AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Uterine Cancer

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: Malignant neoplasm of the uterine corpus — endometrial carcinoma accounts for ~95% of cases,[1] with endometrioid adenocarcinoma the dominant histology; serous, clear cell, and carcinosarcoma represent aggressive non-endometrioid subtypes. Molecular classification (POLE-mutated, MMR-deficient, NSMP, p53-abnormal) increasingly drives prognosis and treatment selection. Cardinal symptom is abnormal vaginal bleeding, present in >90% of postmenopausal[1] patients.

ICD-10 Codes: Primary corpus **C54.0** isthmus/**C54.1** endometrium/**C54.2** myometrium/**C54.3** fundus/**C54.8** overlapping/**C54.9** corpus unspecified (avoid); **C55** uterus part unspecified (avoid — most common upcoding error). Cervical cancer **C53.x** is a distinct family — never substitute. Metastatic: **C77.5** pelvic lymph nodes, **C79.82** secondary genital organs (HCC 18); **C78.6** peritoneum, **C78.7** liver, **C78.0x** lung (HCC 17). Code each metastatic site individually.

Prevalence: ACS projects ~68,270 new diagnoses[2] and ~14,450 deaths[2] in the U.S. in 2026 — the most common gynecologic cancer and the fourth most common cancer in women overall, with **incidence and mortality rising ~2% annually**[2] since the mid-2000s. Median age at diagnosis ~60 years;[1] ~80% diagnosed in postmenopausal women. ~67–70% diagnosed at Stage I; 5-year relative survival: Stage I 95–96%, Stage II 75%, Stage III >41%, Stage IV 17–22%; overall ~81–82%.[1,3]

HCC/RAF V28 Mapping

ICD-10 CODE[1–3]	HCC CATEGORY	RAF WEIGHT	DOCUMENTATION REQUIREMENT
C54.x C54.1, C54.0, C54.2, C54.3, C54.8, C54.9, C55	HCC 23 — Prostate/ Breast/and Other Cancers and Tumors	0.186	**Active uterine cancer**; document **histologic type** (endometrioid, serous, clear cell, carcinosarcoma), **grade**, and **FIGO stage**. C54.1 is the default for endometrial origin; C55 should be used **only** when site is genuinely **indeterminate**

ABBREVIATIONS: ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification | HCC = Hierarchical Condition Category | RAF = Risk Adjustment Factor | CNA = Community Non-Dual Eligible, Aged | FIGO = International Federation of Gynecology and Obstetrics

RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model; values vary across patient populations based on eligibility and care setting

Risk-Adjusted Care Resources per Patient/Year[4]

Risk-adjusted care resource allocation — MA base rate × RAF coefficient for HCC 23 (Prostate/Breast/and Other Cancers and Tumors): 0.186 (CNA segment, CY2026)

UTERINE CANCER

~$1,934

HCC 23 · RAF 0.186 · per active patient/year

RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model; values vary across patient populations based on eligibility and care setting

RAF coefficients are CNA segment, 2026 CMS-HCC Model V28. The impact of this condition varies across patient populations, particularly in individuals with disability, dual eligibility, or those receiving care in institutional settings. All primary uterine codes (C54.x and C55) map to HCC 23 — accurate documentation (C54.1 over C55), thorough comorbidity documentation (E66.xx obesity, E11.xx diabetes), and metastatic site coding remain the documentation leverage points.

2 RECOGNITION AND DIAGNOSIS

Molecular Classification

MOLECULAR SUBTYPE	TCGA CLASSIFICATION	PROGNOSIS	KEY FEATURES
POLE-mutated	POLE ultramutated (POLEmut)	Excellent — even in high-grade tumors	**Ultrahigh tumor mutation burden**; pathogenic mutations in exonuclease domain (P286R, S297F, V411L most common)[5]
MMR-deficient	Microsatellite instability hypermutated (MSI-H/dMMR)	Intermediate	Loss of **MLH1, MSH2, MSH6, or PMS2**; overlap with Lynch syndrome[6]
p53-abnormal	Copy-number high (CNH/p53abn)	Poor — regardless of histologic grade	**Mutant p53 expression**; majority of endometrial serous carcinomas; ~22% of Grade 3 endometrioid[7]
No Specific Molecular Profile	Copy-number low (CNL/NSMP)	Intermediate	**Wild-type p53**; MMR proficient; primarily Type I endometrioid[8]

MOLECULAR SUBTYPE	TCGA CLASSIFICATION	PROGNOSIS	KEY FEATURES

ABBREVIATIONS: POLE = Polymerase Epsilon | POLEmut = POLE-mutated | MMR = Mismatch Repair | dMMR = MMR-Deficient | MSI-H = Microsatellite Instability-High | MLH1 = MutL Homolog 1 | MSH2 = MutS Homolog 2 | MSH6 = MutS Homolog 6 | PMS2 = PMS1 Homolog 2 | CNH = Copy-Number High | CNL = Copy-Number Low | NSMP = No Specific Molecular Profile | TCGA = The Cancer Genome Atlas | FIGO = International Federation of Gynecology and Obstetrics | ER = Estrogen Receptor | PR = Progesterone Receptor

Medicare Screenings (older adults, at-risk population)

TEST	COVERAGE	FREQUENCY	CPT CODE	CLINICAL INDICATION
Endometrial biopsy (Pipelle/office)	Diagnostic only — Medicare does NOT cover screening	As clinically indicated	58100/ 58110	**Postmenopausal bleeding**; endometrial thickness **>4 mm**; atypical glandular cells[9,10]
Transvaginal pelvic ultrasound	Covered when diagnostic — not screening	As clinically indicated	76830	First-line evaluation of **postmenopausal bleeding**; endometrial stripe measurement **>4 mm**; **uterine mass or polyp characterization**; abnormal uterine bleeding unresponsive to treatment[11,12]
Lynch syndrome surveillance — annual endometrial biopsy from age 35	Covered for confirmed Lynch syndrome carriers	Annually	58100	Confirmed **MLH1, MSH2, MSH6, or PMS2** pathogenic variant; personal or first-degree family history of **Lynch-associated cancers**; annual surveillance from **age 35** per NCCN[13]
MMR/MSI tumor testing (universal)	Covered when ordered as part of cancer pathology workup	Once at diagnosis	81288/ 81301/ 88341 (IHC)	**All newly diagnosed** regardless of age, stage, or histology; identifies Lynch syndrome (MLH1, MSH2, MSH6, PMS2 loss); guides **immunotherapy eligibility** (pembrolizumab for dMMR/MSI-H tumors); informs hereditary risk counseling; cascade testing for first-degree relatives[14,15]

