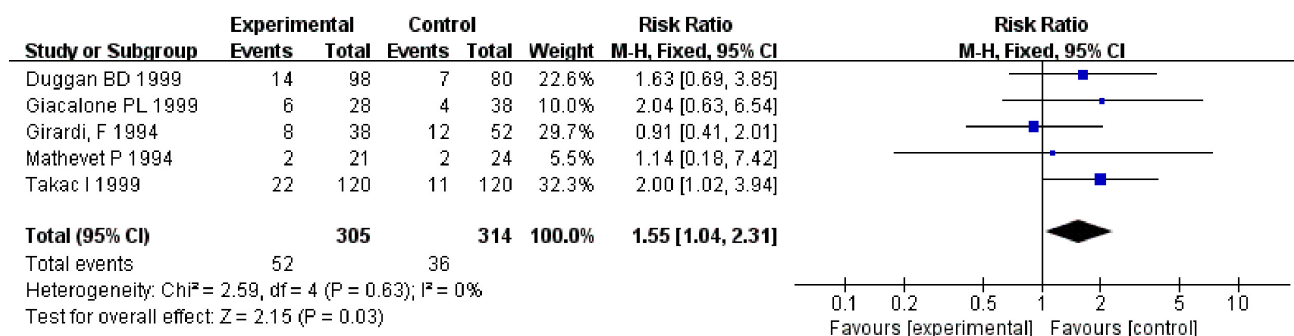


Fig. 6. Forest plot of residual disease.

comes of LEEP versus CKC for the treatment of CIN. CKC demonstrated a significant advantage in reducing residual disease, whereas LEEP showed potential benefits in lowering risks of preterm birth and premature rupture of membranes. However, no significant between-group differences were observed regarding resection parameters (tissue depth, diameter, and positive margins), postoperative safety outcomes (bleeding, cervical stenosis, and infection), or spontaneous abortion risk. Although LEEP appeared to be associated with a higher risk of disease recurrence compared

with CKC, the magnitude of this difference remains uncertain. CKC may offer advantages in reducing cesarean section rates, although this finding requires further validation.

Overall, both procedures possess distinct characteristics: CKC demonstrates superior efficacy in disease eradication, whereas LEEP may offer advantages in specific fertility-preservation indicators. However, the existing evidence remains limited, requiring additional high-quality studies to clarify the relative benefits of these two surgical approaches.

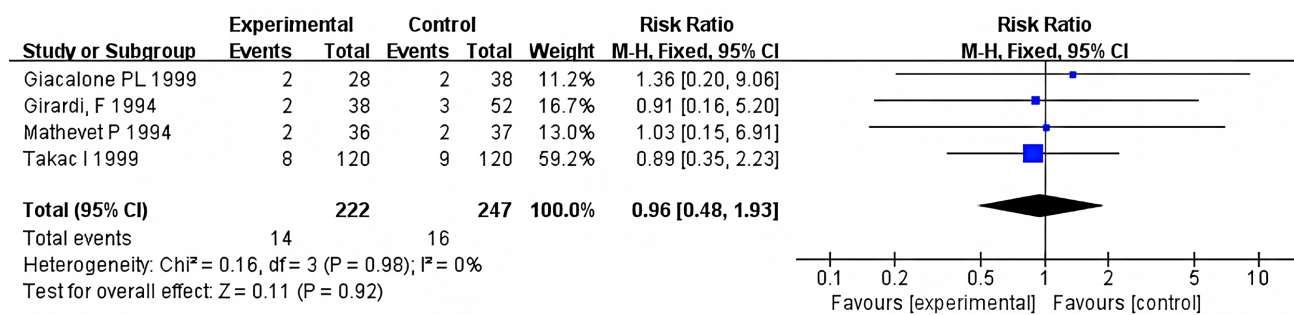


Fig. 7. Forest plot of postoperative bleeding.

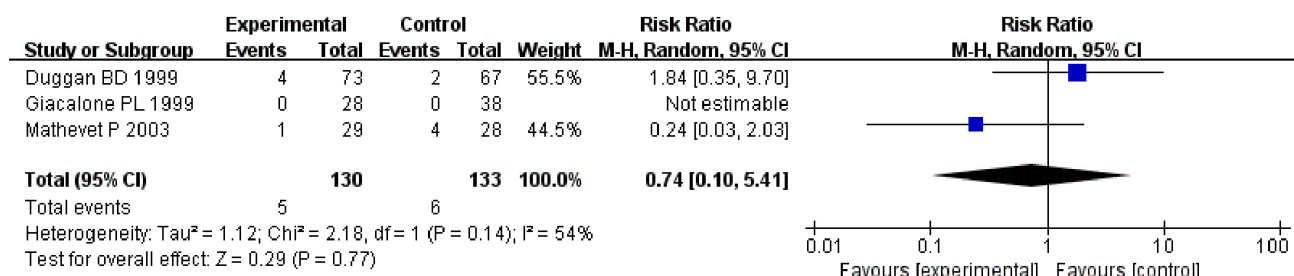


Fig. 8. Forest plot of cervical stenosis.

