

NARRATIVE REVIEW

Advancing equity in endometrial cancer: A narrative synthesis using a cluster-informed framework for resource-stratified implementation

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Abstract

Endometrial cancer incidence and mortality are rising globally, disproportionately affecting health systems facing diagnostic, therapeutic, and survivorship constraints. Rapid innovations—including the International Federation of Gynecology and Obstetrics (FIGO) 2023 staging, molecular classification, sentinel lymph node (SLN) mapping, evolving adjuvant strategies, immunotherapy, and digital tools—risk exacerbating inequities if implementation mismatches system readiness. This narrative review synthesizes key trials, international guidelines, and high-impact implementation studies published between 2010 and September 2025. We summarize contemporary evidence across staging, molecular pathology, imaging, surgery, radiotherapy, systemic therapy, survivorship, equity, and artificial intelligence (AI), translating this into a pragmatic, resource-stratified framework. A previously published principal-component-based structural-readiness clustering model encompassing 68 countries is applied—but not re-derived—to illustrate how health-system capacity shapes access to diagnostics, treatment, and innovation. Persistent gaps include limited availability of universal mismatch repair (MMR) and p53 immunohistochemistry, variable adoption of standardized SLN mapping, uneven radiotherapy access, restricted use of immunotherapy for mismatch-repair deficient (dMMR)/microsatellite instability high (MSI-H) tumors, and fragmented survivorship care. A minimum–core–optimal implementation ladder is proposed to guide diagnostic, surgical, radiotherapeutic, systemic-therapy, and survivorship priorities across varying resource levels. AI-supported quality assurance is discussed alongside essential requirements of local validation, bias mitigation, and robust governance. Rather

than generating new empirical data, this review employs a cluster-informed, equity-oriented lens, applying previously validated system-level typologies to contextualize implementation gaps and support context-sensitive guideline adaptation.

KEYWORDS

cluster analysis, endometrial neoplasms, health equity, health systems, implementation science, molecular classification, radiotherapy, sentinel lymph node mapping

1 | INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy worldwide, with rising incidence—particularly in low- and middle-income countries and among younger women.^{1,2} Parallel increases in high-risk histologic subtypes amplify the clinical and health-system burden, creating new demands for coordinated survivorship care. Noncancer causes of death represent a major competing mortality risk, reinforcing the need to integrate survivorship and cardiometabolic management early in the care pathway.³

Over the past decade, multiple innovations have reshaped endometrial cancer management. The 2023 International Federation of Gynecology and Obstetrics (FIGO) revision integrates histologic and molecular prognostic factors to refine surgical decision making.⁴ Molecular classification has transformed risk assessment and therapeutic planning, identifying biologically distinct subgroups with divergent prognoses and treatment sensitivities.⁵ Sentinel lymph node (SLN) mapping, when performed under standardized ultra-staging protocols, reduces morbidity without compromising staging accuracy.⁶ These advances have recently been summarized in contemporary international updates on corpus uteri cancer care.⁷

Systemic therapies have also evolved. Immune checkpoint inhibitors (ICIs) markedly improve outcomes in mismatch-repair-deficient and microsatellite-instability-high tumors, and smaller—but clinically meaningful—benefits have also been observed in selected mismatch-repair proficient (pMMR) tumors.^{8,9} However, access to ICIs, advanced imaging, and precision diagnostics remains uneven due to infrastructure limitations, cost, reimbursement constraints, and persistent underrepresentation of low- and middle-income countries in clinical trials.¹⁰

Despite broad acknowledgement of the value of FIGO 2023 staging, molecular taxonomy, and SLN mapping, real-world implementation remains inconsistent. Many health systems lack routine immunohistochemistry (IHC), expertise for interpreting POLE variants of uncertain significance, or consistent pathology support for subclonal p53 patterns.^{11–14} In such contexts, proportionate precision—beginning with universal IHC for mismatch repair (MMR) and p53, with selective use of POLE sequencing where feasible—captures most prognostic value at minimal cost. Integrating molecular subtyping with the 2023 FIGO schema may refine adjuvant decision

making.¹⁵ Survivorship care remains fragmented, with limited integration of preventive, psychosocial, and primary-care pathways despite high comorbidity burden.¹⁶

Latin America exemplifies several “gray zones” between guideline-recommended and context-feasible care.¹⁶ Bridging these divides requires frameworks that align scientific innovation with health-system readiness, balancing diagnostic sophistication with implementability. Structural readiness—including diagnostic capacity, workforce, governance, and financing—is essential to ensure that advances in staging, molecular profiling, and systemic therapy narrow rather than widen global disparities.

To our knowledge, no prior review has integrated FIGO 2023 staging, molecular risk stratification, sentinel lymph node mapping, radiotherapy, systemic therapy, survivorship, and emerging artificial intelligence (AI) tools within a single implementation-oriented framework grounded in structural health-system readiness. This distinction is important because the challenge in endometrial cancer care is no longer only defining best practice, but determining how best practice can be adopted progressively and equitably across heterogeneous settings. Opportunities exist for AI to support pathology, imaging, and quality assurance; however, region-specific validation, bias mitigation, and robust governance are mandatory before deployment.^{17,18}

Importantly, most contemporary guidelines define optimal standards of care under ideal conditions, but provide limited guidance on how to prioritize implementation when diagnostic capacity, molecular testing, radiotherapy access, and systemic therapies are unevenly available. This creates a persistent translational gap between evidence-based recommendations and real-world feasibility. Without an explicit implementation framework, innovation may inadvertently widen disparities rather than reduce them. Therefore, the purpose of this review is not simply to restate existing guidelines, but to operationalize their equitable implementation by aligning contemporary advances in endometrial cancer care with structural health-system readiness across diverse settings.

The aim of the present study was to synthesize key clinical evidence and international guidelines and to apply a previously published structural-readiness clustering framework to propose a pragmatic, resource-stratified approach for equitable implementation of contemporary endometrial cancer care.

2 | METHODS

2.1 | Study design and scope

The present study is a narrative review integrating pivotal clinical trials, international guidelines, observational studies, and implementation science literature published between 2010 and September 2025. Although not a systematic review, the evidence exploration was informed by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles to enhance transparency, and the study-selection process is summarized using a PRISMA-style flow diagram. No protocol was prospectively registered. Selection of the 60 included studies was based on relevance to core implementation domains, geographic representativeness, and methodological rigor, with at least one high-quality guideline or clinical trial included per domain. The objective was not to generate new empirical data but to synthesize contemporary evidence across staging, pathology, molecular classification, imaging, surgery, radiotherapy, systemic therapy, survivorship, equity, and AI, and to situate these components within an established structural-readiness framework. Key domains were defined a priori based on major international guidelines and landmark trials.^{11,12}

Because this review was designed to inform implementation rather than to perform pooled quantitative synthesis, evidence was hierarchically prioritized within each domain. Preference was given to contemporary international guidelines, practice-changing randomized trials, high-quality validation studies, and implementation-relevant observational evidence. Studies were selected not only according to methodological rigor, but also according to their

relevance for feasibility, scalability, and equity-sensitive implementation. Lower-priority or redundant studies were not retained if they did not materially alter implementation implications.