ABBREVIATIONS: USPSTF = U.S. Preventive Services Task Force | NPV = Negative Predictive Value | TVUS = Transvaginal Ultrasound | MMR = Mismatch Repair | MSI = Microsatellite Instability | IHC = Immunohistochemistry | NCCN = National Comprehensive Cancer Network | AGC = Atypical Glandular Cells

Subtle Early Signs in Older Adults

SIGN/SYMPTOM	CLINICAL SIGNIFICANCE
Postmenopausal vaginal bleeding (any amount, any episode)	Present in **>90% of postmenopausal patients**[1] with endometrial cancer. Probability that postmenopausal bleeding represents endometrial cancer rises with age: **women <50 yrs, <1% of PMB due to uterine cancer; women >80, 24% of PMB due to uterine cancer**[16]
New-onset abnormal uterine bleeding in premenopausal women >40 with risk factors	Approximately **15%** of endometrial cancers occur premenopausally[17]
Bleeding on tamoxifen	**Tamoxifen increases** endometrial cancer risk **2–7×** (estrogenic effect on endometrium). Bleeding on tamoxifen must **NOT** be attributed to the medication without endometrial sampling[18]
Bleeding on anticoagulants (warfarin, DOACs)	**Anticoagulation may unmask** occult malignancy rather than simply cause bleeding. Genitourinary bleeding on anticoagulants carries HR 5.0 for concordant-site malignancy[19] (HR 11.8). **Tissue sampling** still required
Atypical glandular cells (AGC) on Pap smear	**~3% of AGC results** are ultimately endometrial cancer; AGC mandates endometrial sampling regardless of patient age[20]

ABBREVIATIONS: AGC = Atypical Glandular Cells | DOAC = Direct Oral Anticoagulant | BMI = Body Mass Index | OR = Odds Ratio | HR = Hazard Ratio | PMB = Post-Menopausal Bleeding

Geriatric Risk Factors

FACTOR	RISK SIGNAL	NOTES
Obesity (BMI ≥30)	**57%** of US endometrial cancers attributable to **obesity**; BMI >30 RR 2.5–5.0; morbid obesity (BMI >40) lifetime risk 10–15%[21]	The strongest **modifiable** risk factor. Document obesity class (E66.01, E66.811–813) — independently risk-adjustable and supports HEDIS BMI screening measure
Type 2 diabetes mellitus	RR 3.05 (95% CI 2.35–3.96); HR 1.66 (95% CI 1.53–1.81)[22]	Independent risk factor and a comorbidity that dominates clinical encounters; **insulin resistance promotes endometrial stimulation**. Document diabetes with complication specificity (E11.xx)

FACTOR	RISK SIGNAL	NOTES
Metabolic syndrome	HR 2.20 (95% CI 1.61–3.02)[23] in postmenopausal women	The cluster **(central obesity + hyperglycemia + dyslipidemia + hypertension)** approximately doubles risk
Tamoxifen use (current or recent)	RR 2–7×, particularly in postmenopausal women[18]	Document Z79.899 for current users; **postmenopausal bleeding on tamoxifen requires biopsy**

ABBREVIATIONS: BMI = Body Mass Index | RR = Relative Risk | HR = Hazard Ratio | CI = Confidence Interval | MMR = Mismatch Repair | dMMR = MMR-deficient | MSI-H = Microsatellite Instability-High

Diagnostic Thresholds

TEST/MARKER	DIAGNOSIS CRITERION	NOTES
Endometrial biopsy (Pipelle, office)	Histologic confirmation of endometrial adenocarcinoma or atypical hyperplasia	Sensitivity 0.774 (95% CI 0.565–0.900),[1] specificity 0.985 (95% CI 0.927–0.997). Inadequate sample rates 7–40% in postmenopausal women; **~10% false-negative rate**. If biopsy negative but bleeding persists, refer for D&C[24]
Transvaginal ultrasound (TVUS)	Endometrial stripe ≤4 mm has >99% NPV in average-risk postmenopausal women[25]	ACOG-acceptable initial approach for single-episode bleeding. CRITICAL CAVEAT: in **Black women, the 4-mm threshold has only 47.5% sensitivity** (vs 87.9% in White women)[26] per GUIDE-EC — biopsy-first preferred. Aggressive histologies (serous, clear cell, p53-abnormal) can present with thin stripe
Dilation and curettage (D&C)	Sensitivity 0.880 (95% CI 0.281–0.993),[1] specificity 0.984 (95% CI 0.956–0.995)	Recommended when **Pipelle is inconclusive, inadequate**, or when **focal lesions** are present. Performed under anesthesia; supports hysteroscopy and directed biopsy
MMR/MSI tumor testing	MMR-deficient (dMMR) or MSI-H tumor	**Universal testing** recommended at diagnosis. Identifies Lynch syndrome candidates and informs immunotherapy eligibility for advanced/recurrent disease

ABBREVIATIONS: NPV = Negative Predictive Value | TVUS = Transvaginal Ultrasound | D&C = Dilation and Curettage | MMR = Mismatch Repair | MSI-H = Microsatellite Instability-High | ACOG = American College of Obstetricians and Gynecologists | CI = Confidence Interval

CLINICAL PEARL — CARDINAL SYMPTOM

Clinical Pearl — Cardinal Symptom

Postmenopausal bleeding is the cardinal symptom of endometrial cancer — and the most preventable late-diagnosis scenario. Atrophic vaginitis is the most common cause of postmenopausal bleeding, but it is a concurrent finding, not a rule-out diagnosis.[27] The single most important behavior change: in any postmenopausal woman with bleeding, perform endometrial biopsy first — do not let a thin endometrial stripe, a known fibroid, or anticoagulation use defer tissue sampling.

