Oxygen-rich dressing for hypospadias repair: Systematic review and meta-analysis

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ABSTRACT

Introduction: Postoperative dressing selection after hypospadias repair varies widely and is largely guided by surgeon preference. Oxygen-enriched and ozone-based topical dressings have demonstrated antimicrobial and wound-healing benefits in other settings, but their role after hypospadias repair remains unclear. We performed a systematic review and meta-analysis to evaluate outcomes associated with oxygen-rich or ozone-based dressings compared with standard postoperative care.
Methods: We searched CENTRAL, CINAHL, Embase, MEDLINE, PubMed, Scopus, Google Scholar, and trial registries from inception to July 31, 2025, for clinical studies comparing oxygen- or ozone-based dressings with standard postoperative care. Hyperbaric oxygen therapy, abstracts without full-text, and basic science studies were excluded. Two reviewers independently screened studies and assessed risk of bias using RoB 2. Random-effects meta-analyses were performed using mean differences (MD) and risk ratios (RR).
Results: Of 594 records identified, three randomized controlled trials met inclusion criteria, comprising 264 children undergoing primary distal hypospadias repair. All studies had some concerns or high risk of bias, mainly due to lack of preregistration and incomplete blinding of subjective outcomes. Compared with standard dressings, oxygen- or ozone-based dressings were associated with shorter wound-healing time (MD -9.80 days, 95% confidence interval [CI] -15.85 to -3.75, I^2=89%) and fewer reoperations (relative risk [RR] 0.24, 95% CI 0.07−0.75, I^2=0%). Differences in foreskin dehiscence, wound infection, and urethrocutaneous fistula were not statistically significant.

Conclusions: Limited randomized evidence suggests oxygen-rich or ozone-based dressings may improve early healing and reduce reoperations after distal hypospadias repair, while no statistically significant differences were observed for individual complications. Larger, methodologically rigorous trials are needed before routine adoption can be recommended.

INTRODUCTION

Hypospadias is a common congenital anomaly of the male genitalia, occurring in approximately 1 in 200–300 live male births.[1–3] Surgical correction is usually undertaken in early childhood with the goals of achieving a straight phallus, a terminal meatus with unobstructed urinary flow, acceptable cosmetic appearance, and minimal long-term morbidity. Despite refinements in surgical technique and perioperative management, postoperative wound complications remain an important cause of morbidity and may lead to reoperation, prolonged follow-up, and psychosocial burden for patients and families.[2,4]

Successful wound healing after hypospadias repair depends on multiple factors, including tissue perfusion, oxygen availability, inflammation control, and local wound care. Oxygen plays a central role in collagen synthesis, angiogenesis, fibroblast proliferation, and host defense against infection. Impaired tissue oxygenation has been linked to delayed healing and higher complication rates across a range of surgical settings.[5,6,16] These observations have driven interest in strategies aimed at improving local oxygen delivery to surgical wounds.[7]

Oxygen-rich or oxygen-diffusion dressings are designed to deliver sustained topical oxygen without the logistical burden and systemic exposure associated with hyperbaric oxygen therapy. Available formulations include oxygen-enriched oil-based gels, hydrogels, tubular delivery devices, and ozone-based preparations that release oxygen or oxygen-derived species at the wound surface. In chronic wound care and reconstructive surgery, topical oxygen therapies have been associated with improved healing kinetics and fewer complications.[8,9] Their role in pediatric urogenital reconstruction, however, remains poorly defined.

Several randomized trials published over the past decade have examined oxygen- or ozone-based dressings following distal hypospadias repair, reporting outcomes such as healing time, wound appearance, and postoperative complications.[10–12] While these studies suggest potential benefit, they are limited by small sample sizes, heterogeneity in dressing formulations and comparators, and variability in outcome definitions.

The aim of this systematic review and meta-analysis was to evaluate the efficacy and safety of postoperative oxygen-rich dressings after hypospadias repair, focusing on wound-healing time, postoperative complications, reoperation rates, and wound appearance. We hypothesized that oxygen- or ozone-based dressings would be associated with faster healing and lower complication rates compared with standard postoperative dressings By synthesizing available randomized data, we sought to clarify the current evidence base, identify key limitations, and inform future research and clinical practice.[13,14]

METHODS

Study design and registration

This review was conducted in accordance with the PRISMA 2020 guidelines, was registered prospectively with PROSPERO (Registration number: CRD420251047228)[15] and aimed to evaluate the efficacy and safety of postoperative oxygen-rich dressings following hypospadias repair in pediatric and adult populations.