2.2 | Literature exploration

To ensure comprehensive coverage, structured searches were conducted in PubMed/MEDLINE, Scopus, and Web of Science for January 2010–September 2025. Search terms combined Medical Subject Headings (MeSH)—*endometrial neoplasms*, *neoplasm staging*, *molecular diagnostic techniques*, *sentinel lymph node biopsy*—with free-text terms related to immunotherapy, minimally invasive surgery, radiotherapy, survivorship, equity, and AI. Boolean strings were adapted across databases (Table S1).

The search identified 24 731 records. After removing 7689 duplicates, 17 038 unique citations were screened, and 127 full-text articles were assessed. Ultimately, 60 studies were prioritized based on methodological rigor, relevance to contemporary practice, geographic representativeness, and alignment with at least one predefined review domain. This approach maximizes transparency and breadth while maintaining the methodological integrity of a narrative review (Figure 1). Within each domain, studies were interpreted according to both evidentiary strength and implementation relevance, allowing the synthesis to distinguish between interventions that are evidence-supported yet difficult to operationalize, and those that represent high-yield, scalable priorities across resource settings.

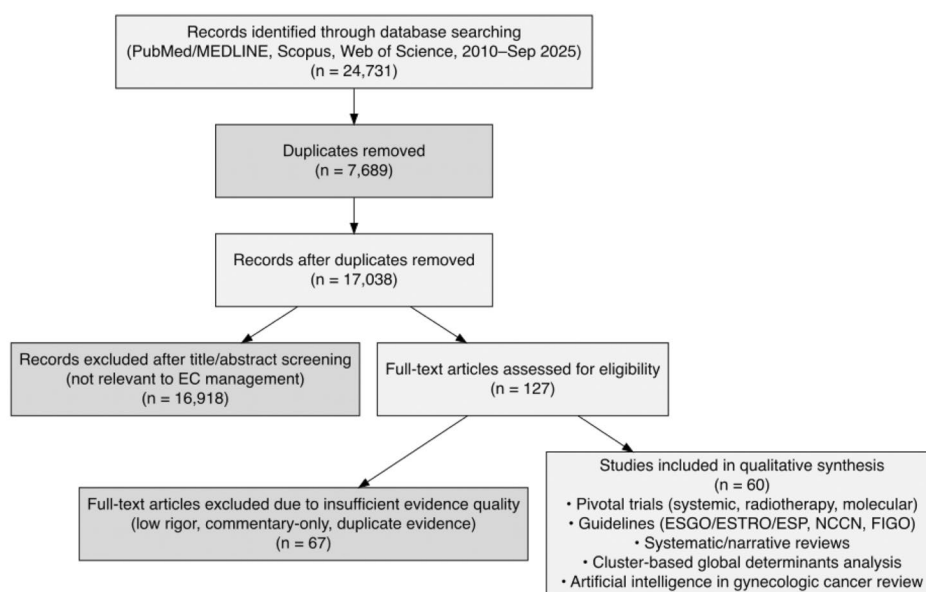


FIGURE 1 Flow diagram summarizing the evidence exploration process. A structured exploration of the literature (2010–September 2025) identified 24 731 records across PubMed/MEDLINE, Scopus, and Web of Science. After removal of duplicates ($n = 7689$), 17 038 unique records were screened. A total of 127 full-text articles were assessed for eligibility, and 60 studies were included based on methodological rigor, relevance to contemporary practice, and alignment with predefined review domains. Because this is a narrative review, the diagram is PRISMA-style and used solely to enhance transparency.

2.3 | Use of artificial intelligence tools

ChatGPT (OpenAI) was used exclusively to support language refinement and to assist in the preliminary organization of search outputs. AI tools did not influence study selection, data interpretation, or the formulation of recommendations. All extraction, appraisal, and synthesis were independently conducted and verified by the authors.

2.4 | Clustering framework

A previously published principal-component-based structural-readiness clustering model—originally developed across 68 countries—was used as a contextual analytic lens.¹³ This typology was not re-derived or statistically updated in the present review. Instead, the original cluster characteristics—reflecting diagnostic capacity, workforce availability, financing, governance, and population health—were applied descriptively to interpret disparities in access to staging, molecular testing, surgery, radiotherapy, systemic therapy, and survivorship care. Table S2 summarizes country-cluster assignments and methodological elements from the original study.

No new clustering or statistical reanalysis was conducted. While the original framework underwent internal and external validation using several multivariate indicators, its use here is purely illustrative and represents a major limitation. Future work should consider endometrial cancer-specific data and contemporary revalidation to refine these structural-readiness archetypes.¹³ Cluster-specific implementation priorities proposed in this review are therefore conceptual, reflecting expert synthesis of the literature rather than outputs of new statistical modeling. Importantly, the cluster framework is not presented as a disease-specific predictive model, but as a structured implementation heuristic. Its purpose is to contextualize which components of contemporary endometrial cancer care are realistically adoptable, scalable, or deferrable across different health-system environments. In this sense, it supports decision making by linking evidence-based recommendations to structural feasibility rather than replacing clinical evidence.

In accordance with journal policy, materials required for independent methodological evaluation will be provided upon request.

2.5 | Evidence synthesis across key domains

2.5.1 | FIGO 2023 staging

Evidence from key validation studies illustrates that the 2023 FIGO revision represents a critical shift toward precision oncology, integrating histologic, surgical, and molecular parameters.⁴ Reliance on morphology alone is insufficient for accurate prognostication or therapeutic planning. Validation studies indicate improved risk discrimination, especially for p53-abnormal and POLE-ultramutated

subtypes, with external reports showing generally consistent prognostic performance.^{14,15,19–21} FIGO 2023 can modify adjuvant therapy allocation when compared with FIGO 2009.^{22,23} However, performance diminishes where molecular data, subspecialist pathology, or ultrastaging capabilities are limited.^{24–26} Reflex immunohistochemistry (p53 and MMR) on diagnostic biopsy represents a scalable strategy to front-load risk information, with POLE sequencing reserved for referral hubs in a minimum-core-optimal adoption ladder.^{11,12,24} Thus, while FIGO 2023 enhances prognostic accuracy, its full implementation requires tailored strategies that account for diagnostic infrastructure, workforce expertise, and resource variability across health systems. Importantly, the incremental clinical value of FIGO 2023 depends on access to pathology quality assurance, molecular testing, and standardized staging workflows; where these are absent, partial adoption may create classification complexity without equivalent gains in care quality.