Common Oversights

OVERSIGHT/SHORTCUT	WHY IT MATTERS — WHAT TO DO INSTEAD
Attributing postmenopausal bleeding to atrophic vaginitis without endometrial biopsy	**Atrophic vaginitis** is the most common cause of postmenopausal bleeding but **does not exclude malignancy**. Tissue sampling required regardless of presumptive atrophy diagnosis
Stopping at 'thin endometrial stripe (≤4 mm) — reassuring' in Black women	GUIDE-EC: 4-mm threshold has only 47.5% sensitivity in Black women vs 87.9% in White women. **Biopsy-first preferred**. Fibroids (more prevalent in Black women) further degrade ultrasound assessment quality
Attributing bleeding on anticoagulants to the medication	Genitourinary bleeding on anticoagulants carries HR 5.0 for concordant-site malignancy.[19] AUB on DOACs/warfarin in postmenopausal women still requires endometrial sampling
Defaulting to C55 or C54.9 when pathology specifies endometrial origin	Pathology that says 'endometrial adenocarcinoma' supports C54.1, not C55 or C54.9. **C55 is the most commonly overused** uterine cancer code; reserve for genuinely indeterminate cases

ABBREVIATIONS: GUIDE-EC = Guidance from Ultrasound for the Identification of Endometrial Cancer (study) | DOAC = Direct Oral Anticoagulant | AUB = Abnormal Uterine Bleeding | HR = Hazard Ratio

Key Differentials in Elderly

PRESENTATION	DIFFERENTIAL	KEY TESTS
Postmenopausal bleeding	Endometrial cancer **vs.** atrophic vaginitis; endometrial polyps; cervical cancer; cervical polyps; coagulopathy; uterine fibroids[16]	**Endometrial biopsy first**; TVUS as adjunct (but not as substitute); Pap if cervical screening due. Do not defer biopsy for endometrial stripe ≤4 mm in high-risk patient[10]

PRESENTATION	DIFFERENTIAL	KEY TESTS
AUB on anticoagulant in postmenopausal woman	Endometrial cancer (**HR 5.0** for concordant-site malignancy) **vs.** drug-related bleeding; uterine fibroids[19]	**Tissue sampling is still** required. Document **anticoagulation status and bleeding pattern**; coordinate INR/DOAC level with sampling timing[19]
Premenopausal AUB in obese woman ≥40	Endometrial hyperplasia/cancer (BMI ≥40 OR 19.79) **vs.** anovulation/PCOS; uterine fibroids; coagulopathy[21]	Endometrial biopsy preferred over TVUS. **TVUS thickness has no diagnostic value premenopausally**
Bleeding on tamoxifen	Endometrial cancer **(RR 2–7×)vs.** endometrial polyps (also tamoxifen-associated); atrophic changes[18]	**Mandatory** endometrial **biopsy**. Tamoxifen-related endometrial change does not exclude malignancy

ABBREVIATIONS: AUB = Abnormal Uterine Bleeding | TVUS = Transvaginal Ultrasound | PCOS = Polycystic Ovary Syndrome | OR = Odds Ratio | RR = Relative Risk | HR = Hazard Ratio | INR = International Normalized Ratio | DOAC = Direct Oral Anticoagulant

Comorbidity Screening

CONDITION	PREVALENCE IN THIS POPULATION	SCREENING APPROACH
Obesity	**57% of US endometrial cancers attributable**;[18] BMI ≥30 RR 2.5–5.0	Document at **every encounter** (E66.01, E66.811–813), counsel on weight management
Type 2 diabetes	**RR 1.89/HR 1.66** for endometrial cancer; complications worsen surgical and chemo outcomes[22,23]	**HbA1c every 3–6 months**; document E11.xx with complication specificity (E11.21 nephropathy, E11.40 neuropathy, etc.)
Metabolic syndrome	**HR 2.20** (95% CI 1.61–3.02)[23]	Address each component (**HTN, dyslipidemia, hyperglycemia, central adiposity**); generates frequent PCP visits — do not let cardiovascular focus eclipse gynecologic symptom evaluation
Atrial fibrillation on anticoagulation	AUB OR 1.81 in anticoagulant users;[28] bleeding may unmask malignancy (HR 4.0–5.0)	Document anticoagulation **type and indication**; AUB warrants endometrial sampling regardless of perceived drug attribution

ABBREVIATIONS: BMI = Body Mass Index | HbA1c = Glycated Hemoglobin | HTN = Hypertension | AUB = Abnormal Uterine Bleeding | OR = Odds Ratio | RR = Relative Risk | HR = Hazard Ratio | CI = Confidence Interval | HEDIS = Healthcare Effectiveness Data and Information Set

Staging/Severity Matrix

STAGE	THRESHOLD/ RANGE	CATEGORY	ACTION REQUIRED
Stage I	Tumor confined to corpus uteri (IA: <50% myometrial invasion; IB: ≥50% myometrial invasion)[1]	Localized — most common at presentation (~67–70%)	**TH/BSO + lymph node assessment**; **hysterectomy**, adjuvant therapy by **grade, LVSI, age, molecular subtype**. 5-year survival ~86%[1,29]
Stage II	Tumor invades cervical stroma (does not extend beyond uterus)	Locally advanced	**TH/BSO ± radical hysterectomy**; adjuvant RT ± systemic therapy. 5-year survival >75%)[1]
Stage III	Local/regional spread (IIIA: serosa/adnexa; IIIB: vagina/ parametria; IIIC: pelvic/para-aortic LN)	Regional	**Systemic therapy ± RT; sentinel or lymph node dissection**. 5-year survival >41%[1]
Stage IV	IVA: bladder/bowel mucosa; IVB: distant metastasis	Distant	Systemic therapy with **immunotherapy backbone** (pembrolizumab/dostarlimab + carbo/paclitaxel); **palliative radiation** as needed. 5-year survival >18%[1]

