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Beyond Modality Choice: Brachytherapy, Chemoradiation, Treatment Deliverability, and Survivorship in Primary Vaginal Cancer: A Critical Narrative Review

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Abstract

Primary vaginal cancer is rare, and its definitive nonsurgical treatment is supported mainly by observational cohorts, technique-specific series, and evidence extrapolated from cervical cancer. Although contemporary reviews and guidelines describe increasingly sophisticated radiotherapy, an unresolved question is how to translate associative treatment signals into decisions that remain feasible, timely, and acceptable to patients.

We undertook a purposive critical narrative synthesis of primary vaginal cancer radiotherapy literature, drawing on author-recorded PubMed searches, citation tracking, landmark historical cohorts, and contemporary guidelines. We examined concurrent chemoradiotherapy, brachytherapy access and technique, cumulative dose, treatment completion, and late morbidity while identifying cohort overlap and threats to causal interpretation.

In a National Cancer Database cohort, median overall survival was 56.2 months with concurrent chemoradiation versus 41.2 months with radiation alone. In a population registry analysis of 2,517 patients, brachytherapy exposure was associated with lower mortality after propensity matching (hazard ratio 0.77, 95% confidence interval 0.68-0.86). The 148-patient Retrospective International Image-Based Adaptive Brachytherapy for Vaginal Cancer (retroEMBRAVE) cohort reported five-year local control of 83%, alongside clinically important severe pelvic morbidity. These observations support multidisciplinary consideration of brachytherapy but cannot establish treatment-specific causal effects.

We propose an evidence-to-delivery framework linking disease phenotype, technically deliverable radiotherapy, treatment continuity, and survivorship. Its accompanying research matrix specifies the confounders, outcomes, and prospective data required to evaluate chemotherapy, brachytherapy, treatment duration, and dose-toxicity relationships. The framework is an unvalidated organising tool, not a predictive score or new clinical guideline.

Categories: Obstetrics/Gynecology, Radiation Oncology, Oncology
Keywords: brachytherapy, chemoradiotherapy, dose-volume metrics, narrative review, radiotherapy, survivorship, treatment time, vaginal cancer

Introduction And Background

Primary vaginal carcinoma is rare, limiting the feasibility of large prospective trials. Accurate classification matters: cervical or vulvar extension and vaginal recurrence after another gynaecological malignancy are distinct from a true vaginal primary. Contemporary guidance addresses different aspects of care. Chin and Damast review modern radiotherapy techniques [1]; the National Comprehensive Cancer Network (NCCN) guidelines cover multidisciplinary management [2]; the French Society of Radiation Oncology (SFRO) recommendations focus on external-beam radiotherapy (EBRT) and brachytherapy (BT) [3]; and the European Society for Radiotherapy and Oncology (ESTRO)/European Society of Gynaecological Oncology (ESGO)/European Society for Paediatric Oncology (SIOPe) guidelines provide further multidisciplinary recommendations [4].

The American Brachytherapy Society also published guidance on pelvic toxicity, surveillance, and sexual health [5]. A separate dose-response synthesis modelled tumour control across vaginal malignancies, although only 293 of its 879 patients had primary vaginal cancer [6]. Because recurrent and primary disease differ, these sources cannot be treated as interchangeable evidence.

This review addresses four questions: which patients benefit independently from concurrent chemotherapy; whether the observed BT survival advantage persists after accounting for patient selection and treatment feasibility; whether overall treatment time influences outcomes independently of disease complexity; and

how dose-volume parameters relate to local control and late morbidity. Its contribution is to examine these questions together rather than to claim a new treatment effect. The questions remain relevant despite limited case numbers: a global population-based analysis estimated 17,908 new vaginal cancer cases in 2020 [7].

