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Regenerative and Energy-Based Interventions in Gynecology: An Umbrella Review of Systematic Reviews on Platelet-Rich Plasma, Vaginal Laser, Radiofrequency, and Reproductive Tissue Regeneration

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Abstract

Background: "Regenerative gynecology" has become a commercially mature field before it became an evidentially mature one. Platelet-rich plasma (PRP), fractional CO_2 and Er:YAG lasers, radiofrequency (RF), and, more recently, cell- and exosome-based products are marketed for genitourinary syndrome of menopause (GSM), vulvar lichen sclerosus, sexual dysfunction, vaginal laxity, stress urinary incontinence (SUI), diminished ovarian reserve, and recurrent implantation failure (RIF). Dozens of systematic reviews now exist, frequently reaching opposite conclusions from largely overlapping primary studies.

Objective: To map, appraise, and reconcile the review-level evidence across four intervention domains — injectable PRP, vaginal laser, radiofrequency, and reproductive tissue regeneration — and to explain *why* conclusions diverge so widely.

Methods: Umbrella-review methodology (overview of systematic reviews) following the logic of the PRIOR reporting standard, with methodological confidence framed by AMSTAR-2, certainty by GRADE, and primary-study overlap by the corrected covered area (CCA).

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Principal findings: Three consistent patterns emerge. First, a sham gradient: effect sizes shrink, and often disappear, as comparators move from before–after designs to active controls to double-blind sham. Second, a surrogate–outcome gap: in reproductive applications, PRP improves laboratory markers of ovarian reserve while pooled pregnancy outcomes do not follow. Third, estimate instability: reviews of essentially the same trials report live-birth odds ratios ranging from 1.23 to 11.02, a spread that cannot be explained by biology.

Conclusions: Across all four domains, the evidence supports biological plausibility and acceptable short-term safety, not established efficacy. The field's central problem is not a shortage of publications but a shortage of standardization: uncharacterized biologics, non-comparable device parameters, before–after designs, surrogate endpoints, and short follow-up. A defined minimum reporting set, a core outcome set, and adequately powered sham-controlled trials with ≥12-month follow-up are the prerequisites for regenerative gynecology to become a specialty rather than a market.

Keywords

Platelet-rich plasma; Genitourinary syndrome of menopause; Fractional CO_2 laser; Radiofrequency; ovarian rejuvenation; Recurrent implantation failure; Umbrella review; Evidence appraisal.

Introduction

Few areas of women's health have expanded as quickly, or with as little methodological discipline, as regenerative and energy-based gynecology. The clinical needs are real and often poorly served: GSM affects a large proportion of postmenopausal women and women on aromatase inhibitors; vulvar lichen sclerosus is chronic, under-diagnosed, and steroid-dependent; SUI and pelvic floor dysfunction carry substantial quality-of-life burden; and diminished ovarian reserve remains one of reproductive medicine's least tractable problems. Into these gaps arrived interventions that are procedural, autologous or device-based, immediately billable, and rhetorically attractive — "regeneration," "rejuvenation," "restoration."

The regulatory environment made the mismatch explicit. In July 2018 the U.S. Food and Drug Administration warned patients and clinicians against the use of energy-based devices for vaginal "rejuvenation" and cosmetic vaginal procedures, stating that safety and effectiveness for these conditions had not been established and citing potential serious adverse events including vaginal burns, scarring, dyspareunia, and chronic pain, as summarized by IUGA's dissemination of the FDA communication and by ACOG's committee guidance on elective female genital cosmetic surgery. A 2019 ICS/ISSVD best-practice consensus concluded that laser should not be used routinely for vaginal atrophy or urinary incontinence outside well-designed trials or arrangements with formal clinical governance, consent, and audit, and the American Urogynecologic Society issued its consensus statement explicitly because strong level I evidence was absent — positions compiled in the AUGS clinical consensus statement on vaginal energy-based devices.

Meanwhile, systematic reviews multiplied. This creates a second-order problem that primary research cannot solve: when twenty reviews of overlapping trials publish incompatible conclusions, the clinician's difficulty is no longer "what does the evidence show?" but "which synthesis should I believe?" That is precisely the question umbrella reviews exist to answer.