ABBREVIATIONS: TH/BSO = Total Hysterectomy with Bilateral Salpingo-Oophorectomy | LVSI = Lymphovascular Space Invasion | LN = Lymph Node | RT = Radiation Therapy | FIGO = International Federation of Gynecology and Obstetrics

⚠ RED FLAG — URGENT ACTION

- Heavy or persistent vaginal bleeding causing hemodynamic compromise, pre-syncope, or symptomatic anemia in a postmenopausal woman → **ED evaluation**
- Bowel obstruction or new severe pelvic pain in a known endometrial cancer patient → **same-da**y surgical/oncologic evaluation

⚠ RED FLAG — RAPID DECLINE

- Atypical glandular cells (AGC) on Pap; postmenopausal bleeding with elevated imaging findings (pelvic mass, ascites); or pathology returning endometrial intraepithelial neoplasia (EIN, N85.02) — ~40% concurrent endometrial cancer rate on hysterectomy → Same- or next-day gynecologic oncology referral[30]

AAVBC PERSPECTIVE

Unlike most gynecologic malignancies, ***uterine cancer symptoms appear early****. Postmenopausal bleeding is present in approximately 90% of uterine cancer cases, making it one of the most visible early warning signs in oncology. Yet mortality continues to rise, in part because the clinical reflex remains ultrasound-first rather than biopsy-first. A thin endometrial stripe does not exclude malignancy, and a negative office biopsy carries a 10% false-negative rate, two facts that must be embedded in primary care workflow, not left to specialist interpretation.* ***The AAVBC recommendation is direct: practices should establish a standing protocol that initiates endometrial biopsy as the primary diagnostic step for any patient presenting with postmenopausal bleeding, independent of imaging findings.***

3 MEAT DOCUMENTATION ESSENTIALS

Endometrial cancer documentation succeeds when it includes (1) the precise anatomic site (C54.1 over C54.9/C55), (2) histologic subtype and grade, (3) molecular classification when available (POLE/MMR/NSMP/p53), and (4) the comorbidities that drive disease risk and care complexity (obesity, diabetes, tamoxifen exposure, family history of Lynch-associated cancers)

A 68-year-old postmenopausal woman with BMI 34, type 2 diabetes (E11.9, A1c 7.4%), and a history of hormone-receptor-positive breast cancer treated with tamoxifen (active, 3 years) presents to PCP with two episodes of postmenopausal bleeding over the prior month. Family history notable for colorectal cancer (mother, age 62) and endometrial cancer (maternal aunt, age 70).

MONITOR: 'Vital signs stable; **BP 132/78**; weight 86.4 kg (**BMI 34.2**). **Hemoglobin 12.6 g/dL** (no anemia). **HbA1c 7.4%** — at goal but not optimized. Bleeding pattern: **2 episodes** of moderate vaginal bleeding over **4 weeks**, lasting 3–5 days each'

EVALUATE: **'Office endometrial biopsy** performed (**CPT 58100**). Results pending. Cervical exam and Pap (R10.30 not applicable; bleeding evaluation indication documented). Pelvic ultrasound ordered as adjunct — **endometrial stripe 8 mm'**

ASSESS: 'Postmenopausal bleeding (**N95.0**) under evaluation in a high-risk patient: tamoxifen use (**Z79.899**), obesity class I (**E66.01** — BMI 34), type 2 diabetes (**E11.9**), prior breast cancer (**Z85.3**), and family history of colorectal/endometrial cancer (**Z80.49**). Endometrial biopsy completed; histology pending. Concurrent differential includes endometrial atrophy, polyp, and malignancy — **biopsy-first approach** selected given high-risk profile'

TREAT: 'Patient counseled on biopsy-first rationale. If histology confirms endometrial cancer or atypical hyperplasia, **urgent gynecologic oncology referral** will be placed; pathology to include **MMR immunohistochemistry**. **Continue tamoxifen** per oncology direction pending biopsy result. **Follow-up scheduled within 7 days** to review pathology and discuss next steps. If biopsy returns negative but bleeding persists or recurs, will **refer for D&C'** (**~10% false-negative** rate of office Pipelle)

Clinical Documentation Elements

- **Link clinical relationships:** Document tamoxifen status (Z79.899) AND bleeding evaluation in the same encounter — postmenopausal bleeding on tamoxifen is not a tamoxifen side effect, it is a malignancy workup. The same applies to anticoagulation: AUB on warfarin or DOAC is not exonerating
- **Include current data:** Note BMI/obesity class with date, A1c with date, tamoxifen duration, anticoagulation type and indication, and any prior endometrial sampling results. Surveillance for Lynch carriers requires dated annual biopsy and TVUS evidence
- **Specify precisely:** Document anatomic site (C54.1 over C54.9/C55), histologic subtype, FIGO stage with sub-stage, grade, lymphovascular space invasion (LVSI), depth of myometrial invasion, and molecular classification (POLE, MMR-deficient, NSMP, p53-abnormal) when available
- **Document chronicity:** Use C54.x while active; transition to Z85.42 once curative treatment is complete and patient is in surveillance with no evidence of disease per oncology
- **Associated conditions:** Co-document obesity class (E66.01–E66.813), type 2 diabetes with complications (E11.xx), metabolic syndrome components, tamoxifen exposure (Z79.899), prior breast cancer (Z85.3), Lynch susceptibility (Z15.04), and family history (Z80.49) — each is clinically meaningful and many carry independent HCC implications

