Research Article

Integrating Genomics into Clinical Gynecologic Practice: Current Methods, Diagnostics, and Ethical Considerations

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Abstract

The completion of the Human Genome Project and the subsequent fall in sequencing costs have transformed most areas of medicine, and gynecology is no exception. Technologies that two decades ago belonged almost exclusively to research laboratories now inform the routine management of patients with endometrial and ovarian cancer and hereditary cancer syndromes. This narrative review synthesizes current evidence on the integration of genomic technologies into gynecologic practice, moving from methodological foundations to clinical applications and, finally, to the ethical and organizational challenges that accompany this transition. We first summarize the evolution of molecular diagnostic tools, from polymerase chain reaction to next-generation sequencing, minimally invasive liquid-biopsy sampling, and artificial-intelligence-assisted analysis. We then review the clinical integration of genomics into the diagnosis of hereditary ovarian and endometrial cancer syndromes, including hereditary breast and ovarian cancer syndrome, Lynch syndrome, Cowden syndrome, and Peutz-Jeghers syndrome, together with the emerging mainstreaming model of genetic testing. A dedicated section addresses molecular diagnostics and personalized treatment, covering the Cancer Genome Atlas-based molecular classification of endometrial cancer, tumor clonality assessment, genomic biomarkers for targeted therapy and immunotherapy, and the prospective role of CRISPR/Cas9 genome editing. Finally, we examine informed consent, genetic privacy and discrimination, disparities in access to genetic services, and the ethical dilemmas surrounding preimplantation and prenatal genetic testing. We conclude that genomic literacy among gynecologists, structured multidisciplinary collaboration, and standardized consent protocols are prerequisites for translating genomic advances into equitable clinical benefit.

Keywords: gynecologic oncology; next-generation sequencing; hereditary cancer syndromes; molecular classification; genetic counseling; reproductive ethics

Introduction

The completion of the Human Genome Project and the subsequent fall in sequencing costs have reshaped most medical specialties, and gynecology is no exception [1]. What two decades ago belonged largely to research laboratories – germline mutation detection, tumor profiling, and the search for molecular targets – is now embedded in the routine management of patients with endometrial cancer, ovarian cancer, and hereditary oncologic syndromes. Genomic technologies are simultaneously reshaping three components of gynecologic care: identification of at-risk women, diagnostic precision, and treatment selection, which is increasingly tied to a tumor's molecular profile rather than to its histologic type alone [1].

The difficulty is that the pace at which genomics has entered laboratory and research practice has outstripped the readiness of practicing clinicians to apply it. Surveys of residents and practicing obstetrician-gynecologists consistently document a gap between what these technologies can offer and how confidently a physician can order genetic testing, interpret a result, and explain it to a patient. A substantial proportion of residents report only episodic exposure to genetics during training and do not feel prepared to independently manage a patient with a hereditary cancer syndrome; those surveyed also describe genetics as competing, in practice, with an already dense clinical workload – a tension that helps explain why training exposure remains episodic even as testing indications multiply [2].

This training gap matters disproportionately in gynecology because obstetrician-gynecologists are often the first clinicians positioned to recognize a hereditary risk pattern. Identifying a pathogenic variant in one patient immediately raises the question of risk for her sisters, daughters, and future generations, underscoring why genomic competence in this specialty carries consequences beyond the individual patient [3].

The purpose of this review is to synthesize current evidence on the integration of genomic technologies into gynecologic practice: from methodological foundations (sequencing, minimally invasive sampling, artificial intelligence) through clinical applications (hereditary syndromes, molecular tumor classification, personalized therapy) to the ethical and organizational challenges that accompany this integration. The review proceeds from

the general to the specific – from the underlying technologies to their clinical application, and from there to the questions that confront clinicians, patients, and health systems alike.

Materials and Methods

This review was prepared as a narrative synthesis rather than a systematic review. The literature was identified primarily through searches of PubMed/MEDLINE, supplemented by Scopus and Web of Science and by manual screening of the reference lists of relevant articles and clinical guidelines. The search was not restricted to a predefined protocol, and the retrieved literature spans publications from the early 2000s to 2026, reflecting both the historical development of molecular diagnostics and the most recent clinical trials and consensus statements.