Review

Review approach and evidentiary safeguards

We conducted a purposive critical narrative review, not a systematic review. The source base comprised two author-recorded PubMed searches covering publications from 2010 to 2026 using two search strings: ("vaginal cancer" OR "vaginal carcinoma" OR "vaginal neoplasm" OR "vaginal neoplasms" OR "primary vaginal cancer" OR "primary vaginal carcinoma") AND (radiotherapy OR radiation therapy OR irradiation OR chemoradiotherapy OR chemoradiation OR brachytherapy) and ("Vaginal Neoplasms"[Mesh] OR "vaginal cancer"[Title/Abstract] OR "vaginal carcinoma"[Title/Abstract] OR "primary vaginal cancer"[Title/Abstract] OR "primary vaginal carcinoma"[Title/Abstract]) AND ("Radiotherapy"[Mesh] OR radiotherap* [Title/Abstract] OR "radiation therapy"[Title/Abstract] OR chemoradiotherap*[Title/Abstract] OR chemoradiation[Title/Abstract] OR brachytherap*[Title/Abstract] OR "external beam radiotherapy" [Title/Abstract] OR "external beam radiation therapy"[Title/Abstract] OR EBRT[Title/Abstract] OR IMRT[Title/Abstract] OR "image guided radiotherapy"[Title/Abstract] OR "image-guided radiotherapy" [Title/Abstract] OR IGRT[Title/Abstract]). Backward citation tracking, selected earlier landmark reports, and contemporary professional guidelines were also used. The searches concerned primary vaginal cancer, radiotherapy, concurrent chemotherapy, brachytherapy, dose, tumour control, survival, and treatment-related morbidity. These are the principal topic concepts used to organise the review.

We prioritised reports addressing confirmed primary vaginal carcinoma and curative-intent EBRT, chemoradiotherapy, BT, clinical outcomes, treatment delivery, dosimetry, or late effects. Larger population-based and multicentre studies were used to assess broad treatment associations; smaller institutional and historical series were retained when they informed technical feasibility, disease subgroups, or late toxicity. Guidance documents were used to describe contemporary practice, not as independent comparative efficacy evidence. Studies of recurrent vaginal malignancies were distinguished from primary cancer, and mixed-population syntheses were explicitly labelled.

The synthesis was organised by clinically relevant questions rather than pooled effect estimates. We retained each study's endpoint, follow-up horizon, denominator, and design limitations. We considered treatment selection, residual confounding, treatment-era changes, and potential overlap among registry and institutional cohorts. In particular, the Wang dose-response study was treated as a secondary synthesis, not as a new independent patient cohort [6].

A complete screening log and a verified final search date were not available for independent reconstruction. We therefore cannot claim exhaustive retrieval, reproducible screening, independent duplicate selection, or a formal study-level risk-of-bias assessment. No meta-analysis or new patient-level statistical analysis was undertaken. This transparency defines the scope of the conclusions: the review critically interprets published associations and generates research questions rather than estimating pooled causal effects.

Historical radiotherapy evidence: the baseline from which modern claims depart

Institutional radiotherapy series remain clinically useful because they capture recurrence patterns and late complications across long treatment eras. In 36 patients treated in Tokyo from 1992 to 2010, Murakami and colleagues reported 2-year local control of 68.8% and argued that brachytherapy should play a central role [8], while the Ottawa experience of Samant and colleagues reported five-year disease-free outcomes in 60% of 28 curatively treated patients and severe late toxicity in 11% [9]. The historical comparison by Kucera and colleagues involved 80 patients treated with high-dose-rate brachytherapy and 110 patients treated with low-dose-rate brachytherapy. Differences in dose rate, source and afterloading technique, and treatment era complicate interpretation of this comparison [10].

These cohorts contextualise but cannot serve as unadjusted controls for modern IGABT. The five-centre Retrospective International Image-Based Adaptive Brachytherapy for Vaginal Cancer (retroEMBRAVE) cohort [11] and a subsequent single-institution MRI-guided interstitial series [12] differ in imaging approach, target definition, dose reporting, treatment combinations, and toxicity grading, and both had median follow-up under 30 months. Apparent improvements cannot be attributed to image guidance alone without controlling for other treatment-era changes.