Reframing Common Documentation Shortcuts

INSTEAD OF…	DOCUMENT…
'Uterine cancer'/'cancer of uterus'/C55	'Endometrial adenocarcinoma, FIGO Stage IB, grade 1, LVSI absent (C54.1) — molecular subtype: NSMP (no specific molecular profile).' Use C54.1 when pathology specifies endometrial origin
'Postmenopausal bleeding — likely atrophy'	'Postmenopausal bleeding (N95.0) — endometrial biopsy ordered to exclude malignancy. Concurrent atrophic vaginitis possible but does not rule out malignancy in this age group'
'On tamoxifen — bleeding likely related'	'Postmenopausal bleeding on tamoxifen (Z79.899). Tamoxifen increases endometrial cancer risk 2–7×; endometrial biopsy performed regardless of presumptive drug attribution'
'On warfarin — bleeding from anticoagulation'	'AUB on warfarin (Z79.01). Anticoagulation may unmask malignancy; endometrial biopsy ordered. Genitourinary bleeding on anticoagulants HR 5.0 for concordant-site malignancy'

ABBREVIATIONS: FIGO = International Federation of Gynecology and Obstetrics | LVSI = Lymphovascular Space Invasion | NSMP = No Specific Molecular Profile | MMR = Mismatch Repair | dMMR = MMR-deficient | IHC = Immunohistochemistry | AUB = Abnormal Uterine Bleeding | HR = Hazard Ratio

DOCUMENTATION IS COMPREHENSIVE CODING

C54.1 over C55 is a documentation choice, not a coding optimization — it reflects the actual pathology and supports the clinical record. Adding the comorbidities that drove the cancer (obesity, diabetes, tamoxifen) and the family history that informs cascade testing is how the chart represents this patient as she actually is.

4 TREATMENT AND REFERRAL QUICK GUIDE

Endometrial cancer treatment is specialist-led and primarily surgical for early-stage disease. The PCP role is concentrated at the front end — biopsy-first evaluation of postmenopausal bleeding — and at the back end — comorbidity co-management, surveillance, and Lynch syndrome cascade testing.

Standard Treatment Pathway

TREATMENT CATEGORY	KEY CONSIDERATIONS
Total hysterectomy (BSO + cervix)	**Standard curative surgery** for Stage I–II. Sentinel lymph node biopsy is now standard for staging. Minimally invasive approach preferred when feasible[31]
Radiation therapy (EBRT/ brachytherapy)	**Adjuvant radiation for intermediate/high-risk** Stage I–II. Brachytherapy reduces vaginal vault recurrence. PCP role: coordinate follow-up and monitor late effects[32]
Chemotherapy (carboplatin + paclitaxel)	Standard for **Stage III–IV and high-risk** histologies. Molecular subtype now guides which patients receive chemotherapy vs. radiation vs. combined modality[33]
Hormone therapy (progestin)	Option for **low-grade**, hormone-receptor-positive recurrent disease. Also used as **fertility-sparing** treatment under **strict criteria**[34]
Immunotherapy (pembrolizumab, lenvatinib)	**FDA-approved** for **dMMR/MSI-H** recurrent disease. PCP role: document Lynch syndrome history and MMR/MSI testing results to support immunotherapy eligibility[35]
POLE/p53-guided treatment modification	**POLE-mutated** tumors **may de-escalate adjuvant therapy**; **p53-abnormal** tumors escalate to **platinum-based** chemo. Molecular documentation in the record is essential[36]

ABBREVIATIONS: BSO = Bilateral Salpingo-Oophorectomy | EBRT = External Beam Radiation Therapy | PCP = Primary Care Provider | dMMR = Mismatch Repair-Deficient | MSI-H = Microsatellite Instability-High | MMR = Mismatch Repair | MSI = Microsatellite Instability | POLE = Polymerase Epsilon | FDA = Food and Drug Administration | NCCN = National Comprehensive Cancer Network | FIGO = International Federation of Gynecology and Obstetrics

Therapy Escalation Criteria

TRIGGER	ACTION
Postmenopausal bleeding (any episode)	PCP — Office endometrial **biopsy (Pipelle) plus TVUS** as adjunct. **Do not defer biopsy** on the basis of thin endometrial stripe in high-risk patients (Black women, anticoagulated patients, tamoxifen users)
Office biopsy fails (cervical stenosis or insufficient tissue)	PCP/Specialist — Refer for D&C under anesthesia, ultrasound-guided **transvaginal biopsy**, or **hysteroscopy with directed biopsy**. Document failed attempt and clinical reasoning
Histology confirms endometrial carcinoma or atypical hyperplasia (EIN)	Specialist — **Urgent gynecologic oncology referral**; MMR immunohistochemistry on tumor mandatory. EIN carries 42.6% concurrent malignancy rate on hysterectomy[1]
Newly identified dMMR/MSI-H tumor	PCP/Genetics — Refer for genetic counseling for **Lynch syndrome** assessment; document Z15.04 if germline confirmed. Cascade testing for first-degree relatives

ABBREVIATIONS: TVUS = Transvaginal Ultrasound | D&C = Dilation and Curettage | EIN = Endometrial Intraepithelial Neoplasia | MMR = Mismatch Repair | dMMR = MMR-deficient | MSI-H = Microsatellite Instability-High | pMMR = MMR-proficient | NCCN = National Comprehensive Cancer Network

NCCN Aligned Recommendations

CATEGORY	RECOMMENDED AGENT/ APPROACH*	NOTES
First-line systemic therapy (Stage III–IV/recurrent, all histology except carcinosarcoma)	Carboplatin + paclitaxel + pembrolizumab	NRG GY018: MMR-D PFS HR 0.30; pMMR **PFS HR 0.54**.[37] **Mandatory MMR testing** on all newly diagnosed EC
First-line — alternative immunotherapy backbone	Carboplatin + paclitaxel + dostarlimab	RUBY/ENGOT-EN6: MMR-D **PFS HR 0.28**[38]
HER2-positive uterine serous carcinoma or carcinosarcoma	Carboplatin + paclitaxel + trastuzumab	**HER2 testing** recommended on serous carcinoma and carcinosarcoma[39]
pMMR recurrent disease (post-platinum)	Lenvatinib + pembrolizumab	Study 309/KEYNOTE-775: PFS and OS improvement[40] vs treatment of physician's choice