Search terms were grouped around three broad concept areas: (1) gynecologic oncology and hereditary cancer syndromes (endometrial cancer, ovarian cancer, hereditary breast and ovarian cancer syndrome, Lynch syndrome, Cowden syndrome, Peutz-Jeghers syndrome); (2) genomic technologies (next-generation sequencing, liquid biopsy, molecular classification, tumor clonality, homologous recombination deficiency, CRISPR/Cas9, artificial intelligence); and (3) ethical and organizational dimensions (genetic counseling, mainstreaming, informed consent, genetic discrimination, health disparities, preimplantation genetic testing, non-invasive prenatal testing). These terms were combined flexibly rather than as a fixed Boolean string, so that the search could accommodate the different terminologies used across laboratory, clinical, and ethics literature.

Priority was given to peer-reviewed publications indexed in Scopus or Web of Science, to studies with clearly described methodology, and to the most recent evidence where findings overlapped. Narrative reviews, editorials, and conference abstracts were used mainly for contextual background and were not relied upon for primary claims. No formal language restriction was applied, although the final reference list is predominantly in English, reflecting the language of the indexed literature.

Because the review is narrative in design, no formal risk-of-bias assessment, PRISMA flow diagram, or quantitative synthesis was undertaken. Study selection was guided by relevance to the review's three organizing domains – methodological foundations, clinical applications, and ethical/organizational challenges – and by the aim of representing the available evidence across its full range, from early-phase feasibility studies to phase III trials and international consensus statements. This approach inevitably introduces selection bias, and the review is therefore offered as a synthesis for clinicians and health-system planners rather than as definitive evidence grading.

Current Genomic Technologies in Gynecology: From Theory to Practice

1.1. The Evolution of Methods: From PCR to NGS

Molecular diagnostics in gynecology relied for decades on the polymerase chain reaction (PCR), a method that rapidly and inexpensively detects a specific, previously known mutation or viral DNA sequence. Its capabilities, however, are limited: PCR answers the question "does this patient carry this particular defect," but it is unsuited to the discovery of unknown or de novo variants, or to the assessment of a tumor's overall mutational burden. Next-generation sequencing (NGS) removed this constraint by allowing hundreds of genes, entire exomes, or whole genomes to be read in parallel within a single run [4]. Over the past decade, NGS platforms have become more reliable, less costly, and faster, which has moved them from the research setting into routine clinical laboratories [4]. In practical terms, this represents a shift from sequential, gene-by-gene testing – characteristic of the PCR era – to parallel analysis of entire candidate-gene panels in a single assay, which is particularly valuable when the clinical picture does not point unambiguously to a single mutation but is compatible with several hereditary syndromes at once.

1.2. Next-Generation Sequencing as a Diagnostic Tool

In gynecologic oncology, NGS addresses several tasks simultaneously: detection of germline and somatic mutations, determination of tumor mutational burden (TMB), assessment of microsatellite instability (MSI), and evaluation of tumor clonality [1]. A retrospective analysis of 108 patients with advanced breast and gynecologic cancers found that targetable mutations were identified by NGS in nearly three-quarters of cases, while an actual clinical action was taken on the basis of these findings in approximately 38% [5]. These figures illustrate both the method's potential and its present limitation: an identified mutation does not automatically translate into a therapeutic option, whether because no corresponding targeted drug exists, because the drug is unavailable or unapproved in a given setting, or because the clinical benefit for a particular patient remains uncertain [6]. Translating an NGS report into an actual treatment decision increasingly depends on structured multidisciplinary review rather than on a single clinician's interpretation. Molecular tumor boards – in which oncologists, pathologists, geneticists, and bioinformaticians jointly evaluate sequencing results and match them against available targeted agents or clinical trials – have become a recommended mechanism for converting a genomic

finding into an actionable plan, particularly for rare or ambiguous variant combinations that fall outside standard guideline pathways [7].

1.3. Minimally Invasive Sampling Methods

One development that is moving genomics out of oncologic surgery and into outpatient gynecology is so-called liquid biopsy. Conventional endometrial biopsy is invasive and poorly tolerated by some patients; an alternative has emerged in the analysis of DNA obtained from uterine lavage, aspirate, or cervico-endometrial smears. In a pilot study using a 12-gene panel, lavage fluid from an asymptomatic patient with no histologic evidence of a premalignant lesion revealed oncogenic PTEN mutations – and ten months later she was diagnosed with a microscopic focus of endometrial cancer [8]. Larger series confirm the feasibility of this approach: genetic alterations were detected in 93% of uterine aspirate samples, and circulating tumor DNA was present in 41% of patients, predominantly those with high-risk tumors [9]. Combining cytologic and genetic analysis of liquid-based cytology specimens likewise improves sensitivity for detecting both endometrial and ovarian malignancies [10,11]. Such specimens can also be obtained from blood and urine, and early recurrence detection based on circulating tumor DNA currently has the strongest evidence base among all liquid-biopsy applications [12,13].