Concurrent chemoradiation: a reproducible association, an unresolved treatment effect

Rajagopalan and colleagues analysed 8,222 irradiated patients in the National Cancer Database (NCDB), of whom 3,932 received concurrent chemoradiotherapy (CRT). Median overall survival (OS) was 56.2 months

with CRT versus 41.2 months with radiotherapy alone [13]. These groups also differed in factors associated with treatment selection, including stage, age, histology, and treating facility.

In a single-centre series of 71 patients, Miyamoto and Viswanathan reported three-year OS of 79% with CRT versus 56% with radiotherapy alone. Three-year disease-free survival (DFS) was 73% versus 43%; the multivariable association with DFS was HR 0.31 (95% CI 0.10-0.97) [14]. However, the CRT group was small and concentrated in later treatment years. Neither study isolates the causal effect of adding chemotherapy.

Smaller series suggest a similar favourable association. Dalrymple and colleagues reported one local failure and no vesicovaginal or enterovaginal fistulae among 14 patients, with nine alive and disease-free at a median follow-up of 100 months [15]. In a 53-patient series, Meixner and colleagues reported an independent association between chemotherapy and outcome on multivariable analysis [16]. Yet chemotherapy regimens, BT exposure, and treatment indications varied; the Meixner series also included postoperative radiotherapy.

Patients offered CRT may differ in performance status, tumour burden, renal function, and specialist access. Systemic-treatment decisions are partly extrapolated from cervical cancer [2]. The available evidence thus supports individualised multidisciplinary assessment, not a universal claim that chemotherapy independently improves survival in every patient with primary vaginal cancer.

Brachytherapy availability and treatment completion: distinct yet interdependent signals

In a Surveillance, Epidemiology, and End Results (SEER) analysis of 2,517 patients receiving radiation treatment, Orton and colleagues reported, in a propensity-matched cohort, median OS of 6.1 years with BT (alone or combined with EBRT) versus 3.6 years with EBRT alone; the matched mortality hazard ratio was 0.77 (95% CI 0.68-0.86) [17]. These estimates indicate a robust observational association, but registries cannot fully measure residual tumour depth, applicator feasibility, detailed target coverage, comorbidity, or reasons why BT was omitted.

In an NCDB study of 1,094 nonmetastatic patients receiving definitive CRT, Reshko and colleagues found propensity-weighted five-year OS of 62.9% with a BT boost versus 49.3% without. Among those receiving BT, treatment completion within 63 days was associated with a five-year OS of 67.8% compared with 54.5% for longer courses [18]. The 63-day distinction is an observational comparison, not a proven biological threshold. Referral pathways, implant complexity, interruptions from toxicity, and aggressive disease could jointly influence treatment duration and survival. Rajagopalan (1998-2011) and Reshko (2021) drew on overlapping NCDB diagnosis years; their cohorts must not be pooled as independent populations [13,18].

Stage, histology, tumour geometry, and dose: avoid false comparability

In the MD Anderson squamous-cancer series of 193 patients treated between 1970 and 2000 (median follow-up 137 months), Frank and colleagues reported five-year disease-specific survival of 85%, 78%, and 58% for stages I, II, and III-IVA, respectively, with corresponding pelvic-control estimates of 86%, 84%, and 71% [19]. The earlier institutional data from Chyle and colleagues (301 patients, 1953-1991) included in situ cases alongside invasive cancers and spanned a historical era with potential overlap with later reports from the same institution [20].