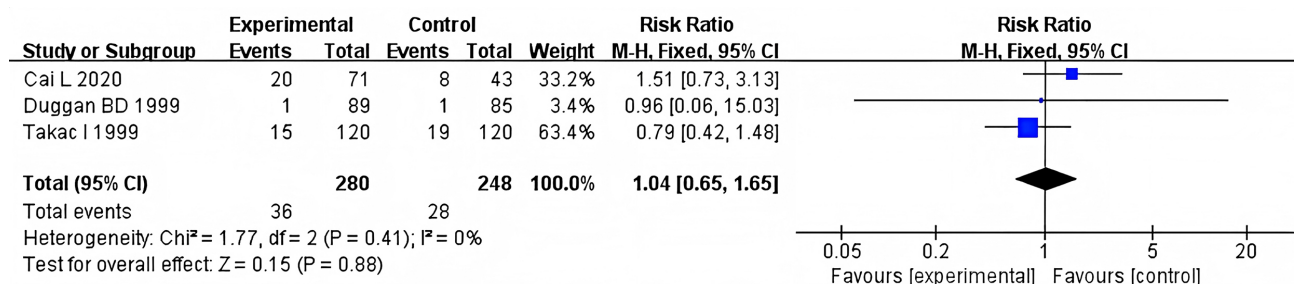


Fig. 9. Forest plot of infection.

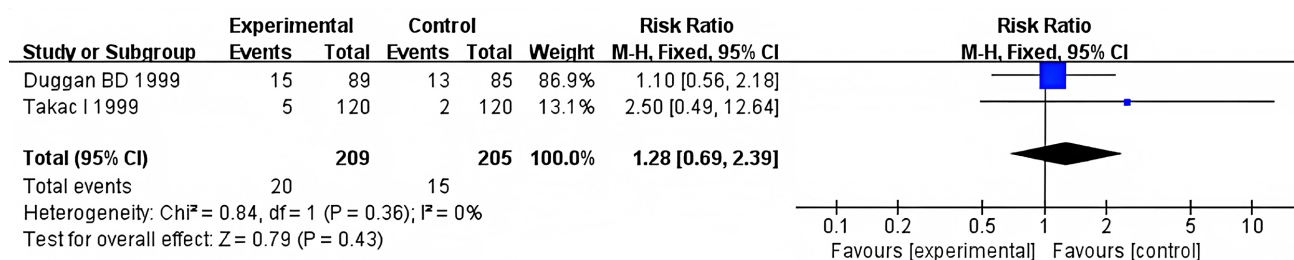


Fig. 10. Forest plot of secondary surgery.

Using the GRADE framework, the quality of evidence was rated as high for residual disease, postoperative bleeding, infection, and spontaneous abortion; moderate for positive resection margins, disease recurrence, resection depth, resection diameter, secondary surgery, and cesarean delivery; and low for cervical stenosis, preterm birth, and premature rupture of membranes. Downgrading was primarily driven by inconsistency (for resection depth, resection diameter, and cervical stenosis) and imprecision (for positive

resection margins, disease recurrence, secondary surgery, preterm birth, premature rupture of membranes, and cesarean delivery). Risk of bias did not result in downgrading for any outcome. This assessment underscores that the evidence base comparing LEEP with CKC requires substantial strengthening, particularly with respect to reproductive-related outcomes (Table 3).