Eligibility criteria

Clinical studies involving pediatric or adult patients undergoing hypospadias repair, including all hypospadias subtypes (distal, midshaft, proximal) and repair techniques (with or without grafts or flaps), were eligible for inclusion. Studies were required to assess postoperative outcomes associated with oxygen-rich or oxygen diffusion–enhancing dressings, including but not limited to oxygenated wound dressings, oxygen diffusion dressings, oxygenating hydrogels, topical oxygen devices, micro-oxygen supply devices, oxyband, Natrox, Oxyzyme, or ozone-based dressings. Eligible comparators included standard postoperative dressings or active controls. Hyperbaric oxygen therapy was excluded. Randomized and nonrandomized clinical studies were included, while abstracts without full text, basic science studies, and non-clinical reports were excluded.

Information sources and search strategy

A comprehensive literature search was performed across multiple electronic databases, including MEDLINE, PubMed, Embase (via Ovid), CENTRAL (Cochrane Central Register of Controlled Trials), Scopus, CINAHL and Google Scholar, from database inception to the date of search completion, without language or date restrictions. Additional sources included reference list screening of included articles, citation tracking (“snowballing”), conference proceedings, dissertation and thesis databases and clinical trial registries (including ClinicalTrials.gov and WHO ICTRP). The full search strategy is detailed in the registered protocol.

Study selection, data extraction, and risk of bias assessment

Study selection was conducted independently by at least two reviewers using predefined eligibility criteria, with discrepancies resolved by discussion or consensus. Data extraction was similarly performed independently using a standardized form and included study characteristics, patient demographics, hypospadias type and repair technique, dressing type, comparator, follow-up duration, and reported outcomes. Risk of bias was assessed independently by two reviewers using Cochrane Risk of Bias 2 (RoB 2) for randomized trials. Disagreements were resolved through consensus.

Outcomes and data synthesis

Primary outcomes were surgical success and overall complication rates. Secondary outcomes included wound-healing time, reoperation, infection, fistula, and wound appearance. Random-effects meta-analyses were performed using inverse-variance or Mantel–Haenszel methods as appropriate. Heterogeneity was assessed using I^2 statistics. Certainty of evidence was evaluated using GRADE methodology.

RESULTS

Study selection

The search yielded 594 records. After removal of 251 duplicates (5 manually and 246 via Covidence), 343 titles and abstracts were screened. Of these, 338 were excluded for failure to meet inclusion criteria. Five full-text articles were reviewed, with two excluded due to study design. No ongoing or unpublished eligible studies were identified. Three randomized controlled trials met inclusion criteria and were included in the qualitative and quantitative syntheses (Figure 1).

Study characteristics

The three included studies were prospective randomized controlled trials published in 2021 (n=2) and 2025 (n=1), enrolling a total of 264 children undergoing primary distal hypospadias repair. All trials compared an oxygen- or ozone-based postoperative dressing with standard, non-oxygenated wound care. Total sample sizes ranged from 64 to 114 patients, with per-arm allocations of 32/32, 57/57, and 43/43. Mean or median age ranged from approximately 14 to 19 months. No studies included adult patients or proximal hypospadias repairs (Table 1).

Risk of bias within studies

Risk of bias assessment using the Cochrane RoB-2 tool identified variability across studies (Table 2-5). All three trials were judged to be at low risk of bias for the randomization process, with adequate sequence generation and allocation concealment and no baseline imbalances. Two trials were assessed as having some concerns overall, primarily related to deviations from intended interventions and outcome measurement.[10,11] Although parents were blinded to allocation, nursing staff performing dressing changes were likely aware of treatment assignment. Several outcomes, including Southampton Wound Assessment Scale (SWAS) scores and cosmetic assessments, were subjective, and reporting of assessor blinding and inter-rater reliability was limited.

The trial by Coppola et al. (2025) was judged to be at high overall risk of bias, driven by outcome measurement.[12] Subjective endpoints—including SWAS, FLACC pain scores, and parental satisfaction—were assessed without effective blinding, which was impractical given visible differences between dressing formulations. No observer calibration or reliability testing was reported. Although attrition was minimal across all studies, none were prospectively registered or reported a predefined statistical analysis plan, raising concerns regarding selective outcome reporting.

Wound-healing time

All three included randomized trials reported postoperative wound-healing time. Two studies reported medians with interquartile ranges; these were converted to approximate means and standard deviations using established methods to permit pooling, while original summary statistics were retained for descriptive reporting. Random-effects meta-analysis demonstrated that oxygen- or ozone-based dressings were associated with a significantly shorter wound-healing time compared with control dressings (pooled MD −9.80 days, 95% CI −15.85 to −3.75). Statistical heterogeneity was substantial ($Q = 18.50$, $df = 2$; $I^2 = 89.2\%$, $\tau^2 = 24.92$), likely reflecting variability in dressing formulation, comparator treatments, and dispersion of healing times in control groups. Despite heterogeneity, all individual study estimates consistently favored oxygen/ozone-based dressings, supporting a robust direction of effect. (Figure 2, Tables 3 and 4)