Hiniker and colleagues analysed 91 squamous cancers: tumour size greater than 4 cm was associated with worse overall survival and locoregional control, while patients experiencing grade 3-4 toxicity received a substantially higher median dose (82.9 versus 70.0 Gy) than those without such toxicity [21]. The Korean KROG 12-09 multicentre cohort of 138 patients reported five-year overall survival of approximately 68% and identified stage as an important prognostic factor [22]. Histology also matters: In an MD Anderson series of 26 non-DES-associated adenocarcinomas, five-year OS was 34% versus 58% and pelvic control was 31% versus 81%, compared with squamous cancers treated at the same institution over the same period [23]. These data should not be used to derive a single prognosis or dose rule across all stages and subtypes.

Contemporary IGABT: promising control, persistent dosimetric uncertainty

The international RetroEMBRAVE cohort included 148 patients treated with image-guided adaptive BT. Estimated five-year local control, DFS, and OS were 83%, 66%, and 68%, respectively, although median follow-up was 29 months [11]. These five-year estimates should therefore be read in light of the shorter median observation period. Gardner and colleagues reported two-year local control of 93% and DFS of 57% among 41 patients receiving MRI-guided high-dose-rate BT [12].

Other series provide complementary but less precise estimates. Huertas and colleagues reported three-year local control of 82% and DFS of 65% in 27 patients; 12 had late sexual morbidity, including three with grade 3 stenosis [24]. The 21-patient TRIDENT pilot reported grade 3 stenosis as its only late toxicity category

described [25]. In the 27-patient Erlangen series, estimated five-year OS and DFS were 90% and 68%, while four of 22 evaluable patients developed grade 3-4 late complications [26]. An earlier 13-patient MRI-guided series reported three-year local control of 92%, alongside fistulae and necrosis [27].

These reports differ in case mix, technique, endpoints, and follow-up. They show that high local control is achievable in selected cohorts but do not establish the independent superiority of a given applicator, dose, or imaging method. Possible overlap between institutional and multicentre cohorts also limits claims of independent replication.

Dose-volume interpretation and intracavitary versus interstitial selection

BT selection should follow the residual geometry after EBRT. Superficial, appropriately distributed disease may be compatible with an intracavitary cylinder or mould, whereas thicker, eccentric, paravaginal, or anatomically irregular targets often require interstitial needles or hybrid application. Pre- and post-EBRT examination and pelvic MRI can help define initial and residual disease, adjacent structures, and whether the proposed applicator can cover the target safely [1-4,11,24]. No fixed depth cut-off is universal across all anatomical configurations.

Modern reporting should specify EBRT technique and fractionation, BT modality, dose rate, applicator geometry, image guidance, relevant clinical target-volume definitions, and cumulative equivalent dose in 2-Gy fractions (EQD2). Target D90 describes the minimum dose delivered to 90% of a specified target volume; organ-at-risk D2cc refers to the dose received by the most exposed 2 cm^3 of a named organ. The linear-quadratic alpha/beta assumption should be stated explicitly, commonly 10 Gy for tumour and 3 Gy for late-responding normal tissues when applying a given study method [6,11,27]. Dose-volume endpoints, organ contouring, and dose summation techniques require consistency before numerical thresholds can be transported across cohorts.

In RetroEMBRAVE, an exploratory univariate association between CTV doses above 80 Gy EQD2 (α/β 10) at the time of brachytherapy and better local control in T2-T4 disease was reported [11]. Wang and colleagues reported a modelled D90 associated with 90% two-year local control of 79.0 Gy EQD2 (95% CI 75.3-96.6), but their 18-study dataset combined 293 primary vaginal cancers, 573 recurrent vaginal malignancies, and 13 unspecified cases [6]. This is a hypothesis-generating mixed-population dose-response relationship, not a validated minimum prescription for every primary vaginal tumour. Apparent dose escalation benefit must be balanced against organ-specific exposure and injury [21,27].