CATEGORY	RECOMMENDED AGENT/ APPROACH*	NOTES

ABBREVIATIONS: PFS = Progression-Free Survival | OS = Overall Survival | HR = Hazard Ratio | MMR = Mismatch Repair | dMMR = MMR-deficient | pMMR = MMR-proficient | MSI-H = Microsatellite Instability-High | EC = Endometrial Cancer | NCCN = National Comprehensive Cancer Network* **Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Non-Pharmacologic Treatment and Lifestyle Modification

INTERVENTION	TARGET/RECOMMENDATION	NOTES
Weight management	Address obesity with all uterine cancer patients and high-risk individuals	**57%** of US endometrial cancers are attributable to **obesity**. **Counseling**, **dietary referral, weight-management pharmacotherapy, or bariatric referral** when appropriate
Comprehensive Geriatric Assessment (CGA)	ACCI ≤4 supports standard-intensity treatment; **ACCI >4** prompts **treatment modification**	**ACCI >4** is the strongest predictor of postoperative complications[41] and reduced overall survival (HR 2.24)
Lynch syndrome cascade testing	All endometrial cancers should have MMR immunohistochemistry; dMMR results trigger genetic counseling	Universal tumor testing identifies **~63% of Lynch** cases that **family history alone misses**.[42] Cascade testing benefits first-degree relatives
Diabetes optimization	HbA1c at goal pre-operatively when feasible	**Diabetes** carries adjusted HR 2.9 for mortality in Stage I endometrial cancer;[22] optimize before surgery and during adjuvant treatment

ABBREVIATIONS: ACCI = Age-Adjusted Charlson Comorbidity Index | CGA = Comprehensive Geriatric Assessment | MMR = Mismatch Repair | dMMR = MMR-deficient | HR = Hazard Ratio | HbA1c = Glycated Hemoglobin

Non-Pharmaceutical Prevention Strategies

Endometrial cancer prevention is anchored in weight management — obesity accounts for 57% of cases in the US, and intentional weight loss of ≥5% reduces risk by 39% (HR 0.61). Bariatric surgery offers the greatest single intervention effect, reducing risk by up to 68%. Physical activity independently contributes a 20% risk reduction, with the highest population-attributable fraction of any cancer type. Oral contraceptive use for ≥10 years reduces risk by 30–40%, with protection persisting for decades after cessation. Unopposed estrogen therapy should be avoided in women with an intact uterus. For Lynch syndrome carriers, annual endometrial biopsy beginning at age 35–40 and prophylactic hysterectomy after childbearing is complete represent the standard of care. No population-level screening is recommended in average-risk women.[1,13,15,16]

Medication Safety and Dose Adjustments

DRUG/CLASS	INTERACTION/CONTRAINDICATION	CLINICAL ACTION
Carboplatin/paclitaxel + pembrolizumab	Immune-related adverse events (thyroiditis, hepatitis, pneumonitis, colitis); chemotherapy cytopenias and neuropathy[37]	Baseline **thyroid** panel, **hepatic** function; monitor for **irAEs** and hold/treat per oncology. Cumulative **paclitaxel neuropathy in elderly** — assess at every visit
Tamoxifen (concurrent or prior breast cancer Rx)	Endometrial cancer risk **2–7×**; postmenopausal AUB	Endometrial sampling for **any AUB on tamoxifen** — do not attribute to the drug. Annual gynecologic surveillance
Anticoagulants (warfarin, DOACs)	AUB OR 1.81; postmenopausal bleeding may unmask malignancy (HR 5.0 for concordant-site)[28]	Endometrial sampling for AUB; coordinate **INR/DOAC** level with biopsy timing. Document anticoagulation indication
Lenvatinib + pembrolizumab (recurrent pMMR)	Hypertension, proteinuria, irAEs[40]	**BP** at every visit; **weekly during titration**. **Urinalysis** for proteinuria. Coordinate with oncology for dose modifications

ABBREVIATIONS: irAE = Immune-related Adverse Event | AUB = Abnormal Uterine Bleeding | DOAC = Direct Oral Anticoagulant | OR = Odds Ratio | HR = Hazard Ratio | BP = Blood Pressure | INR = International Normalized Ratio | pMMR = MMR-proficient

When to Refer

CRITERION	SPECIALIST	URGENCY
Postmenopausal bleeding (any episode) where office biopsy fails or is non-diagnostic	Gynecology/gynecologic oncology	Urgent — within 1–2 weeks
Histologic confirmation of endometrial cancer or atypical hyperplasia (EIN)	Gynecologic oncology	Urgent — within 1 week
dMMR/MSI-H result on tumor IHC	Genetic counseling; gynecologic oncology	Routine — within 4 weeks
Suspected immune-related adverse event during checkpoint inhibitor therapy	Treating oncology team	Urgent/emergent depending on grade

ABBREVIATIONS: EIN = Endometrial Intraepithelial Neoplasia | dMMR = MMR-deficient | MSI-H = Microsatellite Instability-High | IHC = Immunohistochemistry

Follow-Up Timing

STAGE/CATEGORY	FREQUENCY	LABS TO MONITOR
On active treatment (systemic therapy)	Per oncology protocol (typically every 3 weeks)	CBC, comprehensive metabolic, BP, thyroid (if checkpoint inhibitor), hepatic function; toxicity assessment
Post-curative surveillance (Stage I–III, in remission)	Every 3–6 months × 2 years; every 6–12 months × years 3–5; annually thereafter[43]	**Symptom-directed exam**; pelvic exam; vaginal cytology not routinely required. CA-125 not routinely used; imaging only for suspected recurrence
Lynch syndrome surveillance (carrier, no cancer)	Annual endometrial biopsy + TVUS from age 30–35[13]	Per NCCN Genetic v1.2025; **coordinate with colonoscopy** schedule for synchronous **Lynch** cancers
Long-term survivor	Annual	**Cardiovascular risk reassessment**; bone health (especially after surgical menopause); survivorship goals-of-care; continued comorbidity optimization