Reoperations

Re-operation rates were reported in all three trials. Pooled analysis demonstrated a significant reduction in re-operations among patients receiving oxygen/ozone dressings (RR 0.24, 95% CI 0.07–0.75), with no observed heterogeneity ($Q = 0.91$, $df = 2$; $I^2 = 0\%$, $\tau^2 = 0.000$). Absolute event rates were low, but the consistency of effect across studies suggests a clinically meaningful reduction in severe postoperative complications requiring surgical revision. (Figure 3, Tables 6 and 7)

Specific postoperative complications

Meta-analyses of individual complication types showed no statistically significant differences between oxygen/ozone dressings and control dressings. For foreskin dehiscence, the pooled RR was 0.38 (95% CI 0.09–1.65), with minimal heterogeneity ($I^2 = 5.1\%$). For urethrocutaneous fistula, pooled analysis of two studies yielded an RR of 0.28 (95% CI 0.05–1.67; $I^2 = 0\%$). Similarly, wound infection rates did not differ significantly between groups (RR 0.36, 95% CI 0.03–3.95; $I^2 = 0\%$). These analyses were limited by low event counts and wide confidence intervals, indicating imprecision rather than absence of effect. (Figure 4-6, Tables 6 and 7)

Wound appearance and healing quality

Two studies reported wound appearance using the Southampton Wound Assessment Scale (SWAS) at postoperative day 14. Pooled analysis showed that patients treated with oxygen-based dressings were significantly more likely to demonstrate normal wound healing (SWAS ≤ 1) compared with controls (RR 1.56, 95% CI 1.32–1.83), with no heterogeneity ($I^2 = 0\%$). This finding was consistent across studies and suggests a clinically relevant improvement in early wound quality. (Figure 7, Tables 6 and 7)

Composite outcomes
Two studies explicitly reported a composite outcome of any postoperative complication. Random-effects pooling demonstrated a significant reduction in overall complications favoring oxygen/ozone dressings (RR 0.25, 95% CI 0.06–0.95), with no observed heterogeneity ($I^2 = 0\%$). One study was excluded from this analysis because complications were reported only as overlapping individual components without a predefined composite endpoint, precluding valid aggregation. (Figure 8, Tables 6 and 7)

Sensitivity and robustness considerations
Sensitivity analyses excluding studies at higher risk of bias or outcomes requiring imputation of means and standard deviations did not materially alter the direction of effect for wound-healing time or re-operations, although confidence intervals widened. Given the small number of included studies, formal assessment of publication bias using funnel plots was not performed.

DISCUSSION
This systematic review and meta-analysis evaluated the available randomized evidence on oxygen-enriched postoperative dressings following distal hypospadias repair. Across three randomized controlled trials, the use of oxygen- or ozone-based dressings was associated with a shorter time to wound healing and a lower rate of reoperation compared with standard postoperative care.[10,12] Although individual complication outcomes were not statistically significant, patients treated with oxygen-based dressings were more likely to demonstrate normal early wound healing (SWAS ≤1).[11,12] These findings suggest a potential benefit of enhanced topical oxygen delivery in the early postoperative period, while recognizing the methodological constraints of the existing literature.

The pooled reduction in wound-healing time of approximately 1–2 weeks is clinically relevant, as delayed epithelialisation may contribute to discomfort, prolonged wound care, and secondary complications. Early wound quality, assessed using the Southampton Wound Assessment Scale, was also superior in oxygen-treated patients at postoperative day 14.[11,12] Improved early healing may reduce local inflammation and tissue stress during a critical period of urethroplasty maturation. However, substantial heterogeneity was observed for healing time, reflecting differences in dressing formulation, outcome definitions, and dispersion of healing metrics across trials.

A notable finding was the reduced risk of reoperation among patients receiving oxygen-rich dressings. Although absolute event rates were low, reintervention represents a meaningful endpoint, as it reflects clinically significant complications requiring further surgery. Even in distal hypospadias repair, reoperation rates of 5–10% have been reported in experienced centres.[2,4] An adjunct that may lower this risk is therefore of interest. However, these results should be interpreted cautiously given the limited sample size and the absence of long-term follow-up beyond early childhood in most studies.