From an implementation perspective, a phased adoption pathway is essential. At the minimum level, universal MMR and p53 immunohistochemistry provides the highest diagnostic yield at the lowest complexity and should be prioritized. At the core level, POLE sequencing should be incorporated selectively, primarily when results are expected to alter adjuvant decision making, and ideally through referral or centralized laboratory pathways. At the optimal level, full molecular classification can be integrated into routine care. This stepwise model allows health systems to progressively adopt precision oncology without compromising feasibility or equity.

2.6 | Diagnostic imaging and cost-effective pathways

Accurate imaging informs staging, surgical planning, and adjuvant treatment decisions. Standardized transvaginal ultrasonography (TVUS) is the most scalable and widely available modality and, when performed using structured International Endometrial Tumor Analysis (IETA) criteria, can map tumor extension and predict high-risk features with good discriminatory ability.^{27,28} Magnetic resonance imaging (MRI) offers superior soft-tissue resolution for myometrial, cervical, and nodal assessment,²⁹ with updated European Society of Urogenital Radiology (ESUR) recommendations aligning MRI interpretation with FIGO 2023.¹⁹ Positron emission tomography/computed tomography (PET/CT) improves detection of distant disease but is best reserved for indeterminate or metastatic presentations.¹⁹

Diagnostic pathways also play a critical role in implementation. Endometrial sampling—whether through office-based biopsy or hysteroscopy-guided approaches—remains fundamental for timely diagnosis, while hysteroscopic evaluation may improve diagnostic precision in selected settings where expertise and infrastructure are available.

From an equity perspective, a triage pathway prioritizing transvaginal ultrasonography for all patients,¹⁹ MRI for indeterminate or

intermediate/high-risk features, and PET/CT only in select ambiguous/advanced scenarios^{30–32} maximizes diagnostic reach. Training, structured reporting, telementoring, and AI-assisted interpretation may elevate diagnostic consistency where subspecialist radiology is limited.^{10,33}

2.7 | Molecular classification (TCGA/ProMisE)

Molecular classification delineates four biologically distinct subgroups—POLE-ultramutated, mismatch-repair deficient (dMMR), p53-abnormal, and no specific molecular profile (NSMP)—refining risk stratification beyond morphology.⁵ The ProMisE algorithm operationalizes this using sequential immunohistochemistry for MMR and p53, followed by targeted POLE sequencing.^{17,34} Integration into PORTEC-3 confirmed differential prognostic patterns and informed selective adjuvant approaches.^{22,26} Key implementation challenges include interpretation of variants of uncertain significance in POLE,³⁵ the clinical relevance of subclonal p53 staining,^{36,37} and explicit handling of multiple-classifier tumors to avoid misclassification.³⁶

Universal MMR and p53 immunohistochemistry offers the highest diagnostic yield at lowest cost, capturing most prognostic and therapeutic information even where sequencing is unavailable. Regional slide-sharing networks and consensus pathology rounds strengthen quality assurance and reduce interpretive variability at minimal cost. Although molecular classification substantially improves biologic stratification, its real-world value depends not only on assay availability but also on interpretive consistency, referral pathways, specimen quality, and whether results can meaningfully alter treatment decisions in a given setting. In this context, immunohistochemistry-based classification (MMR and p53) represents the most feasible and scalable minimum implementation layer across diverse settings, with additional molecular testing incorporated selectively as resources and referral capacity allow.³⁸

In addition, hormone receptor status (estrogen and progesterone receptors) may provide complementary information in selected clinical contexts, particularly in relation to endocrine therapy, although its role within implementation frameworks remains context-dependent and less standardized across settings.

2.8 | Surgical management and sentinel lymph node mapping

Sentinel lymph node (SLN) mapping has supplanted full lymphadenectomy in most apparent early-stage endometrial cancers. Trials such as FIRES and SHREC demonstrated high sensitivity, excellent reproducibility, and significantly reduced morbidity.^{6,39} Meta-analyses confirm these findings.⁴⁰ Indocyanine-green (ICG)-guided mapping improves bilateral detection in low- and intermediate-risk disease,⁴¹ and professional societies now endorse SLN as standard practice.⁴² If mapping fails unilaterally,

side-specific lymphadenectomy is recommended, with ultrastaging to enhance micrometastasis detection. SLN metastasis size, histologic type, and tumor biology correlate with non-sentinel involvement.⁴²

Dual-tracer techniques, robotic platforms, and enhanced recovery after surgery (ERAS) programs optimize perioperative outcomes.⁴³ In low- and middle-income settings, phased training pathways and regional pathology ultrastaging hubs facilitate safe adoption. Prospective work comparing labeling and injection techniques—including ICG—supports feasibility in early-stage disease.⁴¹

2.9 | Adjuvant therapy

PORTEC-2 established vaginal brachytherapy as standard for high-intermediate risk disease,^{44,45} while PORTEC-3 suggested that any incremental benefit from combined chemoradiation appears concentrated in p53-abnormal tumors; however, the trial was not powered for molecular subgroup analyses, so these findings should be regarded as hypothesis-generating rather than definitive.²³ Ongoing RAINBO and PORTEC-4a trials are refining escalation/de-escalation strategies using integrated molecular and clinical risk.^{46,47} Under the updated FIGO 2023 staging and European Society of Gynecological Oncology (ESGO)–European Society for Radiotherapy and Oncology (ESTRO)–European Society of Pathology (ESP) 2025 guidelines, many patients previously categorized as high-intermediate risk in PORTEC-2 are now considered intermediate risk, whereas contemporary high-intermediate and high-risk profiles—particularly when adverse molecular features coexist—often warrant pelvic external-beam radiotherapy rather than vaginal brachytherapy alone.¹²