ABBREVIATIONS: CBC = Complete Blood Count | BP = Blood Pressure | TVUS = Transvaginal Ultrasound | CA-125 = Cancer Antigen 125 | NCCN = National Comprehensive Cancer Network

Comorbidity Management

COMORBIDITY	APPROACH	CAUTION
Obesity	BMI documented at every encounter; counseling; consider weight-management pharmacotherapy or bariatric referral	**Obesity** is the largest population-attributable **risk factor** (57%) AND a **surgical-risk modifier**; addressing it benefits cancer outcomes and overall health[21]
Type 2 diabetes	HbA1c at goal pre-operatively when feasible; document complication-specific E11.xx codes[22]	Diabetes adjusted HR 2.9 for mortality in Stage I endometrial cancer; optimize before surgery and during chemotherapy
Anticoagulation	Coordinate INR/DOAC level with planned biopsy or surgery timing	**Anticoagulation does not exonerate** AUB — sampling required regardless. Document type, indication, and bleeding pattern[28]
Cardiovascular disease	BP at every visit; particular attention with lenvatinib (HTN risk)[40]	Manage **HTN** to goal during **VEGF-pathway therapy**; address dyslipidemia and metabolic syndrome components

COMORBIDITY	APPROACH	CAUTION

ABBREVIATIONS: BMI = Body Mass Index | HbA1c = Glycated Hemoglobin | INR = International Normalized Ratio | DOAC = Direct Oral Anticoagulant | AUB = Abnormal Uterine Bleeding | HR = Hazard Ratio | BP = Blood Pressure | HTN = Hypertension | VEGF = Vascular Endothelial Growth Factor

Cost-Smart Options

BRAND (EST. COST)	GENERIC/ALTERNATIVE (EST. COST)	EST. MONTHLY SAVINGS	COST-SMART TIP
Pembrolizumab (Keytruda)	No biosimilar available	—	**Patient-assistance** programs and **Medicare Part D** LIS may reduce out-of-pocket; coordinate with oncology pharmacy
Lenvatinib (Lenvima)	No generic/biosimilar available	—	Manufacturer support programs; consider **Patient Access Network** or specialty pharmacy support
Tamoxifen (Solmatox; oral solution, Nolvadex; tablet form—discontinued)	Soltamox — ~$685/150ml (brand-name oral solution, no generic available)[44] Generic tamoxifen tablets — ~$43/100 tablets[45]	~$700 by switching from Soltamox to generic tablets (where clinically appropriate — tablets vs. solution)	**Already low-cost**; ensure fill consistency; reinforce that bleeding on tamoxifen requires sampling not discontinuation

ABBREVIATIONS: LIS = Low-Income Subsidy | Rx = Prescription

AAVBC PERSPECTIVE

AAVBC recognizes that timely, ***targeted patient education is essential to early detection and improved outcomes in uterine cancer.*** *Postmenopausal bleeding is a cancer symptom until tissue sampling proves otherwise; patient education should reinforce that a normal ultrasound does not clear the patient. Risk counseling should cover obesity, diabetes, Tamoxifen use, and Lynch syndrome, as germline mutations confer risk independent of BMI. Treatment planning in older adults requires Comprehensive Geriatric Assessment over chronological age, with prehabilitation addressed prior to surgical referral. Documentation should capture anatomic coding specificity (C54.1), molecular subtype findings, complete FIGO staging components, and post-treatment surveillance activity to support quality metrics.*

QUALITY OUTCOME

There is no direct HEDIS, MIPS or CMS Star Rating measure for uterine cancer. Indirect measures (CCS with AGC follow-up, BCS, COL, BMI) document care-quality elements that materially affect detection and outcomes. The most impactful protocol shift: move from imaging-first to biopsy first for postmenopausal bleeding. A transvaginal ultrasound stripe under 4 mm does not exclude malignancy. Tissue sampling is the primary diagnostic step. The 2026 ACOG and NCCN guidelines highlight to initiate endometrial biopsy directly. If the office biopsy is negative but bleeding persists, refer promptly for fractional D&C.[16]

DOCUMENTATION

Treatment intensity (full surgical staging vs. modified hysterectomy vs. non-surgical approach) is supported by frailty documentation. Document ACCI components and CGA findings: ADL/IADL, nutritional status, polypharmacy review, cognitive screen — these explain treatment plans and support oncology continuity.

5 CODING REMINDERS AND CASE EXAMPLES

Documentation Specificity

- **Stage/Severity:** Document **FIGO stage and sub-stage** (e.g., IA, IB, IIIC), **grade (G1–G3)**, **histologic subtype** (endometrioid, serous, clear cell, carcinosarcoma), **depth of myometrial invasion**, **lymphovascular space invasion (LVSI)**, and **lymph node status**
- **Etiology:** Include **molecular classification** when available: **POLE-mutated**, **MMR-deficient**, **NSMP**, or **p53-abnormal**. Molecular subtype increasingly informs prognosis and treatment. A “low-grade endometrioid” tumor that is **p53-abnormal** behaves aggressively regardless of histologic grade
- **Current status:** Document the **most recent treatment**: surgery date, adjuvant therapy line/cycle, surveillance status, **MMR/MSI tumor result**, and active comorbidities affecting management. For surveillance patients, include the **last symptom-directed evaluation** and any imaging
- **Associated conditions:** Capture clinically relevant associated factors, including **obesity class** (E66.01–E66.813), **diabetes with complication specificity** (E11.xx), **tamoxifen exposure** (Z79.899), **prior breast cancer** (Z85.3), **Lynch susceptibility** (Z15.04), **family history of Lynch-associated cancers** (Z80.49), and any **treatment-related toxicities**

- **Chronicity:** Use **C54.x** — or **C55** only when truly indeterminate — while disease is active. Transition to **Z85.42** once the patient is in surveillance with no active disease per oncology. Do not maintain an active malignancy code for a patient in remission