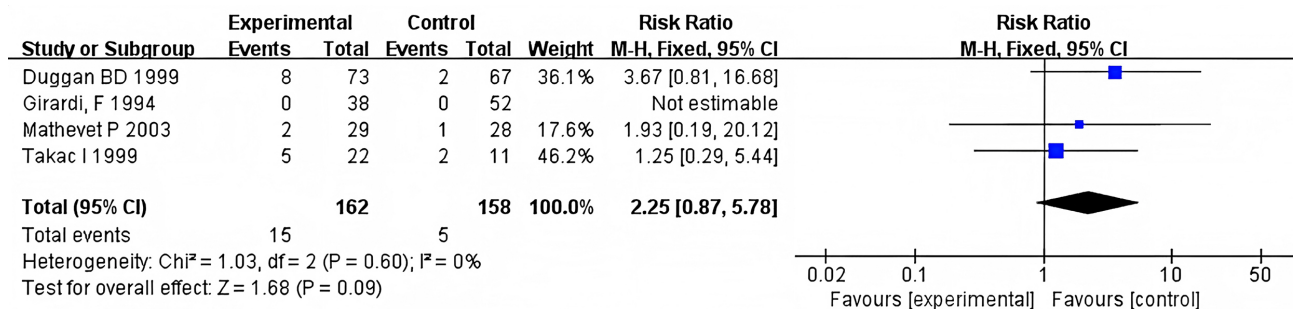


Fig. 11. Forest plot of disease recurrence.

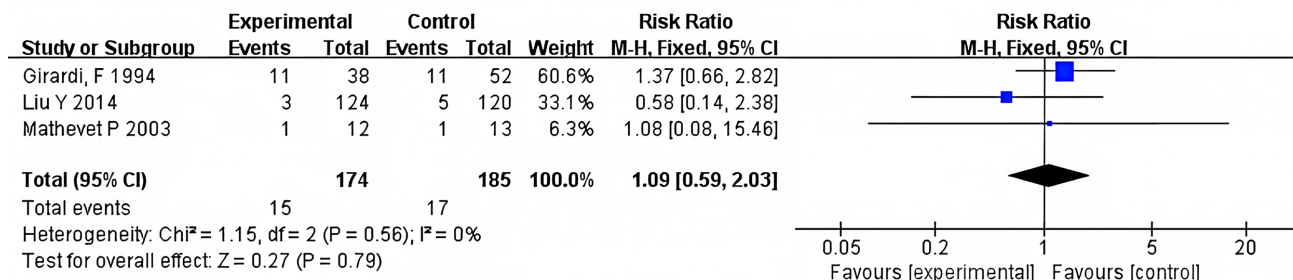


Fig. 12. Forest plot of spontaneous abortion.

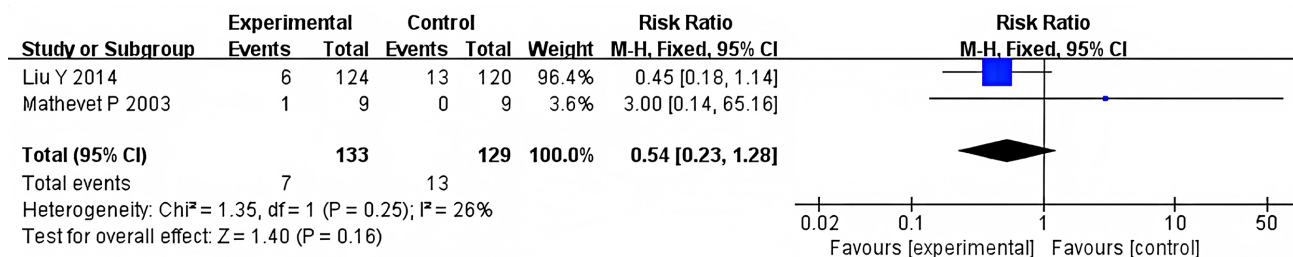


Fig. 13. Forest plot of preterm birth.

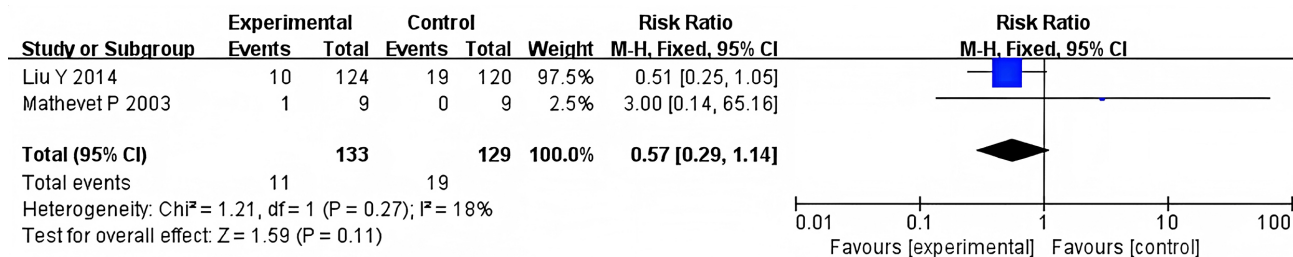


Fig. 14. Forest plot of premature rupture of membranes.