The observed effects are biologically plausible. Oxygen plays a central role in wound healing through its influence on collagen synthesis, angiogenesis, fibroblast proliferation, and host immune defense.[5–7,16] Local tissue hypoxia can impair these processes and delay repair.[8] Topical oxygen therapies aim to augment local oxygen tension at the wound surface, potentially supporting more rapid epithelialization and tissue remodeling. Evidence from chronic wound care and other surgical contexts supports a beneficial role for enhanced oxygen delivery.[8,17] In hypospadias surgery, adjunctive hyperbaric oxygen therapy has also been associated with reduced repair failure in complex cases, reinforcing the principle that improved oxygen availability may support urogenital wound healing.[18]

Despite these encouraging findings, several limitations must be emphasized. Only three randomized trials met inclusion criteria, all conducted in paediatric populations undergoing primary distal hypospadias repair. The results may not be generalizable to proximal hypospadias, staged repairs, redo surgery, or adolescent and adult patients. The interventions grouped as "oxygen-rich dressings" were heterogeneous, including oxygen-enriched gels, impregnated dressing devices, and an ozone-based spray. Although they share a common therapeutic rationale, their mechanisms of oxygen delivery and clinical handling differ. Methodological limitations were also present: none of the trials were prospectively registered, blinding was incomplete or impractical, and several outcomes relied on subjective assessment.[10–12] While objective endpoints such as reoperation are less vulnerable to detection bias, performance bias cannot be excluded.

Follow-up duration was limited in most studies. Although many hypospadias-related complications manifest early, longer-term outcomes—including urethral caliber, scar quality, and cosmetic appearance at later childhood or puberty—were not systematically evaluated.[2] Consequently, it remains uncertain whether the observed early benefits translate into durable long-term advantages.

Future research should prioritize multicenter, preregistered randomized trials with standardized outcome definitions and sufficient power to detect differences in clinically important complications. Studies involving higher-risk repairs, such as proximal hypospadias or staged graft-based reconstructions, may be particularly informative.[18,19] Comparative evaluation of different oxygen-delivery modalities, alongside cost-effectiveness analyses, would further clarify the role of these dressings in routine practice.

CONCLUSIONS

Current randomized evidence suggests that oxygen-enriched postoperative dressings may be associated with faster early wound healing and fewer reoperations following distal hypospadias repair, while their impact on individual postoperative complications remains unclear. However, the certainty of evidence is limited by small sample size, heterogeneity, and risk of bias. At present, oxygen-rich dressings should be considered a promising adjunct rather than an established standard of care, pending confirmation from larger, methodologically robust studies.

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FIGURES AND TABLES

Figure 1. PRISMA flow diagram of study selection.