Annual Clinical Review and Confirmation

- **Annual review:** An **active uterine cancer diagnosis** must be reassessed annually with a **face-to-face** or **synchronous audio-video visit**, with **MEAT documented by 12/31** Use **C54.x** — preferably **C54.1** for endometrial origin — while disease is active; transition to **Z85.42** with confirmed remission
- **Visit modality: In-person** or **video telehealth** qualifies when meaningful evaluation occurs, including **symptom review**, **surveillance status**, **comorbidity assessment**, and **treatment toxicity screening**
- **Clinical context:** Under **HCC V28**, all **C54.x** and **C55** codes map to **HCC 23** (RAF **0.186**); pelvic lymph node and genital-organ metastases (**C77.5**, **C79.82**) map to **HCC 18** (RAF **2.341**); and peritoneal, liver, or lung metastases (**C78.6**, **C78.7**, **C78.0x**) map to **HCC 17** (RAF **4.209**) Documentation precision matters at the **C54.x level** — **C54.1 over C55** when endometrial origin is known — and through clear comorbidity documentation, not through HCC tier alone
- **Avoid rollover:** Do not copy forward the prior year's note Update **treatment status**, **surveillance findings**, **MMR/MSI results**, **current comorbidities**, and any new evidence of **recurrence**

Good Documentation is Comprehensive Coding

EHR SHORTCUT/RISK	PREFERRED DOCUMENTATION LANGUAGE
Defaulting to C55 ('uterus part unspecified') when pathology specifies endometrial origin	Use **C54.1** when pathology says '**endometrial adenocarcinoma**.' **C55** reserved for **genuinely indeterminate** cases
Carrying forward C54.9 once the pathology specifies subsite	Replace with the **specific corpus subsite** (C54.0 isthmus, C54.1 endometrium, C54.2 myometrium, C54.3 fundus, C54.8 overlapping) once documentation supports
Maintaining C54.x after curative treatment ends	Transition to **Z85.42** (Personal history of malignant neoplasm of other parts of uterus) once oncology confirms remission. C54.x should not persist on a surveillance patient
Coding 'metastatic uterine cancer' without site-specific codes	Document each **metastatic site individually**: pelvic LN (C77.5), genital organs (C79.82), peritoneum (C78.6), liver (C78.7), lung (C78.0x). Site determines HCC tier

EHR SHORTCUT/RISK	PREFERRED DOCUMENTATION LANGUAGE
Omitting comorbidities that drove the cancer	Add E66.xx (**obesity class**), E11.xx (**diabetes with complication** codes), Z79.899 (**tamoxifen**), Z85.3 (prior breast cancer), Z80.49 (**family history of genital organ cancer**), Z15.04 (**Lynch** susceptibility) — each is clinically meaningful

ABBREVIATIONS: HCC = Hierarchical Condition Category | LN = Lymph Node | BRCA = BReast CAncer gene | MMR = Mismatch Repair

Brief Case Examples

✓ SUCCESS — COMPREHENSIVE DOCUMENTATION

SCENARIO | 68-year-old postmenopausal woman with BMI 34, type 2 diabetes (E11.9), hormone-receptor-positive breast cancer history on tamoxifen for 3 years (Z79.899, Z85.3), and family history of colorectal (mother) and endometrial (aunt) cancer (Z80.49). Presents with two episodes of postmenopausal bleeding over 4 weeks.

PATIENT

| Stable hemodynamics; A1c 7.4%; recent breast cancer surveillance current.

DOCUMENTATION

| PCP documented: 'Postmenopausal bleeding (N95.0) in a high-risk patient — tamoxifen exposure (Z79.899), prior breast cancer (Z85.3), obesity class I (E66.01, BMI 34), type 2 diabetes (E11.9), and Lynch-relevant family history (Z80.49). Office endometrial biopsy performed (58100) per biopsy-first protocol; not deferring on TVUS findings or tamoxifen attribution. MMR IHC ordered on tissue. Pathology pending.' Pathology returned: endometrial adenocarcinoma, grade 1, MMR-deficient.

OUTCOME

| Same-week gynecologic oncology referral; staging surgery confirmed FIGO Stage IA, grade 1, MMR-deficient, NSMP-equivalent. Genetic counseling: confirmed MSH2 pathogenic variant (Lynch syndrome). Coding documented C54.1 (HCC 23), Z15.04, E66.01, E11.9, Z79.899, Z85.3 — full representation of clinical complexity. Cascade testing offered to first-degree relatives.

⚠ PITFALL — INSUFFICIENT DOCUMENTATION

DOCUMENTATION AS WRITTEN | '68-year-old on tamoxifen with light vaginal spotting. Reassured patient — likely tamoxifen-related. Will reassess in 3 months.' No biopsy ordered. Coded with N95.0 only.

CONSEQUENCE

| Patient returns 6 months later with heavier and more frequent bleeding. Repeat encounter still attributes bleeding to tamoxifen; biopsy deferred a second time. Patient self-refers to gynecology 4 months later — endometrial biopsy returns serous carcinoma, FIGO Stage IIIC1 (pelvic LN+) at diagnosis (~10 months from initial presentation).

RAF IMPACT

| Initial encounters documented only N95.0 (no HCC). After diagnosis, the chart must document C54.1 (HCC 23, RAF 0.186), C77.5 (HCC 18, RAF 2.341 for pelvic LN metastasis), Z79.899 (tamoxifen), Z85.3 (prior breast cancer), and obesity/diabetes comorbidity codes. The clinical cost is greater: Stage IA grade 1 disease has 5-year survival ~95%; Stage IIIC serous carcinoma has substantially worse expected outcome.

FIX

| Postmenopausal bleeding on tamoxifen REQUIRES endometrial biopsy. Tamoxifen is a risk-factor for endometrial cancer (RR 2–5×), not an exonerating cause. The biopsy-first protocol applies regardless of presumptive drug or atrophy attribution.

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