This article synthesizes review-level evidence across four domains — injectable PRP in vulvovaginal and pelvic floor indications; vaginal laser; radiofrequency; and reproductive tissue regeneration (intraovarian

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and intrauterine PRP, cell- and exosome-based approaches) and offers an original diagnostic framework for the field's evidential pathologies.

Methods

Design

This is an umbrella review (overview of systematic reviews), structured according to the conceptual requirements of overview reporting: explicit eligibility at review level, appraisal of included reviews with AMSTAR-2, certainty assessment using GRADE domains as reported by the source reviews, and quantification of primary-study overlap using the corrected covered area (CCA), interpreted in conventional bands (≤5% slight, 6–10% moderate, 11–15% high, >15% very high).

Eligibility

- **Population:** Adult women with GSM, vulvovaginal atrophy, dyspareunia, vulvar lichen sclerosus, female sexual dysfunction, vaginal laxity, SUI or other pelvic floor disorders, thin endometrium, intrauterine adhesions, recurrent implantation failure, diminished ovarian reserve, or premature ovarian insufficiency.
- **Interventions:** Autologous: PRP (any preparation or route), platelet-rich fibrin, fractional/microablative CO_2 laser, Er:YAG laser, hybrid lasers, non-ablative radiofrequency, and cell- or exosome-based products with human data.
- **Comparators:** Sham, placebo, no treatment, vaginal estrogen, moisturizers, pelvic floor muscle training, standard assisted-reproduction care, or before–after self-control (recorded as such and analyzed separately).
- **Outcomes:** Validated symptom and function instruments (Vaginal Health Index [VHI], Female Sexual Function Index [FSFI], Vaginal Laxity Questionnaire [VLQ], VAS for dyspareunia/dryness/burning, ICIQ-SF, UDI-6, IIQ-7), urodynamic parameters, ovarian reserve markers (AMH, FSH, antral follicle count [AFC], estradiol), endometrial thickness, clinical pregnancy, live birth, adverse events, and durability.
- **Study types:** Systematic reviews, meta-analyses, network meta-analyses, and prior overviews. Narrative reviews were used only as contextual sources and are labeled as such; scoping reviews were included for mapping purposes but not for effect estimation.

Interpretive framework

Because pooling across heterogeneous reviews would compound rather than resolve their limitations, this overview privileges structured qualitative synthesis with three original analytic lenses, defined a priori:

- **The sham gradient** — comparison of effect magnitude stratified by comparator rigor (before–after → active control → sham).
- **The surrogate–outcome gap** — divergence between biomarker/instrument responses and patient-important endpoints (live birth, durable symptom relief).
- **Estimate instability** — dispersion of pooled estimates across reviews addressing the same question with overlapping primary studies.

Results

The shape of the evidence base

The review-level landscape is dense but structurally uneven: it is rich in reviews of weak studies and poor in reviews of strong ones.

Domain	Anchor review-level evidence	Evidence volume	Design quality of underlying studies
Vaginal laser for GSM	12 RCTs, 5,147 participants (Pessoa et al., *RBGO* 2024); 7 sham RCTs, 407 women (Prodromidou et al., *JPM* 2023)	High	Moderate; sham-controlled subset now substantial
Radiofrequency / vaginal laxity	38 studies (Pereira et al., *J Sex Med* 2024)	Moderate	Low; dominated by before–after observational data
Vulvovaginal PRP	18 studies, 480 patients, 2 RCTs (De Ponte et al., *J Sex Med* 2026)	Low	Low; single-arm and case-based
PRP for pelvic floor / SUI	15 studies, 600 women (Kurniawati et al., *IJRM* 2024); 8 studies, 257 women (Utama et al., *Front Med* 2026)	Low–moderate	Low; mostly quasi-experimental
Intraovarian PRP	14 studies, 1,632 women, no RCTs (Maged et al., *BMC Pregnancy Childbirth* 2024); 7 RCTs, 422 women (Fang et al., *Front Endocrinol* 2026)	Moderate	Improving; first RCT syntheses now available
Intrauterine PRP / RIF	25 systematic reviews, 112 primary studies (Masiello et al., *Blood Transfus* 2025); 47 SRs in an RIF umbrella review (Almohammadi et al., *IJGO* 2025)	Very high (review-level)	Mixed; severe review redundancy
Cell/exosome-based	199 studies, predominantly preclinical (Applications of Exosomes in Female Medicine, PMC 2026)	Preclinical	Not yet clinically evaluable

Vaginal laser for GSM: the clearest natural experiment in the field

Vaginal laser is the only regenerative-adjacent gynecologic intervention with a substantial double-blind, sham-controlled literature — which makes it the field's most informative case study.