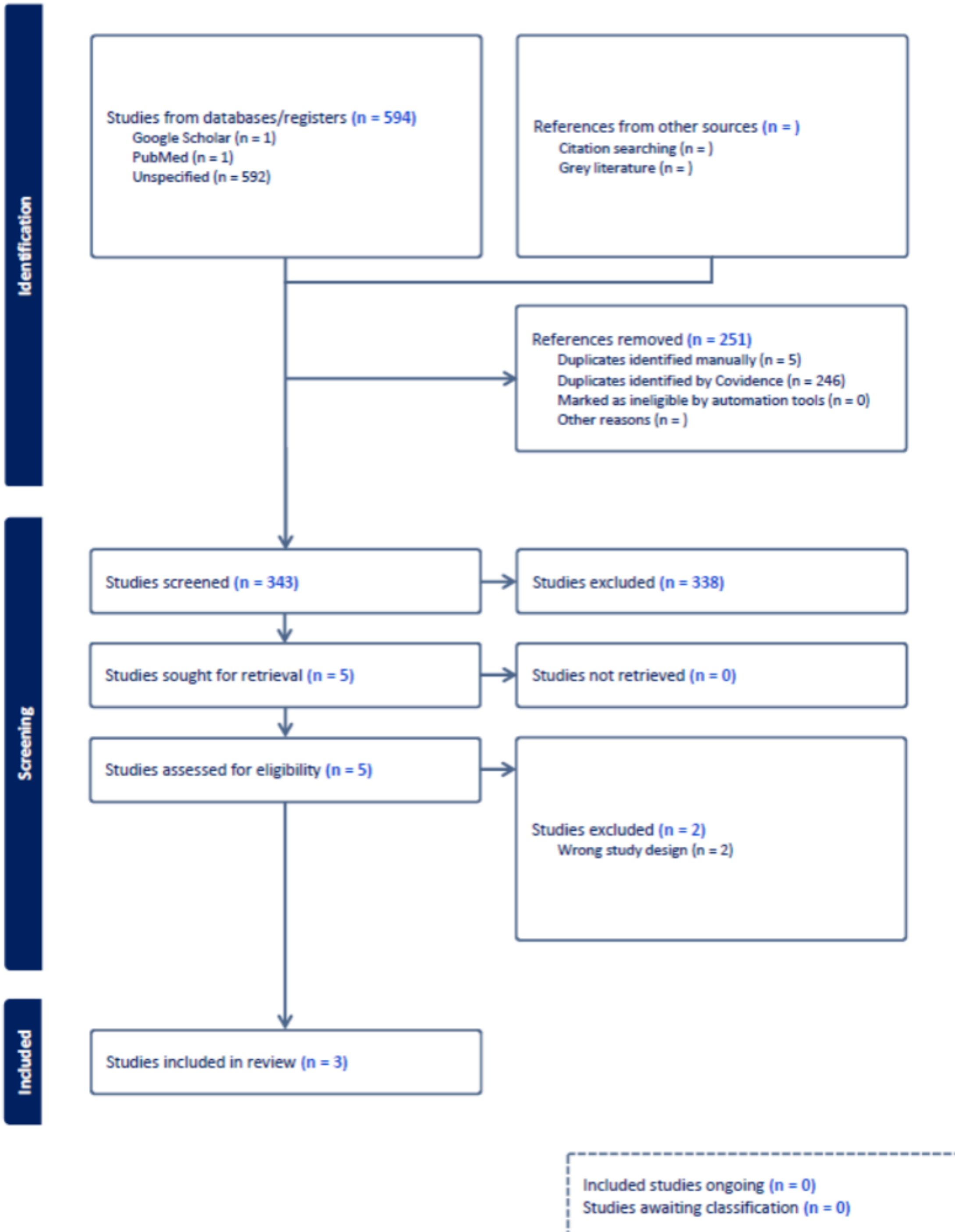

Figure 2. Forest plot of wound-healing time after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings. Negative mean differences favor oxygen-/ozone-based dressings.

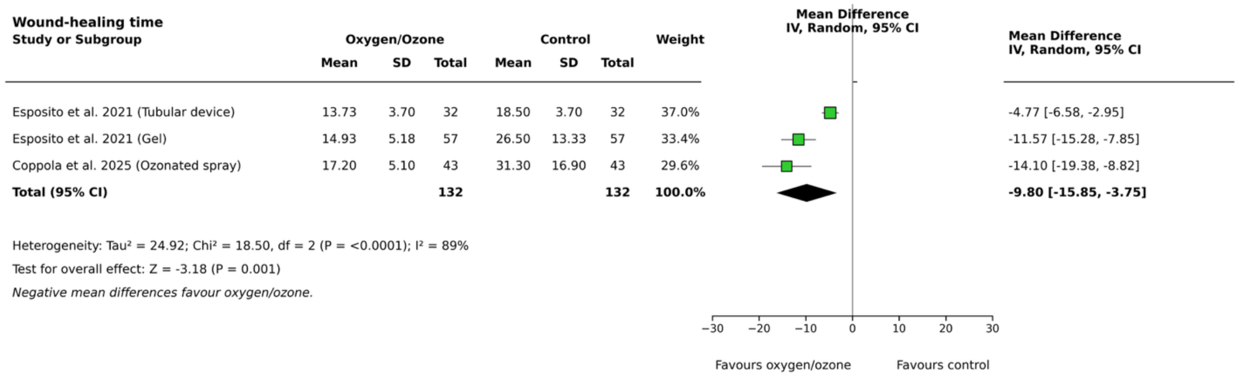

Figure 3. Forest plot of reoperation rates after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings.

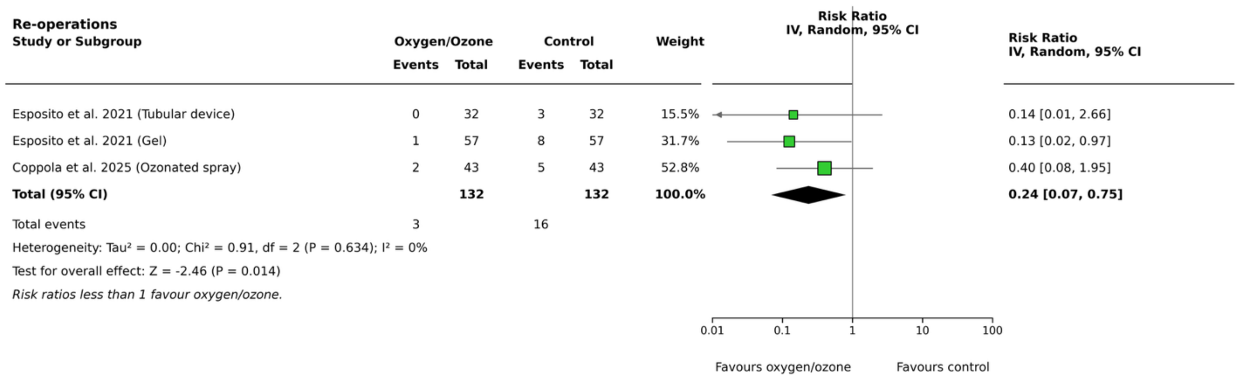

Figure 4. Forest plot of foreskin dehiscence after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings.