Persistent inequities arise where radiotherapy, molecular testing, and subspecialist pathology remain limited.⁴⁸ Universal immunohistochemistry for MMR and p53 and equitable access to vaginal brachytherapy constitute essential investments across all settings. While vaginal brachytherapy is an evidence-based standard for selected intermediate-risk patients,^{44,45} it cannot replace pelvic or extended-field external beam radiation therapy (EBRT) in high-risk cases due to its limited depth and field of coverage. Practical capacity-expansion strategies include selective use of hypofractionation and prioritization of vaginal brachytherapy, particularly in health systems with constrained linear-accelerator capacity. However, hypofractionated regimens—though increasingly explored and feasible in gynecologic malignancies including endometrial cancer—lack robust long-term data on late toxicities and quality-of-life outcomes in the adjuvant setting^{49,50} and cannot yet be recommended as a routine substitute for standard-fractionation pelvic or extended-field EBRT outside clinical trials or carefully monitored programs. These limitations underscore the need for cautious, context-adapted implementation and structured post-treatment follow-up. Cost-effectiveness analyses reinforce the value of intravaginal brachytherapy in high-intermediate-risk disease, particularly in resource-limited settings where standard fractionation EBRT may be unaffordable or inaccessible.⁴⁹ Patterns of recurrence

in patients omitted from postoperative radiotherapy further highlight the importance of appropriate risk stratification and vigilant surveillance.⁵¹

2.10 | Systemic therapy in advanced or recurrent disease

The RUBY and NRG-GY018 trials established immune checkpoint inhibitors plus chemotherapy as new standards, particularly for dMMR/MSI-H tumors.^{8,9} Benefits in pMMR/MSS tumors appear more modest and heterogeneous across available trials.^{8,9} Cost remains a major barrier in low- and middle-income countries, and even high-income systems increasingly evaluate cost-effectiveness.⁵²

Equitable implementation requires universal MMR/MSI testing, differential pricing, health-technology assessment aligned with local cost-utility thresholds, and multidisciplinary adjudication—particularly for pMMR/MSS disease—to ensure appropriate stewardship. Managed-access pathways and outcome-based reimbursement schemes may help bridge affordability gaps.

Accordingly, the main implementation challenge is no longer whether these agents are clinically active, but whether health systems can adopt them in a way that is affordable, selective, and equity-preserving.

2.11 | Survivorship and long-term care

Non-cancer mortality—including cardiovascular and metabolic disease—now surpasses cancer-specific mortality in many endometrial cancer cohorts.^{2,3,53} Survivorship must be integrated early, focusing on cardiometabolic health, physical activity, psychological wellbeing, and functional status. Body-composition metrics and transcriptomic signatures further refine long-term risk.⁵³ Interventions that reduce sedentary time and increase structured physical activity are associated with improved overall survival.⁵⁴

Digital health tools, remote monitoring, and structured follow-up pathways offer scalable survivorship solutions in resource-constrained systems.¹⁰ Embedding survivorship, geriatrics, and palliative care within multidisciplinary discussions aligns treatment decisions with physiologic reserve and patient priorities.

3 | DISCUSSION

This narrative synthesis does not generate new empirical data. Rather, its primary contribution lies in translating multi-domain

evidence into an implementation-oriented, equity-focused framework. By applying a previously validated structural-readiness lens, this review moves beyond descriptive synthesis to identify context-sensitive pathways for adopting, sequencing, and prioritizing endometrial cancer interventions across heterogeneous health systems.

3.1 | Summary of main results

To contextualize inequities in endometrial cancer outcomes, we applied a previously validated structural clustering framework encompassing 68 countries.¹³ Developed through principal component analysis of socioeconomic, healthcare, and environmental indicators, this typology classifies countries into four readiness archetypes: (C1) Foundational health and social development, (C2) comprehensive socioeconomic advancement, (C3) emerging environmental and healthcare focus and (C4) advanced economic and public health integration.

Unlike income-based categories, these clusters reflect structural determinants influencing diagnostic capacity, access to treatment, survivorship pathways, and innovation uptake. The framework allows interpretation of translational gaps by aligning “proportionate precision”—the adaptation of diagnostic and therapeutic intensity to local readiness—with real-world feasibility.^{11–13}

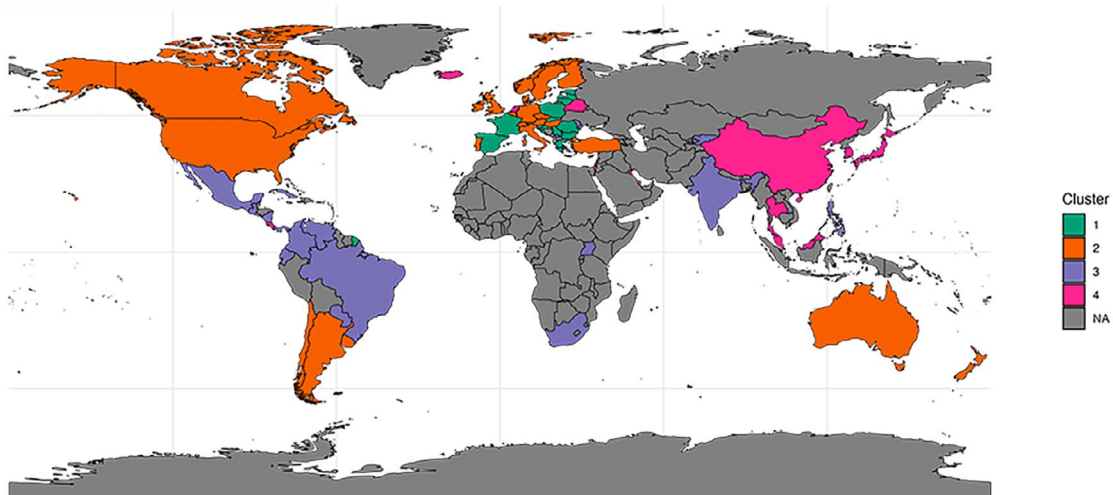
3.2 | Results in the context of published literature

Global patterns of endometrial cancer incidence and mortality (Figure 2) illustrate the complexity of implementation. Higher-incidence regions (C2, C4) frequently reflect enhanced detection capacity, while the steepest mortality gradients appear in clusters with delayed diagnosis and limited treatment access (C1, C3). Age-stratified mortality data (Figure 3) confirm disproportionately higher deaths in older women in C1 and C3, consistent with underdiagnosis, late-stage presentation, and restricted systemic therapy availability. These patterns underscore that the principal implementation challenge is not simply the availability of innovation, but the uneven capacity to absorb and operationalize it. In this context, guideline concordance cannot be assumed to translate into equitable outcomes unless delivery systems are structurally capable of supporting diagnosis, treatment, and longitudinal survivorship care.