The largest RCT-restricted synthesis, covering 12 randomized trials and 5,147 participants, reported statistically significant improvements with CO_2 laser: VHI mean difference (MD) 2.21 (95% CI 1.25–3.16), dyspareunia MD −0.85 (−1.59 to −0.10), dryness MD −0.62 (−1.12 to −0.12), and burning MD −0.64 (−1.28 to −0.01), with no serious adverse effects. Crucially, the same authors rated the certainty of evidence as low and explicitly declined to recommend laser for GSM management (Pessoa et al., 2024).

When the comparator is tightened to sham alone, the signal weakens further. A meta-analysis restricted to seven sham-controlled RCTs (407 women) found CO_2 laser and sham comparable for most parameters, with FSFI MD 3.92 (−2.87 to 10.70; p = 0.26) in the primary analysis, becoming nominally significant (MD 6.29; 0.20–12.37; p = 0.04) only after exclusion of one trial (Prodromidou et al., 2023). A 2025 critical appraisal integrating seven double-blind sham-controlled trials with 401 unique participants across six countries concluded that the evidence does not support fractional CO_2 laser as an efficacious treatment for GSM; for dyspareunia in 260 women, the 16.3% greater absolute improvement with laser was not statistically significant, and the two trials using higher 40 W protocols showed no substantial advantage

over 30 W (Li et al., Climacteric 2025).

A separate synthesis of six RCTs (270 women) comparing CO_2 laser with vaginal estrogen found similar improvement between arms (Jang et al., JAMA Network Open 2022). This is often quoted as evidence of laser efficacy; methodologically it is equivocal, because two active treatments can converge either because both work or because both are dominated by regression to the mean, natural symptom fluctuation, and expectation effects in an unblinded procedural context.

Interpretation: The laser literature demonstrates the sham gradient with unusual clarity: robust before–after improvements, attenuated randomized effects, and largely null double-blind sham-controlled effects. Safety at studied parameters appears acceptable in trials, but efficacy for GSM is not established.

Radiofrequency and vaginal laxity: the before–after illusion

Radiofrequency has no double-blind sham-controlled evidence base comparable to laser. The most instructive synthesis pooled 38 studies of treatments for vaginal laxity and produced two contradictory pictures from the same dataset (Pereira et al., 2024):

Analysis	Result	Heterogeneity
FSFI, before vs. after, 8 observational studies	MD 6.51 (5.61–7.42)	I^2 = 85%
FSFI, radiofrequency, before vs. after	MD 6.00 (4.26–7.73)	I^2 = 80%
FSFI, laser, before vs. after	MD 6.83 (5.01–8.65)	I^2 = 92%
VLQ, radiofrequency vs. **sham**	MD 1.01 (−0.38 to 2.40)	I^2 = 94%
Pelvic floor muscle strength after intervention	MD 4.22 (1.02–7.42)	I^2 = 77%

The apparent improvement in sexual function **disappeared when analysis was restricted to the three randomized trials**, for both radiofrequency and laser, and vaginal tightening did not improve sensation. GRADE certainty was moderate for sexual function and VLQ and low for muscle strength, with all non-randomized studies except one judged to carry serious risk of bias.

This is the single most important quantitative observation in the entire energy-based literature: an effect size of roughly six FSFI points — clinically large, exceeding most published minimal important differences evaporates under randomization. Any clinical or commercial claim built on before–after FSFI data should be regarded as uninterpretable.