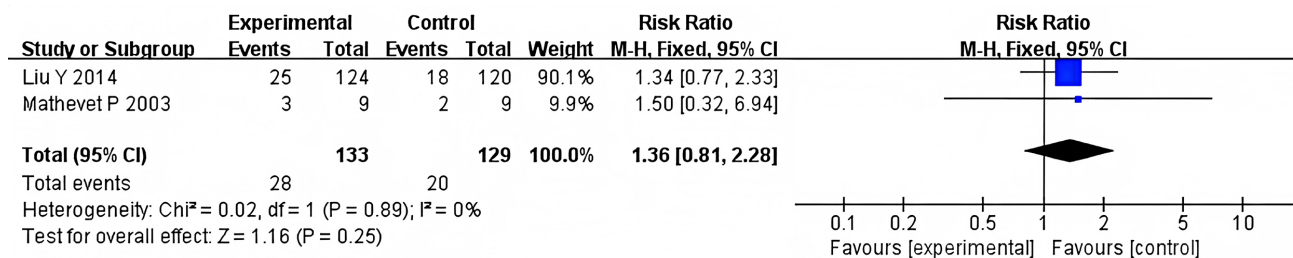


Fig. 15. Forest plot of cesarean delivery.

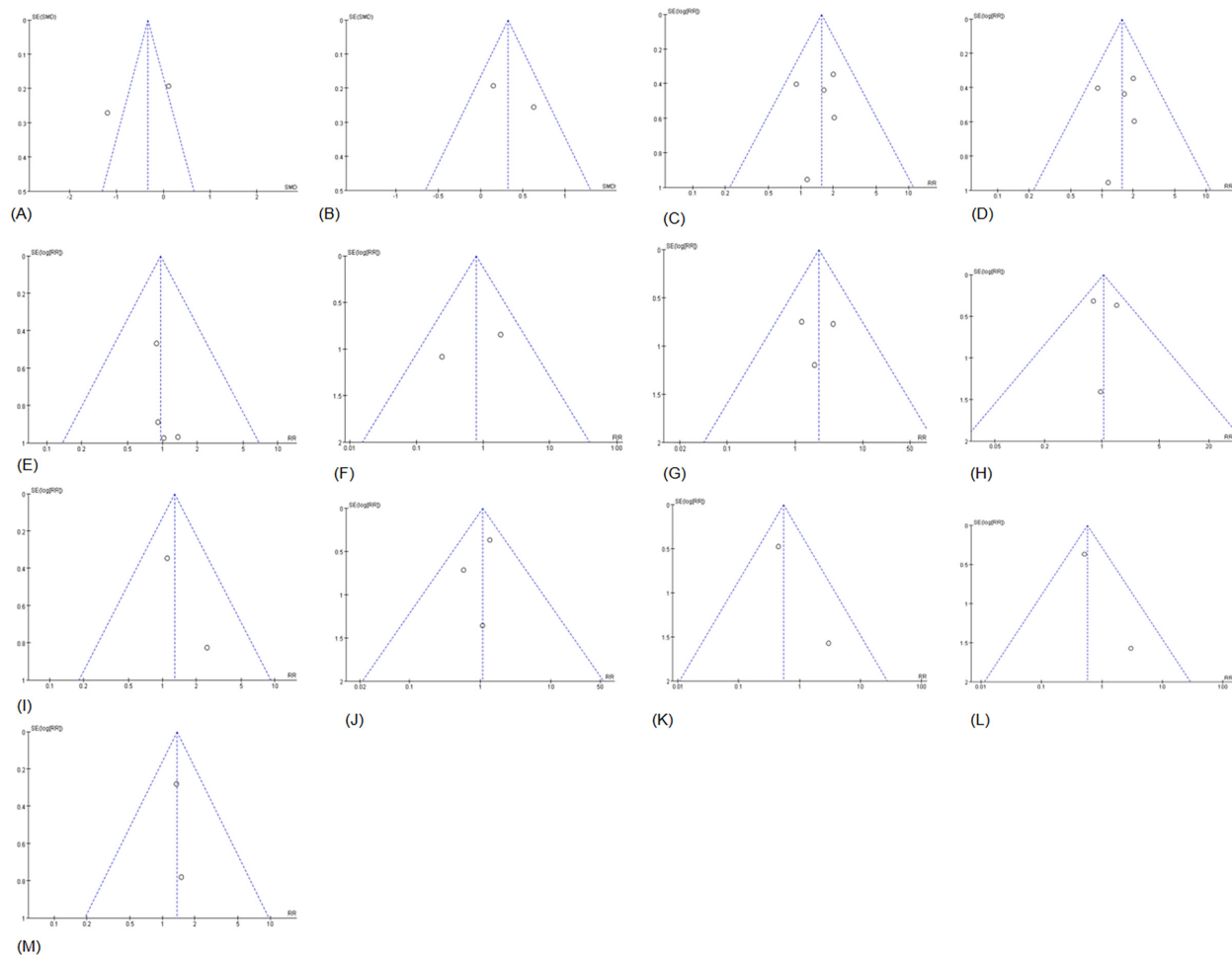


Fig. 16. Funnel plot. (A) Funnel plot of resection depth. (B) Funnel plot of resected tissue diameter. (C) Funnel plot of positive resection margins. (D) Funnel plot of residual disease. (E) Funnel plot of postoperative bleeding. (F) Funnel plot of cervical stenosis. (G) Funnel plot of infection. (H) Funnel plot of secondary surgery. (I) Funnel plot of disease recurrence. (J) Funnel plot of spontaneous abortion. (K) Funnel plot of preterm birth. (L) Funnel plot of premature rupture of membranes. (M) Funnel plot of cesarean delivery.

4.2 Comparison of the Therapeutic Effects of LEEP and CKC in the Treatment of CIN

Overall, this study suggests that LEEP may be inferior to CKC in reducing the risk of residual disease following CIN surgery ($RR = 1.55$, $95\% \text{ CI: } 1.04\text{--}2.31$, $p = 0.03$), consistent with findings from previous studies. In-depth analysis revealed that a key limitation of LEEP lies in its thermal artifact-related tissue damage [53,54]. The extent of thermal damage depends on the surgeon's experience with LEEP [42,55]. As emphasized by Mathevet et al. [42], Duggan et al. [38], and Takac and Gorisek [37], the thermal damage zone is relatively extensive, which can obscure the true morphology of lesional tissue and interfere with accurate pathological assessment of margin status—particularly the endocervical canal margin—thereby increasing the risk of missed residual lesions. The thermal effect of LEEP primarily results in nuclear shrinkage, cytoplasmic vacuolization, and blurred tissue boundaries, producing pseudodysplasia that may resemble high-grade intraepithelial

neoplasia (CIN II/III) and significantly increasing the risk of misinterpretation [56,57]. In contrast, CKC employs cold-knife excision, yielding tissue specimens with clear, well-defined margins that substantially improve pathological assessment conditions, enabling more accurate determination of complete lesion excision. This may underlie its reduced risk of residual disease. Although LEEP offers advantages in operative convenience and surgical duration, the constraint imposed by thermal damage on pathological interpretation accuracy cannot be overlooked. However, surgical outcome evaluation requires comprehensive consideration. Data from Girardi et al. [51] demonstrated no statistically significant difference in excision width between LEEP and CKC (10.2 mm versus 9.7 mm). Similarly, Duggan et al. [38] reported no significant differences in excision depth or diameter, with both techniques effectively achieving complete removal of the primary lesion. Notably, Girardi et al. [51] observed that although mean specimen weight (2.6 g versus 5.6 g) and depth (9.2

Table 3. The certainty of evidence for each outcome was assessed using the GRADE framework.