1.4. Artificial Intelligence and Multi-Omics

Alongside the expanding volume of genomic data, the role of algorithms capable of processing it is also growing. Machine-learning models are used to integrate genomic, transcriptomic, proteomic, and imaging data with the aim of improving risk stratification, predicting treatment response, and identifying new biomarkers [14]. In the digital pathology of gynecologic tumors, deep learning is already used for histologic subtyping and for determining tumor grade and molecular subtype directly from a slide image, without additional sequencing [15,16]. A related direction is AI-based analysis of DNA methylation patterns, which underlies early-stage multi-cancer screening [17]. Ovarian cancer, unlike cervical cancer, lacks a reliable screening test, which makes models that combine classic serum markers (CA-125, HE4) with imaging and multi-omic data of particular interest. A representative example is a multicenter study that trained a machine-learning model on 34 clinical and laboratory parameters – including CA-125, HE4, patient age, and ultrasound characteristics – and showed that this model outperformed conventional logistic regression in distinguishing benign from malignant ovarian masses, pointing toward clinical decision support in gynecologic oncology [18]. A comparable pattern emerges in ultrasound diagnostics, where deep-learning models for distinguishing benign from malignant gynecologic tumors reach accuracies of up to 99.8% and AUCs of up to 0.99, though only three of 26 reviewed studies used a prospective design [19]. Reviewers nonetheless agree that most such models still lack external validation and are not ready for routine use, and that integrating histomorphologic, immunophenotypic, and molecular data remains more a prospect than an everyday reality [20].

Integrating Genomics into the Diagnosis of Hereditary Gynecologic Disorders

2.1. Hereditary Syndromes Conferring High Risk of Ovarian and Endometrial Cancer

A classic example of the clinical application of genomics is hereditary breast and ovarian cancer syndrome (HBOC), associated with germline mutations in BRCA1 and BRCA2. Estimates of cumulative risk vary considerably across populations and study methodologies, but overall, breast cancer develops by age 70 in 55-87% of carriers and ovarian cancer in 15-65%, with risk generally higher among BRCA1 carriers than among BRCA2 carriers [21,22]. The principal method of primary prevention is risk-reducing salpingo-oophorectomy (RRSO), which lowers the incidence of ovarian cancer by approximately 80% on average [23].

The second most clinically important hereditary syndrome is Lynch syndrome, associated with germline mutations in the DNA mismatch repair genes MLH1, MSH2, MSH6, and PMS2. For the gynecologist, its significance lies chiefly in the fact that a carrier's risk of endometrial cancer can exceed her risk of colorectal cancer – the reverse of the popular perception of Lynch syndrome as a "familial colon cancer" condition [24]. Cumulative endometrial cancer risk differs substantially depending on which gene is affected. Across cohorts, including data from the Prospective Lynch Syndrome Database, it is estimated at roughly 21-49% for MSH2 carriers and 16-65% for MSH6 carriers by age 70-75. Because MSH6 carriers often face a higher risk of endometrial cancer than of colorectal cancer, the gynecologist – rather than the colorectal surgeon – may be the first specialist positioned to suspect the syndrome [25,26] (Figure 1). A nationwide Dutch cohort study of the registered population of Lynch syndrome carriers found that systematic gynecologic surveillance combined with timely discussion of risk-reducing surgery allows a substantial proportion of endometrial cancers to be detected at an early, curable stage – while also highlighting the absence of a uniform surveillance protocol across centers [27].

