AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Renal Cancer

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: **Renal cell carcinoma** (**RCC**) is a malignancy arising from the renal tubular epithelium and accounts for the large majority of adult kidney cancers.[1] In the Medicare population it is predominantly a disease of **silent presentation**: more than **60%**[1] of cases are discovered incidentally on abdominal imaging ordered for unrelated reasons, and the classic triad of flank pain, hematuria, and a palpable mass now occurs in fewer than **10%** of patients.[1,2] **Clear cell RCC** is the most common histology (**70-80%** of RCC), followed by papillary (**10-15%**) and chromophobe (**3-5%**) subtypes; each carries distinct biology and treatment implications.[1] Urothelial carcinoma of the renal pelvis is a **separate disease with a** distinct histology and treatment pathway, and is coded under **C65** rather than **C64**.[2,3] Peak incidence falls in the **65-74** age band, placing RCC squarely within primary-care and geriatric oncology practice.[1]

ICD-10 Codes:

Active RCC of the kidney parenchyma is reported with **laterality-specific codes**:[3] **C64.1** (right kidney) and **C64.2** (left kidney); **C64.9** (unspecified laterality) should be used only when laterality is **genuinely undocumented** after review of imaging and operative reports. Renal pelvis tumors (urothelial, not RCC) use **C65.1** (right) and **C65.2** (left) = a distinct anatomic site and histology that is **commonly miscoded as C64**. Metastatic spread to the kidney is captured with **C79.0-** secondary-neoplasm codes, and every confirmed metastatic site is coded separately (for example **C78.00** lung, **C79.51** bone, **C78.7** liver, **C79.31** brain) in addition to the primary **C64.x** code. Presenting hematuria is documented with **R31.0** (gross) or **R31.21** (asymptomatic microscopic). **Z85.528** (personal history of kidney malignancy) is reserved for patients who have **completed treatment with no evidence of disease**; it must not be used while a patient is **on adjuvant therapy or under active surveillance**, where the active **C64.x** code applies.[3,4]

Prevalence and Burden: An estimated ~**81,000** new kidney cancer diagnoses are expected in the United States for 2025, with approximately **735,000 people** living with a prior kidney cancer diagnosis as of January 1, 2025.[5] SEER data show that RCC incidence has been increasing at approximately **1.1% annually** (95% CI: 0.6%–1.5%) from 2008 to 2019, with projected continued increases from **6.92 per 100,000** (2015–2019) to **9.59 per 100,000** by 2040–2044.[6] Peak incidence occurs between ages **60 and 70 years**, with the highest age-standardized incidence rates in individuals aged **70–84 years**.[1,7] About **49%** of U.S. kidney cancer diagnoses occur in adults aged **65 and older**, and approximately 67% of kidney cancer survivors are aged ≥65.[1,5] At presentation, **70%** of cases are **Stage I** and **11%** are **Stage IV**.[1] Five-year relative survival is **stage-dependent**: approximately **93%** for localized disease, **75%** for regional disease, and **17–18%** for distant (Stage IV) disease.[8] The male-to-female ratio is approximately **3:2**.[1] Because incidence rises steeply with age, most disease is found **incidentally** (37–61% of cases), and modifiable risk factors such as hypertension, obesity, and smoking are shared with conditions managed in routine primary care, RCC detection and management are increasingly a **shared primary-care responsibility**.[1]