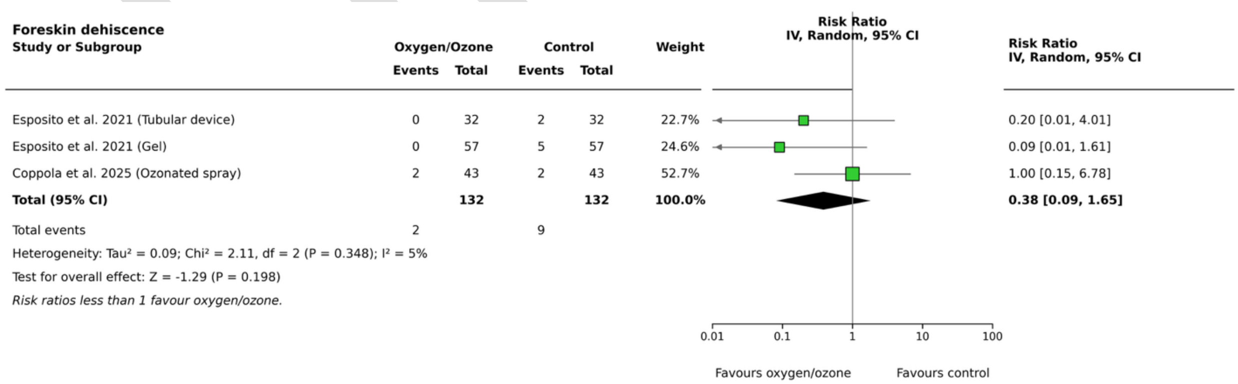

Figure 5. Forest plot of urethrocutaneous fistula after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings.

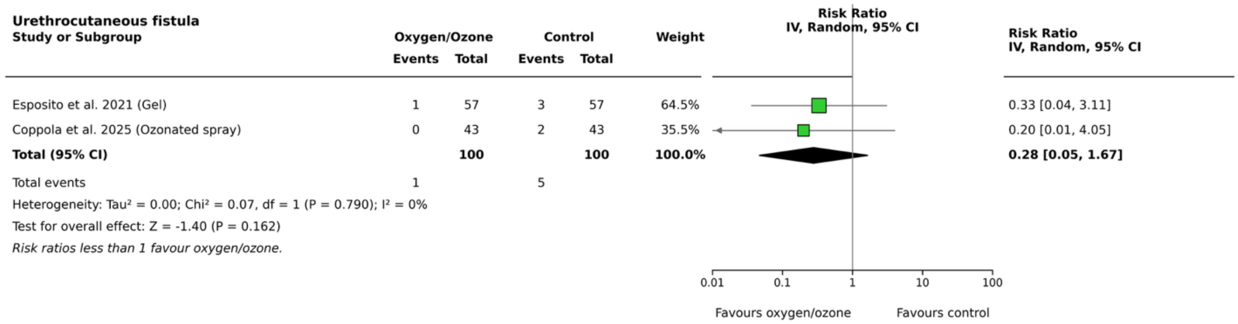

Figure 6. Forest plot of wound infection after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings.

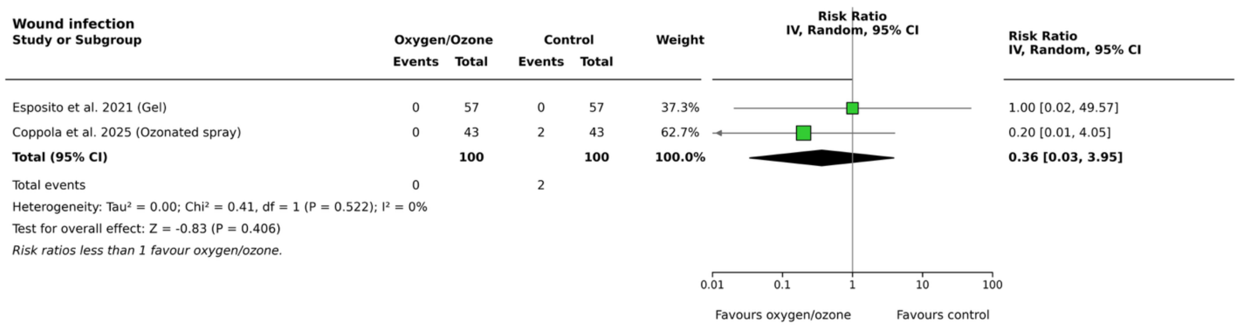

Figure 7. Forest plot of normal wound healing at postoperative day 14, defined as Southampton Wound Assessment Scale score ≤1, comparing oxygen-based dressings vs. standard postoperative dressings.