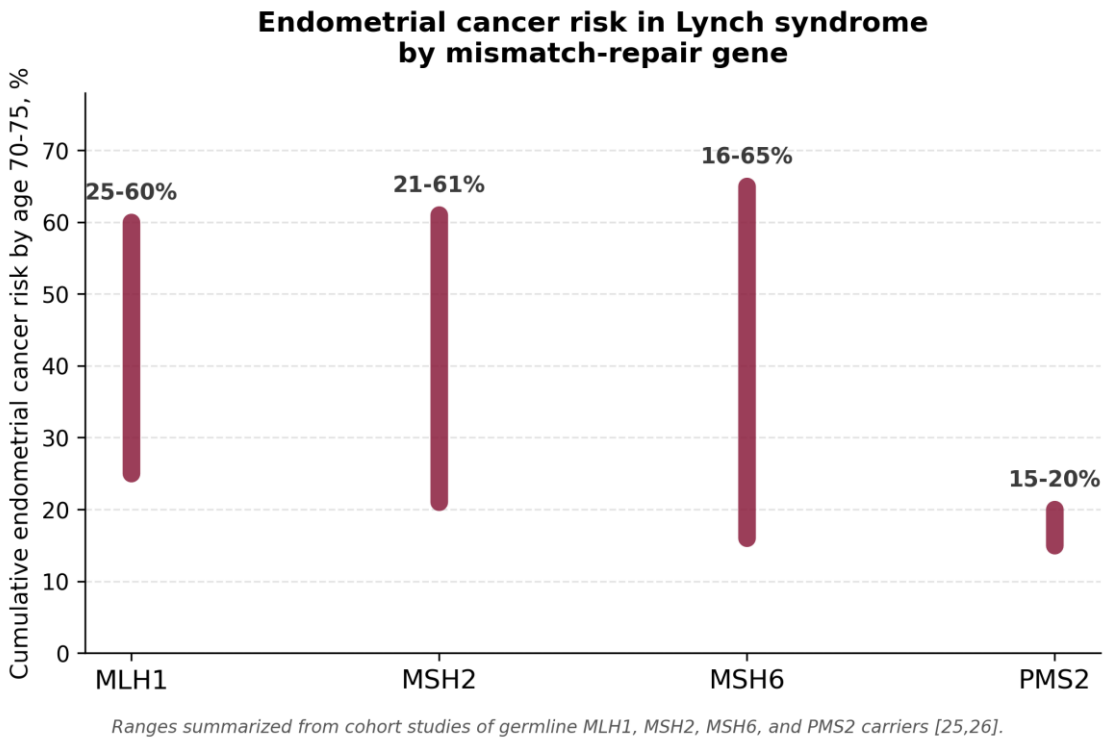

Figure 1. Cumulative endometrial cancer risk in Lynch syndrome by mismatch-repair gene (ranges per [25,26]).

Less commonly encountered in gynecologic practice are Cowden syndrome, associated with PTEN mutations and conferring a 20-30% risk of endometrial cancer, and Peutz-Jeghers syndrome (STK11/LKB1 mutations), in which the risk of gynecologic malignancy by age 50 is estimated at 18-50%, including rare sex cord-stromal tumors of the ovary [28,29]. These figures inform recommendations on the age at which gynecologic surveillance should begin in each syndrome. Within Lynch syndrome, the same risk-stratified reasoning applies to decisions about prophylactic surgery: for MSH6 carriers, whose endometrial cancer risk exceeds that of MLH1 and MSH2 carriers, the higher risk is often cited as an argument for earlier discussion of prophylactic hysterectomy [26]. In Peutz-Jeghers syndrome, cohort studies confirm that the associated cancer risk manifests early and involves several organ sites simultaneously, including gynecologic sites, which calls for coordination between the gynecologist and the gastroenterologist rather than isolated surveillance [30].

2.2. The Role of Genetic Testing in "Mainstreaming"

The traditional model, in which every patient suspected of carrying a hereditary syndrome is referred to a clinical geneticist, scales poorly against the growing number of testing indications. The response has been the concept of "mainstreaming" – incorporating genetic counseling and test ordering into the routine work of the treating gynecologic oncologist, supported by a genetic counselor embedded within the clinical team. One of the first published models of this kind, implemented in an ovarian cancer clinic, achieved testing uptake of 90% within two years of implementation, with the median time from referral to result shortened to five months [31]. A comparable United Kingdom program has likewise proved acceptable to both clinicians and patients, although successful replication requires a dedicated referral pathway, training for non-genetics specialists, and a clear protocol for result disclosure [32,33]. This organizational shift is also bounded by workforce capacity: a national survey of the United States medical genetics workforce found that certified genetic counselors, although the largest single professional group in clinical genetics, remain in short supply relative to demand for direct patient care, particularly outside major academic centers [34]. A systematic review of mainstreaming implementation across cancer care settings nonetheless concluded that the model is feasible and can be integrated into routine practice, provided that pre-test counseling responsibilities are clearly defined and that non-genetics clinicians receive structured training – evidence that the approach is not merely a local experiment but a transferable organizational strategy [35]. The persistent constraint is therefore not the feasibility of mainstreaming itself, but the practical conditions under which it can be sustained: protected time for counseling, accessible genetic expertise for complex results, and a workforce trained to recognize when a mainstreamed pathway reaches its limits.