Vulvoaginal PRP: promising, unstandardized, and under-randomized

The most directly relevant systematic review of injectable PRP in vulvovaginal indications included 18 studies and 480 patients (401 PRP-treated), of which only two were randomized controlled trials; the remainder comprised 10 single-arm clinical trials, one retrospective cross-sectional study, and five case reports. Indications were vulvar lichen sclerosus (179 patients), sexual dysfunction (133), and vulvovaginal atrophy (87). Adverse events were few and mild, but preparation methods, injection techniques, session

numbers, and schedules varied so widely that no pooled estimate was possible; the authors concluded that methodological limitations preclude definitive conclusions (De Ponte et al., 2026).

A broad scoping review of PRP across gynecologic disorders mapped the field's breadth — vulvar lichen sclerosus, sexual dysfunction, vulvovaginal atrophy, Asherman syndrome, intrauterine adhesions, interstitial cystitis/bladder pain syndrome, recurrent UTI, SUI, vesicovaginal fistula, and complications of female genital cutting — with sample sizes from 5 to 200 (median ≈48) and follow-up of 4 weeks to 12 months. No meta-analysis was performed because heterogeneity precluded meaningful quantitative synthesis, and the review itself reports internally inconsistent study counts (43 in the abstract, 46 in the results) (Willison et al., J Clin Med 2025).

Interpretation: Vulvovaginal PRP is currently an indication-generating literature, not an efficacy literature. Its most defensible near-term research target is vulvar lichen sclerosus, where the condition is objectively definable, histologically assessable, symptom-scored with validated instruments, and already has randomized comparisons against placebo underway.

PRP in pelvic floor disorders and stress urinary incontinence

A systematic review of PRP across pelvic floor disorders included 15 studies and 600 women spanning sexual dysfunction and orgasmic disorder (164), SUI (179), perineal rupture (210), vulvovaginal atrophy (20), vesicovaginal fistula (16), and pelvic organ prolapse (10), with designs ranging from RCTs to case reports and largely absent comparators (Kurniawati et al., 2024).

A more recent meta-analysis focused on SUI pooled eight studies (three RCTs, five quasi-experimental) with 257 participants and reported a large improvement in abdominal leak point pressure (MD 51.07; 36.21–65.93; $p < 0.0001$) alongside reductions in UDI-6 and ICIQ-SF at 1–3 months and unchanged functional profile length, with mild, self-limiting adverse events (Utama et al., 2026).

Two cautions apply. First, follow-up of 1–3 months is inadequate for a chronic condition whose comparator therapies are judged over years. Second, urodynamic gains without concordant, durable patient-reported continence outcomes repeat the surrogate–outcome pattern seen in reproductive applications.

Intraovarian PRP: the surrogate–outcome gap in its purest form

Intraovarian PRP is where the divergence between biomarkers and babies is most measurable.

Before–after syntheses are strongly positive. A meta-analysis of 38 human articles (2,256 women), predominantly observational with self-control comparison, reported AMH increases of +0.20 ng/mL at 1 month (0.12–0.28), +0.26 at 2 months (0.07–0.44), and +0.36 at 3 months (0.20–0.52); FSH reductions of −10.20, −7.02, and −8.87 mIU/mL at 1, 2, and 3 months; AFC +1.60 follicles (0.92–2.27); retrieved oocytes +0.81 (0.36–1.26); and embryos created +0.91 (Éliás et al., J Ovarian Res 2024).

Controlled syntheses are markedly less impressive. A review of 14 studies with 1,632 participants containing no randomized controlled trials — found no significant pooled effect on AMH (MD 0.09; −0.06

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to 0.24; p = 0.25) or basal FSH (MD 1.56; −1.53 to 4.64; p = 0.32) (Maged et al., 2024).

Randomized evidence separates markers from outcomes. A meta-analysis restricted to seven RCTs (422 women) found significant improvements in AFC (MD 0.81; 0.31–1.30), AMH (SMD 0.91; 0.41–1.42), FSH (MD −5.72; −7.03 to −4.41) and estradiol (MD 26.03; 19.53–32.53), yet no significant difference in pregnancy rate (six RCTs, 228 participants; logRR −0.25; −0.69 to 0.19; p = 0.26; I^2 = 0%), with live birth insufficiently reported to pool. The authors concluded that current evidence does not demonstrate a corresponding benefit in pregnancy outcomes and that neither optimal regimen nor target population has been established (Fang et al., 2026).