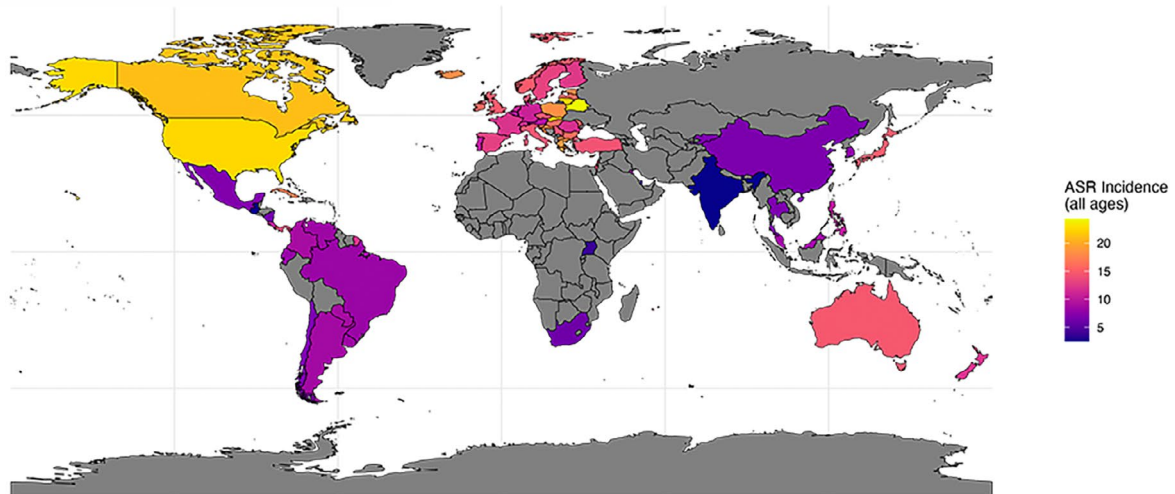
While recent updates have summarized the rapidly evolving standards of endometrial cancer care, including molecularly informed staging and treatment, less attention has been paid to how these advances can be progressively and equitably implemented

FIGURE 2 Global distribution of endometrial cancer burden across structural clusters. (a) Structural cluster assignment for 68 countries (C1–C4) based on previously published principal component analysis of diagnostic capacity, workforce density, financing, governance, and environmental indicators. (b) Age-standardized incidence rates of endometrial cancer (all ages). (c) Age-standardized mortality rates. Clusters with stronger diagnostic capacity (C2, C4) show higher incidence; mortality disparities are steepest in resource-constrained settings (C1, C3).

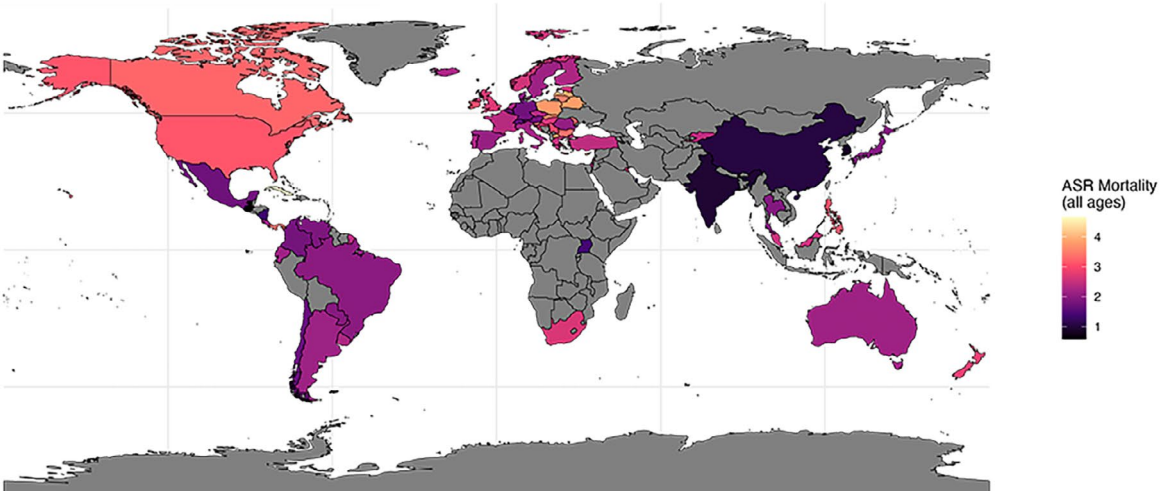
(a) Structural clustering (68 countries)



(b) ASR Incidence Endometrial cancer (all ages, x 100 000 women)



(c) ASR Mortality Endometrial cancer (all ages, x 100 000 women)



Endometrial Cancer: Age-Specific ASR Incidence (a) and Mortality (b) 68 countries stratified into four clusters

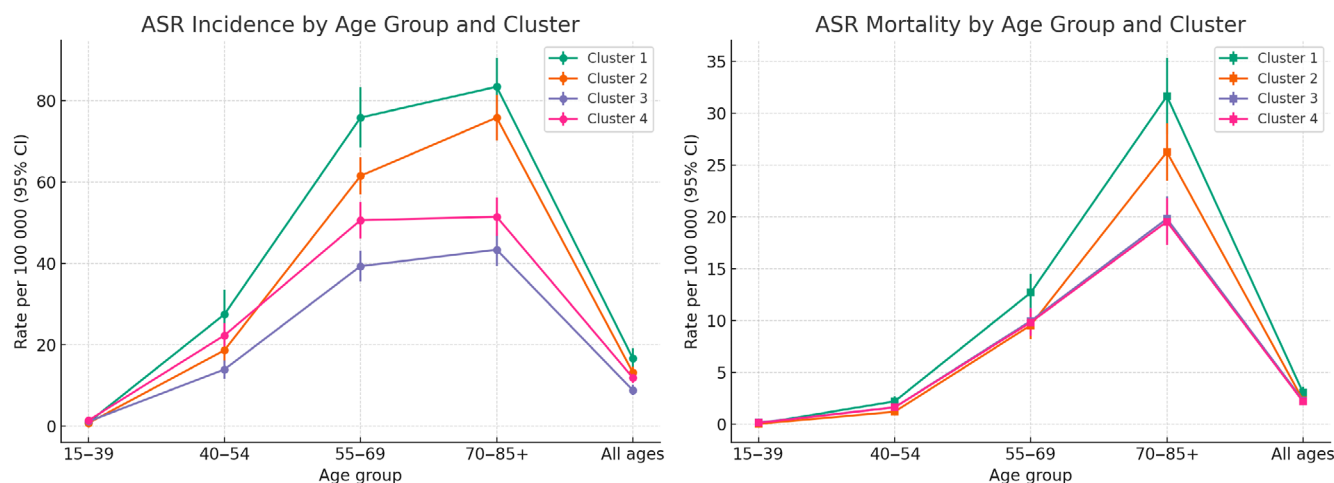


FIGURE 3 (a) Age-specific incidence and (b) mortality of endometrial cancer across four structural clusters. The figure illustrates how older women in clusters with limited diagnostic and treatment capacity (C1, C3) experience disproportionate mortality relative to incidence—suggesting underdiagnosis, delayed presentation, and restricted access to adjuvant or systemic therapies. Error bars represent 95% confidence intervals.

across structurally diverse settings.⁷ Accordingly, the central contribution of this review is not to redefine standards of care, but to clarify how those standards may be prioritized and phased according to structural readiness.