2.3. Genetic Counseling in Gynecology

Shifting part of the geneticist's role onto the gynecologic oncologist does not eliminate the need for specialized counseling; it changes what that counseling must accomplish. A genetic counselor remains the connecting link

between the laboratory, the treating physician, and the patient, particularly in emotionally charged situations such as suspected hereditary cancer, infertility, or pregnancy loss. What mainstreaming adds is a new burden on the treating oncologist: recognizing when a result – most notably a variant of uncertain significance (VUS) – requires escalation to specialized counseling rather than routine explanation. The proportion of VUS rises as gene panels expand, and patients frequently misinterpret such a result, either as covert confirmation of disease or as its definitive exclusion – a state sometimes described as "genetic purgatory": neither anxiety nor relief, but suspended uncertainty [36]. A systematic review of the psychological consequences of receiving a VUS result shows that distress is markedly greater among patients who were not warned in advance of the possibility of such a result – meaning that the quality of pre-test counseling itself shapes how uncertainty is experienced [37].

Molecular Diagnostics and Personalized Treatment of Gynecologic Cancers

3.1. Molecular Classification of Endometrial Cancer

One of the most consequential practical outcomes of the genomic era in gynecology has been the new molecular classification of endometrial cancer, developed from data generated by The Cancer Genome Atlas (TCGA) project. It divides tumors into four groups: POLE-ultramutated (POLEmut), mismatch repair-deficient (MMRd), no specific molecular profile (NSMP), and p53-abnormal (p53abn) [38]. In clinical practice, the TCGA classification is operationalized through the ProMisE (Proactive Molecular Risk Classifier for Endometrial Cancer) algorithm, which replaces full genomic profiling with a surrogate panel – immunohistochemistry for p53, MSH6, and PMS2 combined with hotspot analysis of POLE mutations [39]. Prognosis differs substantially across these groups: survival is best for POLEmut tumors and worst for p53abn tumors, with MMRd and NSMP occupying an intermediate position [40] (Figure 2, Table 2). This classification has proved so consequential that the 2023 FIGO staging system incorporated molecular subtype for the first time as a factor capable of downstaging or upstaging disease. Early-stage POLEmut tumors are assigned a more favorable stage, whereas p53abn tumors may be reclassified to a higher one [39,41].

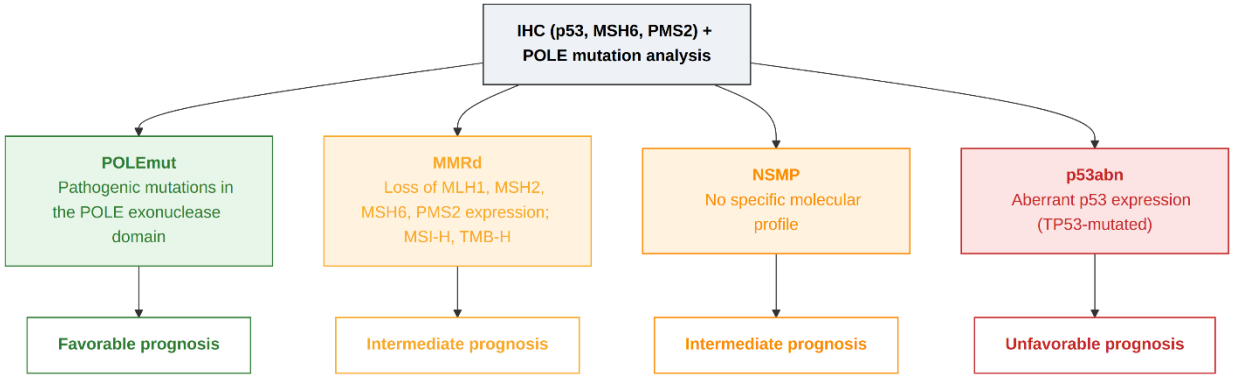

Figure 2. Molecular classification of endometrial cancer (TCGA/ProMisE) and its prognostic correlates [38,39,40].