Outcome	Studies (n)	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Certainty	Interpretation
Residual disease	5	619	None	None ($I^2 = 0\%$)	None	None	None	High⊕⊕⊕⊕	No downgrade
Positive margin	5	643	None	Low ($I^2 = 20\%$)	None	Serious	None	Moderate ⊕⊕⊕○	Downgraded 1 level for imprecision
Disease recurrence	4	320	None	None ($I^2 = 0\%$)	None	Serious	None	Moderate ⊕⊕⊕○	Downgraded 1 level for Imprecision
Depth	2	180	None	Serious ($I^2 = 94\%$)	None	None	None	Moderate ⊕⊕⊕○	Downgraded 1 level for Inconsistency
Diameter	2	180	None	Serious ($I^2 = 55\%$)	None	None	None	Moderate ⊕⊕⊕○	Downgraded 1 level for Inconsistency
Postoperative bleeding	4	469	None	None ($I^2 = 0\%$)	None	None	None	High⊕⊕⊕⊕	No downgrade
Cervical stenosis	3	263	None	Low ($I^2 = 54\%$)	None	None	None	Low ⊕⊕○○	Downgraded 2 levels for Inconsistency and imprecision
Infection	3	528	None	None ($I^2 = 0\%$)	None	None	None	High⊕⊕⊕⊕	No downgrade
Secondary surgery	2	414	None	None ($I^2 = 0\%$)	None	Serious	None	Moderate ⊕⊕⊕○	Downgraded 1 level for imprecision
Spontaneous abortion	3	359	None	None ($I^2 = 0\%$)	None	None	None	High⊕⊕⊕⊕	No downgrade
Preterm birth	2	262	None	Low ($I^2 = 26\%$)	None	Serious	None	Low ⊕⊕○○	Downgraded 2 levels Inconsistency and imprecision
Premature rupture of membranes	2	262	None	Low ($I^2 = 18\%$)	None	Serious	None	Moderate ⊕⊕⊕○	Downgraded 1 level imprecision
Cesarean delivery	2	262	None	None ($I^2 = 0\%$)	None	Serious	None	Moderate ⊕⊕⊕○	Downgraded 1 level for imprecision

Footnotes: ⊕⊕⊕⊕High certainty — we are very confident that the true effect lies close to the estimate of the effect. ⊕⊕⊕○Moderate certainty — we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate, but there is a possibility that it is substantially different. ⊕⊕○○Low certainty — our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate.

mm versus 15.8 mm) were significantly lower with LEEP than CKC (both $p < 0.01$), and thermal damage predominantly affected the endocervical canal margin (columnar epithelium) while sparing the ectocervical margin (squamous epithelium), the authors concluded that this thermal artifact did not substantially compromise histopathological tissue assessment. These findings suggest that LEEP and CKC may achieve comparable lesion clearance efficacy, with differences in residual risk potentially attributable to thermal damage-related difficulties in margin assessment, particularly at the endocervical canal. Therefore, clinical

decision-making requires careful consideration of benefits and limitations with individualized treatment selection. For early-stage lesions or cases requiring high diagnostic precision in pathological assessment, CKC may represent the preferable option; for patients prioritizing surgical convenience, rapid postoperative recovery, and tolerating a degree of thermal damage, particularly when lesions are predominantly located outside the transformation zone, LEEP remains a valuable clinical option. Some studies have focused on optimizing technical parameters (e.g., excision power, electrode design) to minimize thermal damage, a

general principle of energy driven surgery that has been validated in laser laryngeal surgery [58]. With advances in technology, LEEP devices with optimized technical parameters and improved assessment modalities are expected to emerge. These developments hold the potential to resolve the trade-off between thermal injury-related challenges associated with LEEP and the invasiveness of CKC, thereby delivering more efficient, precise, and personalized therapeutic options for patients with cervical intraepithelial neoplasia. At present, evidence-based, patient-tailored surgical selection remains critical for optimizing treatment outcomes, minimizing residual lesion risks, and safeguarding patients' long-term health.

We acknowledge that the inability to conduct subgroup analyses and meta-regression represents an important methodological limitation of this study. This constraint may substantially impact our findings: First, the substantial heterogeneity observed for excision depth and diameter ($I^2 > 50\%$) suggests that pooled effect estimates may mask true differences across clinical scenarios. For instance, both Giacalone et al. (1999) [43] and Girardi et al. (1994) [51] reported significantly smaller LEEP excision depths compared with CKC (approximately 6–7 mm difference), although absolute values varied considerably (LEEP: 9.2 mm versus 12.8 mm). This variation may reflect differences in patient populations (France versus Austria), surgeon experience, or equipment specifications; however, these factors could not be quantified statistically. Second, heterogeneity for residual disease was low ($I^2 = 0\%$) with consistent effect directions across studies (RR: 1.38–1.78), strengthening the robustness of this conclusion. We speculate that the determination of residual disease relies primarily on pathological margin assessment and is relatively less influenced by variations in surgical technical parameters. Finally, because specific heterogeneity sources could not be identified, clinicians should carefully consider individual patient characteristics, surgeon experience, and available equipment when applying these findings. Pooled estimates of surgical technical parameters should not be interpreted as absolute standards but rather as reference ranges. Future methodologically rigorous, standardized large-scale RCTs are warranted to enable reliable subgroup analyses and meta-regression, thereby strengthening the evidence base for individualized surgical selection.