Tables 1 and 2 were designed to translate the evidence reviewed into practical implementation priorities by distinguishing between interventions that are foundational, scalable, or context-dependent across different structural settings. These tables are intended as implementation-support tools rather than prescriptive clinical guidelines, and are meant to facilitate context-sensitive prioritization across structurally heterogeneous settings. Cluster-specific implementation priorities (Table 1; Figure 4) provide a pragmatic roadmap:

- C1: Ensure biopsy access; implement universal MMR/p53 immunohistochemistry; expand radiotherapy, especially brachytherapy.
- C2: Consolidate sentinel lymph node (SLN) mapping; use selective molecular profiling; optimize cost-conscious systemic therapy.
- C3: Reduce diagnostic delay; strengthen survivorship pathways; expand systemic therapy access and pathology infrastructure.
- C4: Integrate full molecular testing; broaden immunotherapy access; embed survivorship and AI-enabled quality assurance.

To further operationalize structural readiness into actionable decision-making, this framework can be conceptually mapped to the minimum-core-optimal resource-stratified model presented in Table 2. In this conceptual mapping, Cluster 1 corresponds to the Minimum tier, where essential investments—such as universal MMR/p53 immunohistochemistry, biopsy access, and transvaginal ultrasound—are prioritized. Cluster 2 aligns with the Core tier, representing settings that can selectively expand capacity toward

MRI, sentinel lymph node mapping, and strategic use of molecular profiling. Cluster 3 bridges the Core and Optimal tiers, enabling broader access to systemic therapies, molecular diagnostics, and structured survivorship care. Cluster 4 approximates the Optimal tier, featuring universal integration of molecular classification, immunotherapy, advanced radiotherapy, and adoption of digital innovations—including AI for quality assurance. This hybrid stratification allows extrapolation to countries and contexts not included in the original 68-country cluster analysis, supporting tailored and scalable implementation strategies across heterogeneous health systems.

Across all settings, multidisciplinary tumor boards enable context-sensitive translation of global guidelines. Radiologists standardize imaging,^{20,21} pathologists ensure quality IHC workflows,^{22,37} surgical teams operationalize SLN mapping,^{6,39,40,42} and radiation oncologists adapt adjuvant approaches to infrastructure while preserving oncologic safety.^{16,23,44,46,49,51} Integrating geriatrics and palliative care ensures that treatment intensity aligns with physiologic reserve and patient goals.

Ultimately, these findings suggest that structural readiness—not national income alone—is more strongly associated with variations in survival and access to innovation. Bridging inequities requires aligning scientific advances with feasible, resource-tailored implementation.

3.3 | Strengths and weaknesses

The principal strength of the present review lies in its attempt to bridge evidence-based endometrial cancer care with implementation feasibility across structurally diverse settings. By incorporating

TABLE 1 Cluster-specific implementation priorities in endometrial cancer care.

Cluster (label)	Structural features	Priority diagnostics	Surgical/pathology focus	Adjuvant/ radiotherapy focus	Systemic therapy focus	Survivorship/ multidisciplinary tumor boards/AI
C1—Foundational health and social development	Limited diagnostic capacity; uneven imaging access; constrained radiotherapy availability; fragmented referral pathways	Transvaginal ultrasonography-first; office endometrial biopsy when feasible; hysteroscopy-guided diagnosis where available; immunohistochemistry-first (MMR, p53); POLE only if treatment- or referral-changing	Total hysterectomy with selective nodal assessment only if results would alter management; SLN often not feasible; prioritize standardized pathology reporting	Prioritize access to vaginal brachytherapy where indicated; use palliative radiotherapy pragmatically; establish referral pathways for salvage radiotherapy when feasible	Prioritize access to platinum-based chemotherapy; test dMMR when feasible; consider referral pathways for trial participation where available	Referral-based multidisciplinary case discussion; early palliative integration; basic survivorship bundle; simple digital tracking tools for delays and attrition where feasible
C2—Comprehensive socioeconomic advancement	Improving diagnostics; growing radiotherapy capacity; better coordination	Selective MRI for staging; immunohistochemistry-first with targeted POLE sequencing; strengthen quality assurance in TVUS and MRI interpretation	Adopt SLN mapping where training and pathology support are available; MIS + ERAS as preferred pathways; synoptic pathology reporting	Biology-adapted adjuvant treatment; vaginal brachytherapy for appropriately selected intermediate-risk patients; reserve EBRT for higher-risk indications	Prioritize access to immunotherapy for dMMR disease; maintain chemotherapy backbone for pMMR disease; apply value-based assessment for combination strategies	Routine multidisciplinary tumor boards; structured survivorship pathways; selective use of AI-assisted imaging appropriateness or reporting support
C3—Emerging environmental and healthcare focus	Underdiagnosis; variable imaging quality; fragmented referral and treatment systems	Close diagnostic gaps through TVUS and biopsy access; targeted MRI for selected cases; minimum immunohistochemistry package (MMR, p53)	Build SLN capacity in referral hubs; strengthen regional pathology QA; improve pathways for timely salvage radiotherapy	Improve imaging-informed radiotherapy selection; expand access to salvage radiotherapy; strengthen basic brachytherapy capacity	Stagewise immunotherapy access beginning with dMMR disease; reduce delays to first chemotherapy; integrate early palliative care	Use multidisciplinary tumor boards to reduce fragmentation; establish survivorship frameworks; consider AI-supported triage or prioritization tools where locally validated
C4—Advanced economic and public health integration	Full diagnostics; robust radiotherapy/systemic access; integrated networks	Routine MRI; selective PET/CT for advanced or ambiguous cases; full molecular classification (MMR, p53, POLE)	SLN mapping as standard staging approach where appropriate; MIS + ERAS; molecularly informed tumor board discussion	Fully biology-adapted adjuvant treatment; high-quality brachytherapy and advanced radiotherapy planning	Frontline chemo-immunotherapy for eligible dMMR disease; value-conscious adoption in pMMR disease; trial participation when available	Comprehensive survivorship care; multidisciplinary tumor boards with geriatrics and palliative integration; AI-assisted quality assurance in pathology and imaging