Table 2. Molecular subtypes of endometrial cancer (TCGA/FIGO 2023)

Molecular subtype	Molecular marker	Prognosis	Clinical significance
POLEmut	Pathogenic mutations in the POLE exonuclease domain	Favorable	Adjuvant therapy de-escalation may be feasible in early-stage disease
MMRd	Loss of MLH1/MSH2/MSH6/PMS2 expression; high microsatellite instability (MSI-H) and tumor mutational burden (TMB-H)	Intermediate	Candidate for immune checkpoint inhibitor therapy (pembrolizumab, dostarlimab)
NSMP	No specific molecular profile	Intermediate	Further stratification by histologic and hormone receptor factors
p53abn	Aberrant expression / mutation of TP53	Unfavorable	Most intensive adjuvant therapy; investigation of additional targets (e.g., HER2)

3.2. Determining Tumor Clonality

Synchronous detection of endometrial and ovarian carcinoma is not rare, accounting for up to 10% of all tumors at either site [42]. The clinical dilemma this raises is substantial: the clinician may be facing two independent

primary tumors, each requiring its own staging and generally carrying a more favorable prognosis, or a single metastatic disease process that changes the entire treatment strategy. Morphology and immunohistochemistry do not always provide an unambiguous answer. NGS can resolve this question more precisely. In one series, calculating a clonality index from shared somatic mutations confirmed clonal relatedness in 92% of cases, pointing to a single origin rather than two independent processes; such clonally related cases showed a markedly better outcome than genuinely metastatic disease [42]. A case reported in the literature illustrates this well: a morphologic diagnosis of two independent primary tumors was revised, after sequencing of both sites, to metastatic spread from a primary uterine tumor to the ovary, based on a shared mutational profile and mismatch repair protein status – with direct consequences for the choice of adjuvant therapy [43]. A larger series applying a 73-gene sequencing panel across 22 cases of synchronous endometrioid carcinoma confirmed the same pattern: clonal origin was demonstrable even in tumor pairs that conventional clinicopathologic criteria had classified as independent, low-stage primaries – a "favorable" morphologic picture alone does not guarantee that two foci are truly independent [44]. The practical conclusion is a cautious one. Molecular profiling adds prognostic and predictive information that can influence adjuvant-therapy decisions, but it does not replace established morphologic staging criteria; rather, the two are complementary, and the molecular result is most useful when it is interpreted alongside, not instead of, the clinicopathologic assessment [42].

3.3. Genomic Biomarkers for Targeted Therapy and Immunotherapy

Molecular classification of a tumor is not only a prognostic tool but also a predictive one. Mismatch repair deficiency and high microsatellite instability, which are usually accompanied by a high tumor mutational burden, have become the basis for approving immune checkpoint inhibitors – pembrolizumab and dostarlimab – in endometrial cancer [45,46]. In the KEYNOTE-158 trial, single-agent pembrolizumab produced a durable response in a substantial proportion of patients with MSI-H advanced endometrial cancer [47]; for tumors lacking these markers (microsatellite-stable tumors), efficacy is improved by combination with lenvatinib [48,49,50]. Large phase III trials – RUBY and NRG-GY018 – have shown that adding checkpoint inhibitors to standard carboplatin-paclitaxel chemotherapy as first-line treatment improves progression-free and, in the dMMR/MSI-H subgroup, overall survival in advanced or recurrent endometrial cancer [48]. A comparable principle applies to ovarian cancer: roughly half of high-grade serous carcinomas carry homologous recombination deficiency, which confers sensitivity to PARP inhibitors (olaparib, niraparib, rucaparib) via synthetic lethality [51,52]. The clinical value of this strategy, however, depends on how reliably homologous recombination deficiency itself is measured; testing standardization remains an unresolved methodological issue. A multi-assay comparison conducted through the Friends of Cancer Research HRD Harmonization Project, together with independent concordance studies, found substantial but incomplete agreement between commercial and laboratory-developed HRD assays, with discordant calls concentrated among tumors near each assay's specific threshold [53]. A subsequent international expert consensus concluded that no single platform can yet serve as a universal reference standard and recommended that laboratories report the specific assay and cutoff used alongside the result, so that clinicians can interpret borderline cases appropriately [54].