An AFC gain of well under one follicle and an AMH shift of a few tenths of a nanogram per milliliter are, in candid clinical terms, below the threshold at which most reproductive endocrinologists would change management — and the randomized pregnancy data are compatible with no benefit at all. Ovarian "rejuvenation" should therefore be presented to patients as an experimental intervention with unproven fertility benefit, not as a treatment.

Intrauterine PRP and recurrent implantation failure: estimate instability

Here the problem is not scarcity of synthesis but its overproduction. An overview of systematic reviews identified 25 systematic reviews published 2020–2024, encompassing 306 overlapping reports derived from only 112 individual primary studies, with a corrected covered area of 1.9% (slight overlap) at report level. Only two reviews met all AMSTAR-2 methodological requirements; twelve had one or two requirements partly met or unspecified; eleven had three or more partly met; only two reported funding sources of included studies; ten failed to fully report excluded studies with reasons (Masiello et al., 2025).

The consequence is visible in the live-birth estimates extracted by that overview from reviews addressing substantially the same trials:

Systematic review	Comparison	Live birth estimate (95% CI)	GRADE certainty
Wang, 2021 (NMA)	PRP vs. placebo, 3 RCTs	OR 1.23 (0.33–4.64)	Low
Jin, 2022 (NMA)	PRP vs. no intervention, 4 RCTs	OR 5.96 (3.38–10.52)	Moderate
Li, 2022	PRP vs. no treatment, 4 studies	RR 2.92 (2.22–3.85)	Low
Liu, 2022 (RCT subset)	PRP vs. no treatment/placebo, 2 studies	OR 11.02 (5.72–21.21)	Low
Anitua, 2023	PRP vs. no PRP/placebo, 4 low-RoB RCTs	RR 2.90 (1.06–7.96)	Low
Deng, 2023	PRP vs. standard treatment, 4 trials	RR 2.83 (1.45–5.52)	Low
Hu, 2023	PRP vs. no PRP, 2 trials	RR 7.03 (3.9–12.6)	Low

Shalma, 2023	PRP vs. no PRP/standard, 10 trials	RR 1.75 (1.24–2.47)	Moderate

All estimates derive from a small, shared, largely single-center trial pool, yet the point estimates span a nine-fold range, and nearly all carry low or very-low GRADE certainty because of risk of bias, imprecision, inconsistency, or indirectness. Chemical- and clinical-pregnancy estimates are more consistently positive (chemical pregnancy RR/OR ≈1.79–2.92 across reviews), but positivity across redundant reviews of the same weak trials is not independent confirmation — it is correlated noise.

Independently, an umbrella review of 47 systematic reviews of interventions for recurrent implantation failure found PRP associated with improved clinical pregnancy in 6 of 10 meta-analyses (60%) but improved live birth in only 1 of 5 meta-analyses (20%) — a pattern shared with G-CSF (69.2% for clinical pregnancy vs. 14% for live birth) (Almohammadi et al., 2025). The consistency of that dissociation across unrelated interventions is itself informative: it points to shared design and reporting artefacts rather than to intervention-specific biology.

Cell- and exosome-based approaches: preclinical, appropriately

Exosome and stem-cell strategies dominate mechanistic discourse but not clinical evidence. A large synthesis of exosome applications in female medicine screened 350 articles and included 199, focused on basic and early clinical science, with quality assessed by the Newcastle–Ottawa Scale and Cochrane risk-of-bias tools and no pooled clinical effect estimates for fertility, pregnancy, or symptom outcomes (Applications of Exosomes in Female Medicine, 2026). Clinical use of exosome products in gynecologic indications is therefore not supported by controlled human efficacy data, and marketing that implies otherwise outruns the evidence by a wide margin.

Cross-cutting synthesis: five structural pathologies

Rather than repeat "more research is needed," this overview names the specific, correctable failures that generate the field's contradictions.