Note: Recommendations presented in this table were developed through iterative author consensus, anchored to the synthesized evidence across key domains, and structured according to feasibility, infrastructure requirements, workforce capacity, and likely equity impact. They are intended to guide implementation prioritization rather than replace clinical guidelines. The table summarizes diagnostic, surgical, adjuvant, systemic-therapy, survivorship, and multidisciplinary priorities across the four structural clusters (C1–C4). Recommended strategies include transvaginal ultrasonography, MMR/p53 immunohistochemistry, sentinel lymph node mapping, minimally invasive surgery with ERAS protocols, scalable radiotherapy options (vaginal brachytherapy, EBRT), selective immuno-oncology for dMMR tumors, geriatric assessment, palliative care integration, and AI-based quality assurance. These priorities were defined through expert consensus informed by the synthesized evidence, not through formal decision-analytic or cost-effectiveness modeling.

Abbreviations: AI, artificial intelligence; dMMR, mismatch-repair deficient; EBRT, external-beam radiotherapy; ERAS, enhanced recovery after surgery; MIS, minimally invasive surgery; MMR, mismatch repair; MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; MMR, mismatch-repair proficient; SLN, sentinel lymph node; pMMR, mismatch-repair proficient; TVUS, transvaginal ultrasound.

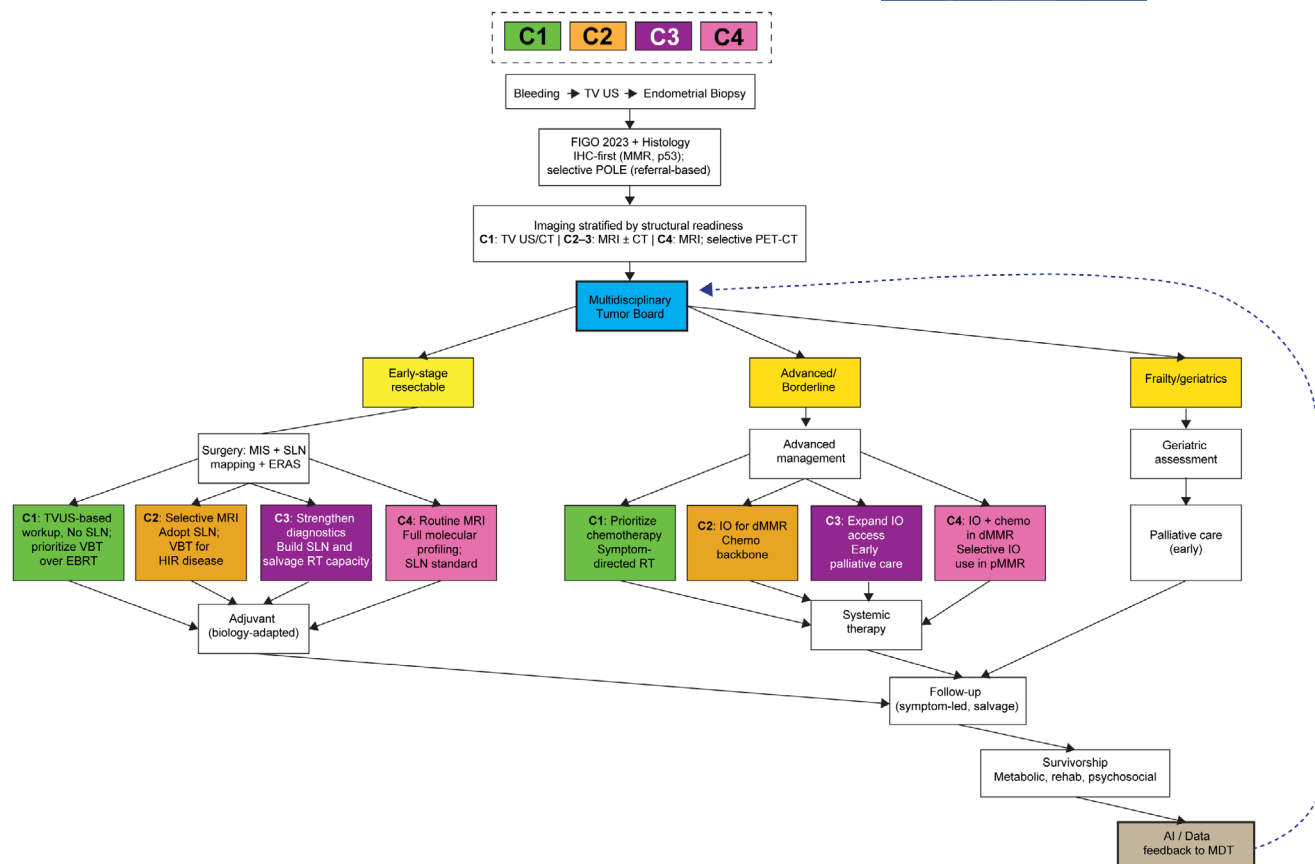


FIGURE 4 Resource-stratified implementation framework for endometrial cancer management across structural-readiness clusters. This schematic illustrates a cluster-informed pathway beginning with symptom-triggered diagnostic evaluation (transvaginal ultrasonography and endometrial biopsy), followed by FIGO 2023 staging, histology, and IHC-first molecular stratification (MMR, p53, with selective referral-based POLE testing where indicated). Imaging, surgical staging, adjuvant therapy, systemic therapy, survivorship, and supportive care are then adapted according to structural readiness and implementation feasibility. The framework incorporates multidisciplinary tumor board input, geriatric assessment, early palliative care, and AI-supported data feedback as mechanisms to support quality assurance and context-specific adaptation. This figure is intended to support implementation prioritization rather than replace formal clinical guidelines. dMMR, mismatch-repair deficient; EBRT, external-beam radiotherapy; ERAS, enhanced recovery after surgery; IO, immune-oncology; MDT, multidisciplinary tumor board; MIS, minimally invasive surgery; PET/CT, positron emission tomography/computed tomography; pMMR, mismatch-repair proficient; SLN, sentinel lymph node; TVUS, transvaginal ultrasound; VBT, vaginal brachytherapy.

multidisciplinary tumor boards remains central to contextualizing evidence and minimizing unwarranted variation.^{11,12,24,25}

Future priorities include:

1. Local validation of molecular and AI-based tools, ensuring reliability and calibration across populations and infrastructures.
2. Health economic modeling comparing phased versus full-scale adoption of advanced diagnostics and therapeutics.
3. Implementation trials testing resource-stratified pathways with real-world endpoints.
4. Inclusive clinical research, expanding participation of low- and middle-income countries to reduce enduring evidence gaps.