3.4. CRISPR/Cas9 and the Future of Therapy

Genome-editing technologies remain, for now, predominantly research tools, but the direction of their application in gynecologic oncology is already discernible: restoring the function of tumor-suppressor genes such as TP53 or PTEN, silencing genes responsible for drug resistance, and increasing the sensitivity of tumor cells to chemotherapy [55]. In preclinical models of ovarian cancer, CRISPR/Cas9-mediated knockout of BCL2 increased cellular chemosensitivity, while editing of the ABCB1 transporter, which mediates efflux of cytotoxic drugs from the cell, enhanced the effect of doxorubicin and paclitaxel [56]. A separate research line addresses nanoparticle- and liposome-based delivery systems, without which clinical application remains constrained [57]. Multiplexed editing of several tumor-suppressor genes simultaneously in model systems can already reproduce the molecular and morphologic features of high-risk, aggressive endometrial cancer, and functional CRISPR screening helps identify genes that determine tumor sensitivity to PARP inhibitors and carboplatin – establishing this technology as not only a potential therapeutic tool but also an important research instrument [58,59].

Ethics and Ethical Considerations in the Implementation of Genomics

4.1. Informed Consent and the Challenge of Understanding Risk

Obtaining informed consent for genomic testing is more complex than for most other medical procedures, because the result concerns not only the patient herself but potentially her relatives, and sometimes future children as well. A review of the ethical, legal, and social issues surrounding genetics and genomics in oncology notes that physicians without specialized genetics training often struggle specifically with preparing a patient for the possibility of incidental or uncertain findings [60]. A related problem arises during tumor sequencing: the detection of a germline variant that was not the original aim of testing requires a carefully considered protocol. Evidence from pediatric oncology suggests that such protocols are often lacking even at specialized centers [61],

and there is little reason to assume that adult gynecologic oncology is better prepared. A separate ethical question concerns "whose patient" a genetic result belongs to. Genetic information about one family member is, by its nature, information about all blood relatives, and a physician can face a dilemma between the duty to maintain confidentiality for the individual patient and the moral obligation to warn those for whom the information could be lifesaving [62,63]. A further tension arises when genomic testing is embedded in a research protocol rather than purely clinical care: participants may struggle to distinguish an investigational study from individualized treatment, a distinction the same review identifies as a recurring source of ethical and legal ambiguity in obtaining consent [60].

4.2. Confidentiality and Discrimination

In the United States, the principal legal safeguard against discrimination on the basis of genetic information is the Genetic Information Nondiscrimination Act (GINA), enacted in 2008, which prohibits employers and health insurers from using genetic data in employment and coverage decisions [64]. The law, however, does not extend to life, disability, or long-term care insurance – leaving a substantial share of the potential financial consequences of a positive result outside its protection, a limitation that remains the subject of active debate among health-law scholars [64]. An international review of genetic discrimination concludes that the issue retains its salience into the 2020s: fear of possible consequences continues to be cited as one reason why some patients decline recommended genetic testing, despite formal legislative safeguards [65]. For a patient found to carry a BRCA1 mutation or Lynch syndrome, this means that the decision to undergo testing is often weighed not only in terms of medical benefit but also in terms of possible practical consequences outside the health care system.

4.3. Access and Inequality

Data from multiple centers show that access to genetic counseling and testing is unevenly distributed. Among patients at a hereditary breast and ovarian cancer center, Black and Hispanic women were more likely to undergo testing only after a cancer diagnosis had already been established, and less likely to be tested on the basis of family history alone – representing a missed opportunity for prevention [66]. Lower testing rates are associated with public insurance coverage, language barriers, and older age at diagnosis [67]. Some centers that have implemented point-of-care testing have shown that this gap can be narrowed through organizational measures rather than financial investment alone [67]. Nevertheless, overall outcomes for cervical, ovarian, and uterine cancer remain worse for Black patients, and germline and somatic tumor testing is only one of several points at which this inequity manifests [68]. Notably, inequity does not end once testing has been performed: among patients who are tested, variants of uncertain significance are found significantly more often in members of ethnic minority groups – simply because reference databases have historically been built predominantly from populations of European ancestry, making result interpretation inherently less reliable for these patients [69]. This turns equity from a purely organizational question (who is referred for testing) into a methodological one: even with equal access, the clinical value of a result may remain unequal. Equity concerns extend to the genetics workforce itself: the same national workforce survey cited above found that certified genetic counselors – the professionals most directly responsible for delivering pre- and post-test counseling – were overwhelmingly White and female, a demographic composition that does not mirror the diversity of the patient population served and may itself shape how comfortably patients from minority backgrounds engage with genetic services [34].