Among the 7 RCTs included in this evaluation, 5 were published in the 1990s (Girardi et al. 1994 [51]; Mathevet et al. 1994 [42]; Duggan et al. 1999 [38]; Giacalone et al. 1999 [43]; and Takac and Gorisek 1999 [37]), and 2 were published after 2000 (Liu et al. 2014 [46]; and Cai et al. 2020 [34]). This temporal distribution raises concerns regarding extrapolation, as LEEP devices used in the 1990s differed in power control and electrode design from contemporary devices. Accordingly, the difficulties in margin assessment observed in early studies may have been partially mitigated by technological advances. This temporal

effect should be considered when interpreting data on residual disease and positive margins, and large-scale RCTs using contemporary equipment are required.

4.3 Comparison of LEEP and CKC Safety in the Treatment of CIN

In terms of safety, minimal differences exist between LEEP and CKC [59]. However, El-Nashar et al. [60] reported that LEEP offers safety advantages, including significantly shorter operative time, reduced intraoperative bleeding, shorter hospital stay, and less tissue excision compared with CKC. Our meta-analysis demonstrated no statistically significant between-group differences in postoperative bleeding (RR = 0.96, 95% CI: 0.48–1.93, $p = 0.92$), cervical stenosis (RR = 0.74, 95% CI: 0.10–5.41, $p = 0.77$), or postoperative infection (RR = 1.04, 95% CI: 0.65–1.65, $p = 0.88$), findings consistent with previous investigations [34,37,38,42,59]. These observations may reflect the fact that both surgical approaches effectively remove lesional tissue and employ comparable postoperative care protocols. In summary, LEEP and CKC demonstrate similar safety profiles for the treatment of CIN, with comparable rates of postoperative bleeding, cervical stenosis, and infection. Therefore, surgical selection should prioritize operative convenience and individual patient characteristics.

Several investigators have improved conventional excision by incorporating vaginal endoscopic guidance with the explicit aim of reducing procedural risk. Current evidence suggests that this hybrid approach achieves higher rates of complete dysplasia excision. Concurrently, cohort studies have reported improved obstetric outcomes following the combined procedure, including reduced rates of preterm delivery. Collectively, these findings place endoscopically assisted excision as a clinically promising strategy for fertility preservation in women treated for CIN [61].

4.4 Comparison of LEEP and CKC in Fertility Preservation for CIN

The pathogenesis of preterm birth is believed to involve cervical shortening and impairment of local immune defense mechanisms following removal of cervical glands [62,63,64,65,66], with greater tissue excision conferring an increased risk of preterm delivery and impaired fertility. Regarding fertility preservation, LEEP may offer advantages [67,68,69,70,71]. Our study found that, although differences did not reach statistical significance, the LEEP group demonstrated lower risks of preterm birth (RR = 0.54, 95% CI: 0.23–1.28, $p = 0.16$) and premature rupture of membranes (RR = 0.57, 95% CI: 0.29–1.14, $p = 0.11$) compared with the CKC group. These findings are consistent with several previous studies. For example, Liu et al. [46] and Mathevet et al. [52] reported lower preterm birth rates in the LEEP group, potentially attributable to reduced cervical tissue trauma and a consequent lower risk of cervical insufficiency. Mathevet et al. [42] and Takac

and Gorisek [37] similarly observed that LEEP is associated with less cervical tissue damage, thereby reducing infection risk. Additionally, Noehr et al. [69,72] demonstrated in a large-scale cohort study that increasing cone excision depth was directly associated with an elevated risk of preterm birth, with each 1 mm of tissue removed increasing this risk by 6%. In LEEP procedures with a mean cone depth of 8 mm, positive margin rates were not higher than those observed with CKC at a mean depth of 15 mm. However, some studies suggest that total cervical volume or the proportion of cervical canal excised may be more predictive than absolute excision depth [73,74,75,76], underscoring the value of preoperative cervical canal length assessment. Our study also observed a nonsignificant trend toward higher cesarean section rates in the LEEP group (RR = 1.36, 95% CI: 0.81–2.28, $p = 0.25$), which may be related to alterations in cervical function following LEEP. The CIs for preterm birth and premature rupture of membranes crossed 1.0, indicating that these findings represent potential trends requiring confirmation in larger RCTs. We explicitly acknowledge the limitations of the current evidence base and do not recommend formulating definitive clinical recommendations based on these observations. Notably, a recent study by Palumbo et al. [77] indicates that the extent of cervical tissue excision and resulting anatomical and functional changes may play a crucial role in determining obstetric risks, emphasizing the importance of personalized surgical approaches that balance oncologic safety with fertility preservation. However, the fertility-preserving advantages of LEEP are not absolute, and the risk of postoperative disease recurrence requires careful consideration. Low serum folate levels may increase the risk of CIN and cervical cancer [78]. When residual human papillomavirus (HPV) persists, the risk of CIN recurrence increases substantially to 18%, even in the presence of negative surgical margins [79]. Postoperative folate supplementation and HPV vaccination can reduce CIN2+ recurrence rates following surgery, decrease reoperation requirements, prevent progression to cervical cancer, and preserve female fertility [80,81]. In recent years, non-surgical treatments have demonstrated potential advantages for fertility preservation in patients with CIN [82,83]. Studies have reported remission rates for CIN 2 ranging from 43% to 93% with topical agents. Local pharmacotherapy may provide more personalized treatment options for patients with CIN who have fertility concerns [83]. Therefore, treatment selection should integrate the patient's reproductive plans and individual circumstances to determine the most appropriate therapeutic strategy.