HCC/RAF V28 Mapping

ICD-10 CODE(S)[3]	HCC CATEGORY (V28)[9]	RAF (CNA)*[10]	DOCUMENTATION REQUIREMENT[3,4,11,12]
C64.1/C64.2 Malignant neoplasm of right/ left kidney, except renal pelvis	**HCC 22** Prostate/ Breast/**Other Cancers** and Tumors	0.363	**Active primary RCC confirmed by pathology**; specify laterality (right or left) = **avoid C64.9** unless laterality is truly unknown; document **histologic subtype** (clear cell, papillary, chromophobe, etc.) and **AJCC 8th Edition stage**; state "**carcinoma**," not "mass" or "lesion"
C65.1/C65.2 Malignant neoplasm of right/ left renal pelvis	**HCC 22** Prostate/ Breast/**Other Cancers** and Tumors	0.363	**Distinct from C64**: document renal pelvis origin and urothelial histology; **not RCC**; specify laterality; if urothelial carcinoma is suspected (e.g., central mass), urine cytology or ureteroscopy may support coding
C78.01/ C78.02/ C78.00 Secondary malignant neoplasm of right/ left/ unspecified lung	**HCC 17** Cancer Metastatic to **Lung**/Liver/ Brain	4.209	Lung is the most common RCC metastatic site (**~70%**); specify laterality: use **C78.01** (right) or **C78.02** (left) when known; **C78.00 only if laterality is undetermined**; sequence **after C64.x**; document imaging confirmation
C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct	**HCC 17** Cancer Metastatic to Lung/**Liver**/ Brain	4.209	Liver metastases occur in **~18%** of mRCC; sequence **after C64.x**; document imaging or biopsy confirmation; note association with poor prognosis (median CSS ~14 months)
C79.31 Secondary malignant neoplasm of brain	**HCC 17** Cancer Metastatic to Lung/Liver/ **Brain**	4.209	Brain metastases occur in **~8%** of mRCC (more common in clear cell subtype); sequence **after C64.x**; document location, number of lesions, and imaging modality; **brain MRI recommended** when clinically indicated
C79.51 Secondary malignant neoplasm of bone	**HCC 18** Cancer Metastatic to **Bone**/Other	2.341	Bone metastases occur in **~32%** of mRCC; document specific bone site(s) involved; sequence **after C64.x**; specify method of detection (bone scan, PET/CT, MRI) and whether pathologic fracture is present
C79.71/C79.72/ C79.70 Secondary malignant neoplasm of right/ left/ unspecified adrenal gland	HCC 18 Cancer Metastatic to Bone/**Other**	2.341	Adrenal metastases occur in **~10%** of mRCC; specify laterality; distinguish from **direct T4 invasion** (which remains C64.x with T4 staging); sequence **after C64.x**

ICD-10 CODE(S)[3]	HCC CATEGORY (V28)[9]	RAF (CNA)*[10]	DOCUMENTATION REQUIREMENT[3,4,11,12]
C77.2 Secondary malignant neoplasm of intra-abdominal lymph nodes	**HCC 18** Cancer Metastatic to Bone/**Other**	2.341	Lymph node metastases occur in **~45%** of mRCC; must be coded alongside **C64.x** when confirmed; document specific nodal station(s) involved and method of confirmation (pathology, imaging)
Z85.528 Personal history of other malignant neoplasm of kidney	No HCC	—	**AVOID for active disease**: Use **ONLY after** definitive treatment with no evidence of disease; patients on active surveillance, adjuvant therapy, or with detectable recurrence retain **C64.x**
D41.01/D41.02/ D41.00 Neoplasm of uncertain behavior of right/left/ unspecified kidney	No HCC	—	**AVOID premature C64**: Use for indeterminate renal masses pending surgical pathology or biopsy; convert to **C64.x** only after confirmed malignancy; specify laterality

ABBREVIATIONS: ICD-10 = International Classification of Diseases, 10th Revision; HCC = Hierarchical Condition Category; RAF = Risk Adjustment Factor; CNA = Community Non-Dual Eligible, Aged; RCC = renal cell carcinoma; AJCC = American Joint Committee on Cancer; CT = computed tomography; PET/CT = positron emission tomography/computed tomography; MRI = magnetic resonance imaging; mRCC = metastatic renal cell carcinoma; CSS = cancer-specific survival; AS = active surveillance

***RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model;[10] values vary across patient populations based on eligibility and care setting**

Risk-Adjusted Care Resources per Patient/Year[9,10]

Risk-adjusted care resource allocation — MA base rate (~$10,402.34) × RAF coefficient

PRIMARY RCC AND UCC	METASTATIC BRAIN/LIVER/LUNG	METASTATIC BONE/ LYMPH NODE
$3.8K	~$48K	~$28K

AAVBC PERSPECTIVE

***From the AAVBC's perspective**, value-based care in renal cell carcinoma requires shifting primary care from passive recognition to **accountable diagnostic stewardship**, while recognizing that contemporary RCC guidelines are derived largely from younger, healthier surgical populations and provide **limited evidence** for the older, medically complex adults who comprise much of the Medicare Advantage population.[4] The central failure is **not missed symptoms alone**, but **failure to act** on hematuria or incidental renal masses with timely, guideline-concordant follow-up.*

*PCPs should treat visible hematuria—or clinically significant microscopic hematuria in adults >60 years—as a trigger for a **formal suspected renal cancer pathway**, initiating contrast-enhanced CT (or MRI when appropriate) and timely urologic referral rather than attributing findings to urinary tract infection, nephrolithiasis, or other benign causes. Urinalysis is a **trigger tool**, not a diagnostic endpoint, and repeated hematuria substantially increases the likelihood of underlying malignancy.*