The sham gradient

Across every domain in which both design types exist, effect size is inversely proportional to comparator rigor. Before–after FSFI gains of ~6.5 points collapse under randomization (Pereira et al., 2024); ovarian marker improvements of +0.36 ng/mL AMH in self-controlled data shrink to null in controlled synthesis (Maged et al., 2024); GSM symptom benefits that appear in mixed-comparator meta-analysis are not confirmed in double-blind sham trials (Li et al., 2025). Procedural interventions in symptom-driven, stigmatized, intimate conditions are close to a worst case for expectation effects — vaginal speculum-based procedures with visible technology, therapeutic ritual, and highly motivated self-selected patients.

The surrogate–outcome gap

The field consistently improves what is easy to measure. AMH, AFC, endometrial thickness, leak point pressure, and VHI move; live birth, durable continence, and long-term symptom control largely do not, or are not reported. The 60%-versus-20% dissociation between clinical pregnancy and live birth in RIF interventions (Almohammadi et al., 2025) and the marker-positive/pregnancy-null pattern in intraovarian

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PRP RCTs (Fang et al., 2026) are two views of the same problem.

The uncharacterized intervention

"PRP" is not one intervention. Across reviews, preparation used single or double centrifugation, variable activation (calcium chloride, thrombin, none), and injected volumes ranging from 0.2 mL to 8 mL intraovarian and 0.3 mL to 40 mL intrauterine, with platelet concentration reported inconsistently and leukocyte content usually not reported at all (Maged et al., 2024; Maged et al., J Assist Reprod Genet 2023). Energy-based devices have a parallel problem: 30 W versus 40 W protocols, dwell times of 800–1000 µs, dot spacing 800–1000 µm, SmartStack 1–3, and 2–5 sessions at 4–6-week intervals (Prodromidou et al., 2023). Pooling uncharacterized biologics or non-equivalent energy doses produces heterogeneity that no statistical model can repair.

Review redundancy as pseudo-replication

Twenty-five systematic reviews built on 112 primary studies is not twenty-five confirmations (Masiello et al., 2025). Redundant syntheses inflate perceived certainty, and because reviews differ in inclusion thresholds, model choice, and outcome definitions, they generate the nine-fold live-birth spread documented above. Journals and authors should require overlap quantification (CCA) and justification for any new review in a saturated question.

Terminology as an evidential hazard

"Rejuvenation," "revitalization," and "regeneration" are not endpoints. Regulators specifically flagged the imprecision of "vaginal rejuvenation," and the FDA has not cleared any energy-based device for vaginal cosmetic procedures or for symptoms of menopause, incontinence, or sexual function (ACOG, 2020; AUGS consensus statement). Scientific writing should name the condition (GSM, lichen sclerosus, SUI, dyspareunia, vulvovaginal atrophy) and the instrument, never the marketing category.

Summary of confidence by indication

Indication	Intervention	Direction of evidence	Best current certainty	Clinical positioning
GSM symptoms	Fractional CO_2 laser	Positive in mixed-comparator pooling; null in double-blind sham	Low (Pessoa 2024; Li 2025)	Not recommended as routine care
GSM vs. vaginal estrogen	CO_2 laser	Comparable to estrogen in small RCTs	Low (Jang 2022)	Estrogen remains first-line
Vaginal laxity / sexual function	Radiofrequency, laser	Large before–after gains; null in RCT-restricted analysis	Moderate for the null (Pereira 2024)	Research setting only
Vulvar lichen sclerosus	PRP	Encouraging, minimally randomized	Very low (De Ponte 2026)	Investigational adjunct; steroids remain standard
Vulvovaginal atrophy / sexual dysfunction	PRP	Signal present, protocols incomparable	Very low (De Ponte 2026)	Investigational
Stress urinary incontinence	Injectable PRP	Short-term urodynamic and symptom gains	Low (Utama 2026)	Investigational; durability unknown

Diminished ovarian reserve	Intraovarian PRP	Markers improve; pregnancy does not	Low (Fang 2026)	Experimental; no proven fertility benefit
Recurrent implantation failure	Intrauterine PRP	Positive but unstable; live birth inconsistent	Low to moderate (Masiello 2025; Almohammadi 2025)	Promising; confirmation required
Any gynecologic indication	Exosome products	Preclinical only	Insufficient (Exosomes review 2026)	Not for clinical use outside trials

Safety signals across reviews were reassuring at studied parameters — few, mild, self-limiting adverse events — but follow-up rarely exceeded 12 months, and regulators have documented serious harms including burns, scarring, and chronic pain in post-market surveillance of energy-based devices (ACOG, 2020). Absence of harm in short, small trials is not evidence of long-term safety.