Late toxicity and sexual survivorship are treatment outcomes, not appendices

Pelvic injury may include vaginal stenosis, shortening or fibrosis, vaginal necrosis, dyspareunia, dryness, fistulae, urinary or bowel dysfunction, and psychological consequences. The 71-patient University of Florida cohort reported grade 3-4 complications in 23%, despite five-year locoregional control of 79%; the older 71-patient interstitial series of Tewari and colleagues also described clinically meaningful complications in 13%, including four necroses and four fistulae [28,29]. In RetroEMBRAVE, crude incidences of late grade 3 or higher urogenital, gastrointestinal, and vaginal morbidity were 8%, 3%, and 8% at a median follow-up of 29 months; these categories may overlap and should not be summed [11].

Physician-graded toxicity alone may miss aspects of sexual and functional burden reported by patients. The 2026 American Brachytherapy Society working-group report supports structured attention to vaginal and sexual health, pelvic floor symptoms, and individualised supportive strategies following gynaecological radiotherapy [5]. Prospective primary vaginal-cancer cohorts should collect baseline sexual and urinary function, repeated validated patient-reported outcome measures, clinician-assessed adverse events, and treatment-specific anatomical dose. Outcomes must be contextualised by follow-up duration, competing mortality, pre-existing symptoms, and recurrence. Table *1* summarises the principal comparative studies and their interpretive limitations.

Study	Cohort and design	Key observed outcome	Interpretive limitation
Rajagopalan et al., 2014 [13]	NCDB, 8,222 RT; 3,932 CRT	Median OS 56.2 vs 41.2 months, CRT vs RT	Confounding by treatment selection; limited dosimetry
Miyamoto et al., 2013 [14]	Single centre, n=71 (20 CRT)	3-year OS 79% vs 56%; DFS 73% vs 43%	Small nonrandomised comparison
Orton et al., 2016 [17]	SEER, n=2,517	Matched mortality HR 0.77 (95% CI 0.68–0.86) with BT	BT technical eligibility incompletely observed
Reshko et al., 2021 [18]	NCDB, n=1,094 definitive CRT	5-year OS 62.9% vs 49.3% with vs without BT; treatment time signal	Partly overlapping registry era; residual confounding
Hiniker et al., 2013 [21]	Single centre, n=91 SCC	Tumour >4 cm adverse; high dose associated with severe toxicity	Historical planning and nonrandom dose assignment
Chang et al., 2016 [22]	Multicentre, n=138	5-year OS approximately 68%; stage prognostic	Mixed technique and prognostic heterogeneity
Westerveld et al., 2021 [11]	Five centres, n=148 IGABT	5-year LC 83%, DFS 66%, OS 68%	No controlled modality comparator
Gardner et al., 2025 [12]	MRI-guided HDR, n=41	2-year LC 93%; DFS 57%	Small, selected contemporary cohort
Huertas et al., 2018 [24]	IGABT, n=27	3-year LC 82%; 12 patients with late sexual morbidity	Variable toxicity capture; possible overlap
Merten et al., 2024 [26]	Single centre, n=27	5-year OS 90%; DFS 68%	Small sample; toxicity denominator, n=22

TABLE 1: Comparative primary evidence for definitive radiotherapy in vaginal cancer

Cohorts and endpoints must not be pooled.

BT, brachytherapy; CRT, chemoradiotherapy; DFS, disease-free survival; LC, local control; OS, overall survival; NCDB, National Cancer Database; SEER, Surveillance, Epidemiology, and End Results.

A four-domain evidence-to-delivery framework: an original organising synthesis

We propose a four-domain evidence-to-delivery framework (Table *2*) that treats observed survival signals as products of interacting clinical, technical, organisational, and functional factors. This is a conceptual synthesis derived from the reviewed literature; it has not been prospectively validated or shown to improve outcomes. Its purpose is to make the decision and its potential biases visible, rather than to replace multidisciplinary recommendations.