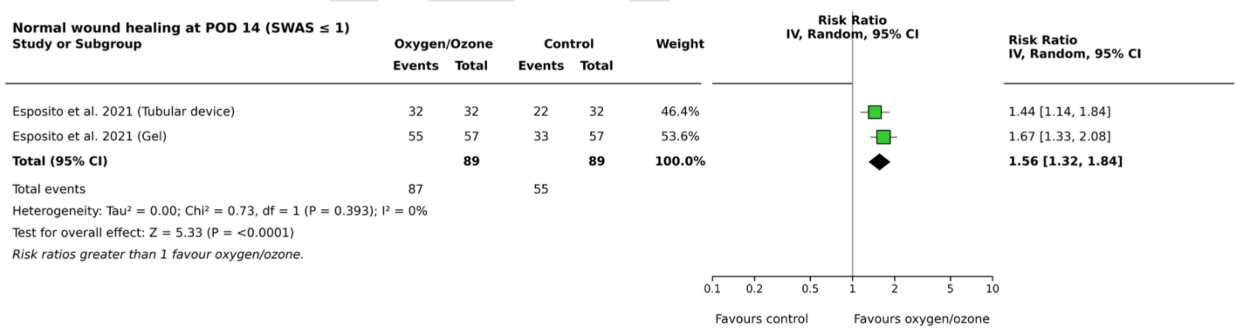

Figure 8. Forest plot of any postoperative complication after hypospadias repair comparing oxygen-/ozone-based dressings vs. standard postoperative dressings.

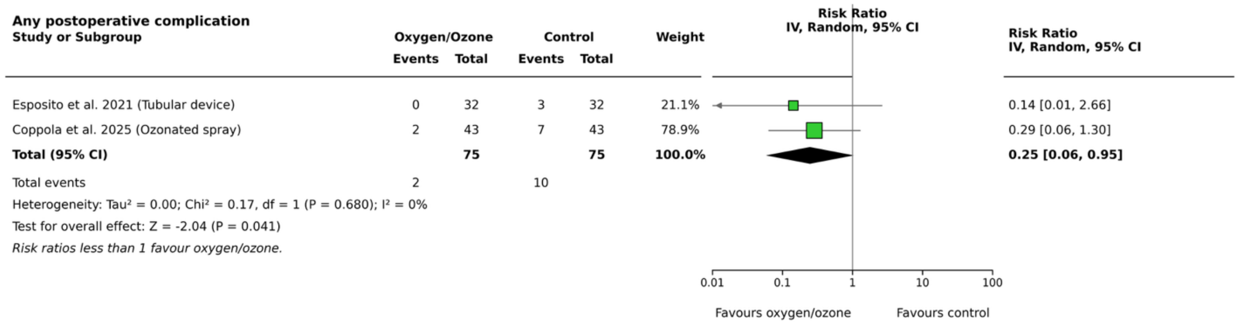

Table 1. Characteristics of included studies

Study	Year	Country	Population	Intervention	Comparator	Sample size (I/C)	Key outcomes
Esposito et al, *World J Urol*	2021	Germany	Children, distal hypospadias (median age ~18 mo)	Oxygen-enriched oil-based gel	Hyaluronic-acid cream	57 / 57	Healing time; SWAS; HOPE; complications; re-operations; costs
Esposito et al, *Front Pediatr*	2021	Switzerland	Children, distal hypospadias (median age 14 mo)	Tubular finger oxygen-enriched oil device	Elastic bandage + oxygen gel	32 / 32	Healing time; SWAS; edema; penile diameter; complications; nurse handling
Coppola et al, *Children (Basel)*	2025	Switzerland	Children, distal hypospadias (mean age ~18–19 mo)	Ozonated olive oil spray + vitamin E	Hyaluronic-acid cream	43 / 43	Healing time; complications; re-operations; day-7 wound features

Table 2. Summary of cochrane RoB-2 assessment of included randomized controlled trials

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of outcomes	Selection of reported results	Overall RoB
Esposito et al, 2021 (Gel)	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Esposito et al, 2021 (tubular device)	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Coppola et al, 2025 (ozonide spray)	Low	Some concerns	Low	**High risk**	Some concerns	**High risk**

Table 3. Cochrane RoB 2 — Critical appraisal of study 1: Esposito et al, 2021 (oxygen-enriched oil gel dressing)

Domain	Judgment	Reasoning
1. Randomization process	Low	Sequence generation and allocation via opaque envelopes described. No baseline imbalances reported.
2. Deviations from intended interventions	Some concerns	Claimed single-blind; only parents blinded via unlabelled packaging. Nurses were likely aware, potentially influencing care or parental reporting (e.g. discomfort, adherence).
3. Missing outcome data	Low	All 114 patients completed the 180-day follow-up.
4. Measurement of the outcome	Some concerns	Primary outcome (SWAS, HOPE) includes subjective clinical judgment (erythema, “normal appearance”); though assessors were independent, their blinding may have been incomplete.
5. Selection of reported results	Some concerns	Protocol was not registered. Outcomes reported are reasonable, but selective reporting risk cannot be excluded. No mention of pre-specified statistical analysis plan.