Governance, capacity building, and sustained workforce development will be essential to translate molecular and digital advances into equitable outcomes.

3.5 | Resource-stratified, stakeholder-oriented framework

A tiered, stakeholder-oriented model can ensure that evidence-based strategies translate into realistic, equitable practice:

- Patients: accessible education and shared decision making tools promote adherence and informed choice.^{43,54}
- Clinicians: simplified, high-yield diagnostic anchors (MMR/p53 IHC+SLN mapping) enable globally feasible pathways. ERAS and MIS, supported by SLN-based staging,^{6,39} improve recovery and reduce disparities.
- Policymakers: prioritize scalable, high-value interventions—universal IHC, SLN over full lymphadenectomy, and expanded brachytherapy.
- Health systems: centralize diagnostics (pathology, imaging QA) while decentralizing treatment (surgery, radiotherapy, systemic therapy) through hub-and-spoke networks.

This coordinated model supports sustainable adoption of precision oncology across resource settings.

3.6 | Artificial intelligence as a catalyst for equity

AI is rapidly maturing across pathology, imaging, prognosis, and survivorship.¹⁸ Properly deployed, AI can standardize IHC interpretation, enhance MRI-based staging, and generate molecular-subtype predictions through radiomics where sequencing is unavailable.^{33,55} Models designed specifically for high-mortality type II phenotypes in under-resourced regions highlight region-specific opportunities.^{56,57}

Yet safeguards are essential: transparent reporting, local calibration, drift monitoring, and governance must accompany all deployments to avoid reinforcing biases. Algorithms trained solely on high-resource populations may underperform elsewhere, making inclusive datasets and co-development with low- and middle-income countries ethical imperatives.

Within multidisciplinary tumor boards, AI may support deliberations through structured summaries and outcome-based feedback loops,⁵⁸ potentially contributing to more standardized and feedback-informed decision making.

While AI holds potential to augment quality assurance and tumor boards, its deployment must be grounded in local validation, inclusive training datasets, and robust governance frameworks. Limitations include algorithmic bias, overfitting to high-resource environments, and ethical constraints around data privacy.

3.7 | Real-world implementation: Locally validated innovation

Although not specific to endometrial cancer, this local implementation example illustrates how low-cost, context-validated AI tools may support oncology care pathways in structurally constrained settings. The experience at Hospital Sótero del Río (Chile) illustrates equitable AI deployment. A lightweight Phi-3-based small-language model classified unscheduled oncology visits with 99.4% sensitivity and 95.3% accuracy, identifying >85% of visits as driven by uncontrolled symptoms rather than logistics.⁵⁹ By prioritizing transparency, interpretability, and independence from cloud-based infrastructure, this approach enabled real-time, resource-aligned deployment.

This case demonstrates that equitable AI does not require maximal computational complexity—only contextualized design and local validation.

3.8 | Real-world implementation: Cluster examples

Implementation feasibility varies across health-system archetypes:

- Cluster 1 (sub-Saharan Africa): prioritize biopsy access, transvaginal ultrasonography, and brachytherapy; molecular tools remain limited.
- Cluster 2 (Asia, parts of Latin America): expand SLN mapping, MIS, and selective molecular profiling while addressing fragmentation.
- Cluster 3 (Andean/Central America): reduce diagnostic delay; build pathology, survivorship, and systemic therapy capacity.
- Cluster 4 (Europe/North America): refine omission of adjuvant therapy in selected cases; expand immunotherapy access with sustainability monitoring.

Latin America, spanning C2–C3, exemplifies both progress and persistent structural barriers, making it an ideal setting for adaptive oncology frameworks.

4 | CONCLUSIONS AND CALL TO ACTION

Scientific advances in endometrial cancer—spanning molecular classification, precision surgery, radiotherapy optimization, systemic therapy, and emerging digital tools—risk widening global inequities unless implementation is deliberately matched to health-system readiness. Such disparities reflect systemic challenges across low- and middle-income contexts, where inadequate infrastructure and uneven access to innovations further compound mortality gaps.⁶⁰ The cluster-informed framework used in this review provides a more nuanced lens than income-based classifications by capturing diagnostic capacity, system integration, workforce availability, and epidemiologic context as key determinants of equitable outcomes.

Grounded in a Latin-American perspective, this analysis highlights that disparities are driven less by gaps in scientific evidence than by gaps in implementation. Expanding access to high-value, scalable interventions—including universal immunohistochemistry for MMR and p53, selective molecular testing, cost-effective radiotherapy, and structured survivorship care—is essential to realizing precision oncology globally.

Artificial intelligence has significant potential to strengthen diagnostic accuracy, quality assurance, and system monitoring; however, its contribution to equity depends on transparent reporting, local validation, and governance structures that prevent algorithmic bias. Solutions must be adapted to the realities of low-resource environments, prioritizing feasibility and sustainability.

A tiered, multiperspective model is therefore proposed:

- For patients: equity begins with accessible education and shared decision making.
- For clinicians: simplified diagnostic anchors (MMR/p53 immunohistochemistry, sentinel lymph node mapping) and biology-informed adjuvant strategies support individualized yet feasible care.
- For policymakers: prioritization of scalable, cost-effective interventions—vaginal brachytherapy, ERAS protocols, selective molecular testing—and financing strategies that ensure sustainability.

- For health systems: centralization of diagnostics and decentralization of treatment delivery through coordinated hub-and-spoke networks.

Equity also requires attention to survivorship, frailty, and palliative care—particularly as non-cancer mortality increasingly surpasses cancer-related mortality in many populations. Integrating geriatrics and supportive care within multidisciplinary tumor boards ensures biologically informed, person-centered treatment planning.

Building minimum-core-optimal implementation ladders provides practical and scalable pathways for diverse health systems. Starting with immunohistochemistry, transvaginal ultrasonography, and vaginal brachytherapy, progressing to sentinel lymph node mapping and selective POLE testing, and ultimately expanding to comprehensive molecular profiling and safe, sustainable use of immune checkpoint inhibitors, this approach supports proportional, achievable, and equitable precision oncology.

AUTHOR CONTRIBUTIONS

MAC conceived the manuscript and led the writing. CI, MB, AH, RG, JB, EO, MIB, KG, NS, EP, MU, VP, OP, MS, JR, SR, BW, JTB, JPC, CL, and CM contributed to literature review, critical revision of the text, and development of the framework. All authors approved the final version.

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The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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