Domain	Minimum pre-treatment questions	Decision or reporting output
1. Disease phenotype	Is this a true primary? What are histology, FIGO stage, dimensions, nodal status, and distal-vaginal extent?	Explicit treatment eligibility and tumour-risk profile
2. Technical deliverability	What residual geometry requires intracavitary, hybrid, or interstitial BT? Can target D90 and organ-specific D2cc be achieved?	Early expert BT plan; documented achievable dose and trade-offs
3. Treatment continuity	Are MRI, implant expertise, chemotherapy fitness, transport, and BT slots arranged before EBRT completion?	Record start-to-end time, interruption causes, and actual treatment completion
4. Survivorship	What are baseline sexual, vaginal, bladder, bowel, and patient-reported symptoms?	Report late toxicity and meaningful function alongside control and survival

TABLE 2: Four-domain evidence-to-delivery framework (proposed; not validated)

FIGO: International Federation of Gynecology and Obstetrics; BT: brachytherapy; D90: dose received by 90% of the target volume; D2cc: dose received by the most exposed 2 cm^3; MRI: magnetic resonance imaging; EBRT: external beam radiotherapy.

The causal pathway is clinically important. Disease phenotype influences both prognosis and BT eligibility; technical deliverability can determine whether an adequate boost is possible; organisational delays may reflect implant complexity, toxicity, or referral access; and dose intensity interacts with later function. Comparing "BT versus no BT" or "short versus long treatment" without measuring the upstream drivers conflates treatment effect with deliverability and selection. The framework deliberately joins radiotherapy planning with treatment completion and patient-centred outcomes, unlike a modality-focused summary.

Why this review adds to contemporary guidance and other syntheses

The 2026 Chin-Damast narrative review clarifies modern RT and adaptive BT technique [1]; the 2026 NCCN guidance and 2023-2025 European recommendations provide multidisciplinary treatment recommendations [2-4]; the 2026 ABS working-group report concentrates on surveillance and pelvic/sexual toxicity management across gynaecological malignancies [5]; and Wang and colleagues quantify a pooled dose-control association from heterogeneous primary and recurrent vaginal cancer populations [6]. Our narrower contribution is the interpretive interface: how comparative RT/CRT/BT signals, feasibility of dose delivery, clock time, and patient-centred harm should be analysed together without claiming unsupported causal certainty.

The framework is intentionally falsifiable: its proposed value could be tested by whether prospective registries capture the key confounders, record the timing of each treatment component together with the documented reasons for any prolongation, and yield more interpretable comparative treatment effects. We make no claim of being the first review of primary vaginal cancer, the first dose framework, or the first discussion of survivorship. Table *3* summarises the points that this review highlights beyond existing publications from 2023 to 2026.

Existing contribution	Principal emphasis	Additional question examined here
Chin and Damast 2026 [1]	Modern RT and adaptive-BT technique	Biases in comparative survival claims
Abu-Rustum et al. 2026 [2]; Nout et al. 2023 [4]	Multidisciplinary treatment guidance	Unresolved treatment-effect questions
Quick et al. 2026 [5]	Pelvic toxicity and sexual health	Vaginal-cancer-specific dosimetry and PROs
Wang et al. 2024 [6]	Mixed primary/recurrent dose–control model	Transferability of modelled D90 to primary disease

TABLE 3: What this review contributes beyond existing 2023–2026 publications

RT: radiotherapy; BT: brachytherapy; PROs: patient-reported outcomes; D90: dose received by 90% of the target volume.

Unresolved causal questions: a feasible rare-cancer research agenda

Table *4* translates four recurring uncertainties into defined comparisons and prospective measurement

priorities. These are proposed research designs, not analyses performed in this review. In a rare cancer, carefully coordinated multicentre registries with pre-specified adjustment and consistent core outcomes may be more realistic than conventional randomised trials. Such analyses should explicitly account for calendar time, centre-level expertise, histology, nodal disease, comorbidity, prior pelvic treatment, and reasons for omission of indicated modalities.