Table 4. Cochrane RoB 2 — Critical appraisal of study 2: Esposito et al., 2021 (tubular finger device)		
Domain	**Judgment**	**Reasoning**
1. Randomization process	Low	Opaque sealed envelope method reported; allocation concealment likely adequate.
2. Deviations from intended interventions	Some concerns	Described as single-blind, but nurses who performed dressing changes likely knew group assignments, potentially influencing subjective assessments (e.g. ease of dressing).
3. Missing outcome data	Low	No attrition; all patients completed 60-day follow-up.
4. Measurement of the outcome	Some concerns	SWAS includes subjective components (erythema, exudate). Assessment performed by one surgeon and one nurse (not clearly both blinded). No inter-rater reliability data.
5. Selection of reported results	Some concerns	No pre-registered protocol. Though SWAS was appropriate, additional subjective parameters (nurse ease-of-use scores, comfort) lack justification or pre-specification.

Table 5. Cochrane RoB 2 — Critical appraisal of study 3: Coppola et al, 2025 (ozonide spray dressing)		
Domain	**Judgment**	**Reasoning**
1. Randomization process	Low	Adequate allocation via sealed envelopes; no baseline imbalances.
2. Deviations from intended interventions	Some concerns	Parents were instructed not to disclose group, but blinding was fragile — obvious differences between spray vs. cream likely revealed assignment to parents and assessors. No double-dummy.
3. Missing outcome data	Low	Only one dropout (included in ITT); impact negligible.
4. Measurement of the outcome	High risk	Subjective measures (SWAS, FLACC pain scale, parental satisfaction) highly vulnerable to bias. Use of different dressing forms makes blinding implausible. No observer calibration or reliability testing.
5. Selection of reported results	Some concerns	No trial registration or statistical analysis plan. Use of numerous secondary endpoints raises reporting concerns (e.g. parent-reported ease, satisfaction, FLACC scale).

Table 6. Summary of pooled meta-analytic outcomes				
Outcome	**Studies (n)**	**Effect measure**	**Pooled estimate (95% CI)**	**I^2 (%)**
Wound-healing time	3	Mean difference (days)	**-9.80 (-15.85 to -3.75)**	89.2
Reoperations	3	Risk ratio	**0.24 (0.07–0.75)**	0
Foreskin dehiscence	3	Risk ratio	0.38 (0.09–1.65)	5.1
Urethrocutaneous fistula	2	Risk ratio	0.28 (0.05–1.67)	0
Wound infection	2	Risk ratio	0.36 (0.03–3.95)	0
SWAS ≤1 at day 14	2	Risk ratio	**1.56 (1.32–1.83)**	0
Any postoperative complication	2	Risk ratio	**0.25 (0.06–0.95)**	0

Table 7. GRADE summary of findings for oxygen-rich dressings compared with standard postoperative dressings after distal hypospadias repair.					
Outcome	**No. of studies (participants)**	**Relative effect (95% CI)**	**Absolute effect***	**Certainty of evidence (GRADE)**	**Explanation**
Wound-healing time (days)	3 (264)	MD −9.80 days (−15.85 to −3.75)	~10 days faster healing	Moderate	Downgraded for serious inconsistency (I^2 = 89%) and use of estimated means from medians; consistent direction of effect across studies
Reoperations	3 (264)	RR 0.24 (0.07–0.75)	~8 fewer re-operations per 100 patients	Moderate	Downgraded for risk of bias (lack of blinding, no trial registration); no heterogeneity

Any postoperative complication	2 (150)	RR 0.25 (0.06–0.95)	~10 fewer complications per 100 patients	Low	Downgraded for risk of bias and imprecision (low event rates, wide CI)
Foreskin dehiscence	3 (264)	RR 0.38 (0.09–1.65)	Possible reduction	Low	Downgraded for imprecision and risk of bias
Urethrocutaneous fistula	2 (200)	RR 0.28 (0.05–1.67)	Possible reduction	Low	Downgraded for imprecision (rare events)
Wound infection	2 (200)	RR 0.36 (0.03–3.95)	Uncertain effect	Low	Downgraded for very serious imprecision
Normal wound healing (SWAS ≤1 at day 14)	2 (178)	RR 1.56 (1.32–1.83)	~30 more patients per 100 with normal healing	Moderate	Downgraded for risk of bias (subjective outcome, incomplete blinding)

[*]Absolute effects are approximate and based on pooled control-group risks.
Population: Children undergoing primary distal hypospadias repair. Intervention: Oxygen-rich, oxygen-based, or ozone-based postoperative dressings. Comparator: Standard postoperative dressings. Study design: Randomized controlled trials.