4.4. Reproductive Dimensions and "Future Generations"

The most ethically sensitive application of genomics in gynecology concerns reproduction. Preimplantation genetic testing of embryos and non-invasive prenatal screening confront the couple and the clinician with questions that extend beyond purely medical competence: what constitutes a "sufficiently serious" indication for embryo selection, and where prevention of disease ends and trait selection begins [70,71]. Some couples and specialists regard preimplantation embryo selection as ethically more acceptable than terminating an established pregnancy after prenatal diagnosis, since the decision precedes implantation rather than concerning an ongoing pregnancy [72]. At the same time, the very possibility of selection raises concern about a gradual expansion of indications, from severe single-gene disorders toward less clear-cut conditions [70]. A separate methodological problem concerns the quality of informed consent for non-invasive prenatal testing: decisions made before the possible consequences of a positive result are fully understood have been shown to undermine the very reproductive autonomy that these technologies were designed to protect [71]. This also sharpens the question of the right not to know and the right to decline. A systematic analysis of more than two hundred sources on the ethics of preimplantation and non-invasive prenatal testing shows that the criteria used to judge the acceptability of such selection for medical indications rest primarily on the notion of "severity" of the condition – even though no consensus definition of severity itself has been established in the literature, leaving clinicians and couples with a wide, often personally unsettling, margin for subjective judgment [71].

One application of these technologies deserves separate attention because of how rapidly it has entered routine care. Non-invasive prenatal testing (NIPT) has already become the standard of care in many countries for detecting chromosomal aneuploidies such as trisomy 21, 18, and 13. From an ethical standpoint, the technology cuts both ways: on one hand, it reduces the number of invasive diagnostic procedures, such as amniocentesis, that carry a risk of miscarriage [73]; on the other, the steady broadening of its scope – from major trisomies toward microdeletions and single-gene disorders – intensifies concerns about informed consent and raises the risk of selection against conditions of uncertain clinical significance, which calls for continued, deliberate oversight by professional societies [71].

Conclusion

Genomics is no longer an adjunct to gynecologic practice – it is embedded within it, at the level of hereditary-syndrome screening, diagnosis, and treatment selection for endometrial and ovarian cancer. The principal drivers of this shift remain next-generation sequencing, minimally invasive sampling methods, and artificial-intelligence algorithms capable of working with data at multiple levels, from the genome itself to the histologic slide image.

The practical challenges, however, are no less substantial than the achievements. The gap between the pace at which new tests appear and clinicians' readiness to use them persists. Mainstreaming models built around an embedded genetic counselor have proved workable but require systematic, rather than piecemeal, implementation. Interpreting results – particularly variants of uncertain significance – remains a source of distress for patients unless it is accompanied by carefully structured pre-test counseling.

From a practical standpoint, successful integration of genomics into day-to-day gynecologic practice requires three key elements: first, training clinicians in the basic principles of interpreting NGS results and in the criteria for referring patients for testing; second, establishing multidisciplinary teams – comprising a gynecologic oncologist, a genetic counselor, and a pathologist – to discuss complex cases; and third, standardizing informed-consent protocols that explicitly address the possible range of results, including variants of uncertain significance.

These measures address the technical and organizational side of integration. Yet as genomics becomes more deeply embedded in clinical care, the questions it raises grow correspondingly harder to resolve through technical progress alone: how to obtain informed consent when a result concerns more than the individual patient; who bears responsibility for protecting that information from discrimination outside the health care system; and how to ensure that access to these technologies does not reproduce existing social inequities. The further evolution of personalized medicine in gynecology – the expansion of multi-omic approaches, genome editing, and deeper ethical reflection – will depend not only on new technologies but on how consistently health systems address these accompanying challenges.

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