Unresolved question	Essential adjustment variables	More informative future analysis or outcome
Who benefits independently from concurrent chemotherapy?	Stage, tumour burden, performance status, renal fitness, histology, RT intensity, treatment centre	Target-trial emulation of eligible patients; predefined survival and toxicity endpoints
Does BT improve survival beyond selection for suitable geometry and access?	Residual depth/volume, tumour site, contraindications, referral centre, EBRT dose, BT non-use reasons	Prospective BT-eligibility cohort; propensity/causal methods with LC, OS and late toxicity
Does shorter overall treatment time independently improve outcome?	Initial plan, implant complexity, toxicity, patient frailty, interruptions, facility capacity	Time-dependent analysis of preventable versus clinical delays; recurrence and treatment completion
Which D90 and organ-specific D2cc predict control with acceptable morbidity?	Primary vs recurrent status, stage, dose summation, target definition, baseline function, follow-up	Individual-patient dosimetry with prospective vaginal/sexual PROs and adjudicated fistula/necrosis

TABLE 4: Priority comparative questions and study designs

RT: radiotherapy; BT: brachytherapy; EBRT: external beam radiotherapy; LC: local control; OS: overall survival; D90: dose received by 90% of the target volume; D2cc: dose received by the most exposed 2 cm^3; PROs: patient-reported outcomes.

Practical multidisciplinary translation

The proposed implementation is a short pre-treatment BT deliverability discussion: (i) confirm primary tumour classification and map baseline extent; (ii) define whether an intracavitary, interstitial, or combined implant is technically appropriate; (iii) anticipate chemotherapy fitness, image-guidance requirements, and capacity constraints; (iv) schedule BT assessment early rather than after an EBRT delay has developed; and (v) document baseline functional symptoms and survivorship support. Every recommendation must remain subject to current guidance, multidisciplinary clinical judgement, and patient preference [2-5].

At treatment completion, the record should distinguish planned from delivered EBRT and BT, provide the cumulative dose-volume summary using consistent target and organ definitions, state reasons for chemotherapy omission and schedule interruptions, and initiate structured late-effect follow-up. This approach promotes auditability and patient-centred discussion; its effects on survival or toxicity have not yet been tested.

Strengths and limitations

This review integrates historical disease-control and toxicity studies, large observational treatment comparisons, modern IGABT experience, contemporary national and European guidelines, a dose-response secondary synthesis, and a 2026 survivorship consensus. It distinguishes non-overlapping clinical questions and explicitly prevents double-counting of NCDB, potential SEER, and sequential institutional populations. The comparative tables preserve design limitations and endpoints rather than providing artificial pooled statistics.

Important limitations remain. Literature identification was purposive and PubMed-centred. Exact search strings, a complete screening record, and a verified final search date were not available; independent dual screening and formal study-level risk-of-bias assessment were not undertaken. Neither the proposed four-domain framework nor its decision pathway has undergone Delphi consensus, prospective testing, or external validation. In some cohorts, full technical or subgroup detail requires consultation of original full texts; not every historical series permits consistent adjustment for disease severity and treatment technique. No original patient data were obtained, and the causal questions presented are hypotheses for future work rather than findings from new statistical analyses.

Conclusions

Brachytherapy remains an important component of definitive radiotherapy for suitable primary vaginal cancers, and observational comparisons associate both BT and selected use of concurrent chemotherapy with improved outcomes. Contemporary image-guided techniques enable individualised target coverage, but

these studies do not establish the independent causal contribution of each modality. The importance of dose delivery, coordinated treatment completion, anatomical suitability, and long-term pelvic function should inform patient-specific decisions.

This review offers a four-domain evidence-to-delivery framework that connects disease phenotype, technical deliverability, treatment continuity, and survivorship. Its principal contribution is an explicit agenda for separating treatment effect from treatment selection while measuring patient-centred benefit and harm. Prospective multicentre reporting with consistent primary-site eligibility, dosimetry, completion metrics, and functional outcomes is needed before more precise causal claims or universal dose thresholds can be justified.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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