A research agenda that would actually change the evidence

- **A minimum reporting set for biologics:** Every PRP study should report, at minimum: whole-blood volume; anticoagulant; centrifugation protocol; final platelet concentration (absolute, $\times 10^9$/L, and fold over baseline); leukocyte and erythrocyte content; activation method; injected volume per site; needle gauge; anatomical plane; imaging guidance; number and interval of sessions; and any co-intervention. Adoption of a published classification system (e.g., leukocyte-based or DEPA/MARSPILL-type coding) should be a condition of publication.
- **Dose transparency for energy-based devices:** Wavelength, power, dwell time, spacing, stacking, fluence in J/cm², probe geometry, treated compartments, and session schedule must be reported so that trials become comparable rather than merely similar.
- **A core outcome set for regenerative gynecology:** Proposed minimum: (a) a validated condition-specific symptom instrument; (b) FSFI or an equivalent sexual-function measure; (c) an objective tissue or functional measure (VHI, maturation index, pH, urodynamics, or histology when ethically justified); (d) a patient global impression of improvement; (e) treatment-emergent adverse events by severity; (f) durability at 6 and 12 months minimum; and, for reproductive indications, live birth as the primary endpoint rather than biochemical or clinical pregnancy.
- **Design requirements:** Double-blind sham control wherever ethically feasible; power calculations anchored to established minimal clinically important differences rather than statistical convenience; multicenter recruitment to break the single-center pattern; prospective registration; and pre-specified analysis plans. Where sham is impossible, three-arm designs with an active standard comparator (vaginal estrogen, topical steroid, pelvic floor training) are preferable to unblinded two-arm designs.
- **The highest-yield trials to run next**. Three studies would move this field more than fifty additional observational series: (1) a multicenter, double-blind, saline-controlled RCT of standardized PRP in vulvar lichen sclerosus with histologic and symptom co-primary endpoints; (2) a sham-controlled RCT of injectable PRP for SUI with 12-month ICIQ-SF and objective leakage outcomes; and (3) an adequately powered intraovarian PRP RCT in a defined POSEIDON population with live birth as the primary endpoint.

Limitations

This overview is limited by the quality of the reviews it summarizes: several reported internally inconsistent study counts, few reported funding of included studies, and GRADE assessments were unevenly applied. Because comparators, populations, and outcome instruments were incompatible across domains, no quantitative pooling was performed at overview level, and the synthesis is therefore interpretive rather than statistical. Reviews published after the search window, non-English syntheses, and grey literature may add evidence not captured here. Finally, publication and reporting bias almost certainly inflate the positive signal in a field where negative single-arm studies are rarely written and rarely published.

Conclusion

Regenerative and energy-based gynecology occupies a genuinely important clinical space and rests on defensible biological reasoning. What it does not yet possess is the evidentiary architecture of a therapeutic specialty. The most rigorous syntheses in each domain converge on the same verdict: vaginal laser is not established for GSM, radiofrequency benefit for vaginal laxity does not survive randomization, vulvovaginal PRP is promising but essentially unrandomized, intraovarian PRP improves markers without demonstrated pregnancy benefit, intrauterine PRP is positive but unstable across redundant reviews, and exosome-based therapy remains preclinical.

The field's deficit is not enthusiasm, volume, or ingenuity — it is standardization, comparator rigor, endpoint honesty, and follow-up duration. These are solvable problems, and solving them is the necessary condition for regenerative gynecology to convert plausibility into proof. Until then, the ethically correct framing for patients is unambiguous: these are investigational interventions with acceptable short-term safety profiles, uncertain benefit, and no established durability — offered, where offered at all, with explicit consent, transparent pricing, structured outcome collection, and, ideally, inside a trial.

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