4.5 Clinical Implications

CKC is the priority consideration: CKC is preferred when the lesion is extensive or extends into the cervical canal, requiring adequate depth of resection; when there is suspicion of microinvasive cancer or AIS, requiring precise

histopathological assessment of the margins; after failed LEEP or in cases of positive margins; when the patient has completed childbearing and has no concerns about fertility; and when sufficient medical resources are available and the patient can tolerate a longer operation time and hospitalization.

LEEP is the priority consideration: LEEP is the priority when the lesion is mainly located on the ectocervix within the transformation zone, with limited extension into the cervical canal; when fertility preservation and cervical function are priorities; when rapid outpatient treatment is required in resource-limited settings; when the patient has multiple comorbidities and cannot tolerate general anesthesia, or when precise excision is feasible under real-time colposcopy guidance.

Further assessment is needed for the following situations: adolescent or young patients with infertility concerns (both techniques should be used with caution; observation or ablative therapy may be considered); and multiple recurrent CIN (may require a larger resection, for which CKC may be more suitable).

4.6 Advantages and Limitations

This systematic review and meta-analysis comprehensively evaluated the efficacy, safety, and fertility-preservation outcomes of LEEP versus CKC in the treatment of CIN. Using a large multinational sample and rigorous methodology, it analyzed multidimensional clinical outcomes and publication bias, providing clinically relevant evidence to support decision-making in patients with reproductive considerations. However, several limitations remain. Unclear risk of bias in some studies, particularly regarding allocation concealment and blinding, may affect accuracy. High heterogeneity in certain outcomes, likely driven by variations in patient characteristics and surgical techniques, limits definitive conclusions. Additionally, nonsignificant results for key outcomes and inconsistent follow-up durations hinder long-term assessments. The absence of quality-of-life evaluations also prevents comprehensive impact assessment. Future studies should strengthen randomization and blinding protocols, report detailed patient and surgical characteristics to reduce heterogeneity, and incorporate long-term follow-up alongside quality-of-life measures. However, some of these limitations may be difficult to completely eliminate given population and technique variations, as well as the need for individualized clinical management.

5. Conclusions

This systematic review and meta-analysis compared the efficacy, safety, and fertility-preservation outcomes of LEEP versus CKC for the treatment of CIN. The results indicate that CKC is superior in reducing residual disease, whereas LEEP shows a potential trend toward lower risks of premature birth and premature rupture of membranes;

however, these differences were not statistically significant. Moreover, given the limited number of studies, the certainty of evidence was low. No significant differences were observed between the two methods in terms of resection efficacy, postoperative safety, or risk of spontaneous abortion. Although LEEP showed a higher risk of disease recurrence compared to CKC, the magnitude of this difference remains unclear. These findings suggest that selection of surgical technique should comprehensively consider the accuracy of pathological assessment, procedural convenience, and the patient's fertility plans. Future studies should optimize study design to reduce the risk of bias, conduct long-term follow-up, and incorporate quality-of-life assessments to more comprehensively compare the advantages and disadvantages of the two surgical methods.

Availability of Data and Materials

The datasets utilized and analyzed in the current study are available from the corresponding author upon reasonable request.

Author Contributions

HX and YL conceived and designed the study; YL and PL performed the literature search and collected the data; HX and YL contributed to the data analysis and wrote the manuscript; PL and YL revised the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/CEOG51629>.

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