*Equally important is avoiding reflexive treatment of every detected renal mass. Many small renal masses (≤4 cm) are **biologically indolent or benign**, and among older adults with substantial competing comorbidity, non-cancer mortality frequently **exceeds RCC-specific mortality**. For appropriately selected patients with T1a disease, **active surveillance and thermal ablation** are NCCN-supported alternatives with cancer-specific survival comparable to surgery.[4,13] **The value-based objective** is therefore to eliminate failures in diagnostic follow-up while avoiding unnecessary intervention through individualized, risk-based management **in partnership with urology**.*

2 RECOGNITION AND DIAGNOSIS

No major medical organization recommends **population-wide screening for renal cell carcinoma** in asymptomatic adults. The USPSTF **does not recommend screening for hematuria** as a marker of occult urinary tract cancer, citing inadequate evidence that benefits outweigh harms.[14] The **American College of Physicians** similarly advises against routine urinalysis for cancer detection in asymptomatic patients.[15] The relatively low prevalence of RCC in untargeted populations (**0.10–0.22%**) limits the cost-effectiveness of population screening.[16,17] **This recommendation does not apply to patients with**: hematuria (visible or microscopic), incidental renal masses on imaging, hereditary RCC syndromes, or other clinical findings warranting evaluation.

Diagnostic Tests Covered Under Medicare Part B (Older Adults, At-Risk Population)

TEST	FREQUENCY	CPT/ HCPCS	CLINICAL INDICATION
Urinalysis with microscopy: hematuria confirmation	**At symptom trigger**; confirm dipstick-positive heme with microscopy **before referral**	81001	**Confirm ≥3 RBC/HPF on microscopic UA** before initiating workup; dipstick alone is **insufficient**[15,18]

TEST	FREQUENCY	CPT/ HCPCS	CLINICAL INDICATION
Renal/bladder ultrasound: intermediate-risk hematuria	Per AUA/SUFU risk stratification	76770/ 76775	**Intermediate-risk MH** (men 40–59, women 50–59, 11–25 RBC/HPF, 10–30 pack-years): renal US + cystoscopy recommended; US **avoids radiation/ contrast** while maintaining high NPV for cortical lesions[18]
CT urography (CT abdomen/pelvis without then with contrast): high-risk hematuria	Per AUA/SUFU risk stratification	74178	**High-risk MH** (age ≥60, >25 RBC/HPF, >30 pack-years, or prior gross hematuria): CT urography + cystoscopy; pooled sensitivity 96%, specificity 99% for upper tract malignancy[18,19]
CT abdomen/pelvis with and without contrast (renal protocol): incidental renal mass workup	**At mass detection**; dedicated renal-protocol imaging	74178	Any **solid enhancing renal mass ≥1 cm** detected incidentally requires dedicated renal-protocol CT or MRI and urology referral; **>60%** of RCC is found incidentally[1,4]
MRI abdomen without then with contrast: renal mass characterization	**At mass detection** or for contrast-allergic/ CKD patients	74183	**Alternative to CT** for renal mass characterization; preferred when CT is contraindicated (contrast allergy, CKD with eGFR <30); also preferred for **hereditary RCC surveillance** to minimize radiation[4]
CT abdomen/pelvis with and without contrast: active surveillance imaging	**Within 6 mo** of AS initiation, then ≥annually	74178	**T1a SRM on AS**: abdomen CT or MRI within 6 months of surveillance initiation, then CT, MRI, or US **at least annually**; mean growth ~0.56 cm/yr; delayed intervention does not increase upstaging risk[4,20]
Renal/ retroperitoneal ultrasound: active surveillance follow-up	**Annually** after initial cross-sectional imaging	76770/ 76775	**Acceptable alternative to CT/MRI** for annual AS follow-up after initial cross-sectional imaging confirms baseline; reduces cumulative radiation[4]
Chest imaging (X-ray or CT): metastatic survey	**Baseline and annually** as clinically indicated during AS	71046/ 71250	Chest x-ray or CT at baseline and annually to assess for pulmonary metastases; repeat if intervention is being contemplated[4]

TEST	FREQUENCY	CPT/ HCPCS	CLINICAL INDICATION
Cystoscopy: hematuria evaluation	Per AUA/SUFU risk stratification	52000	Recommended for **intermediate- and high-risk MH** to evaluate bladder urothelium; gold standard for bladder cancer detection[18]
Advance Care Planning (AWV)†	**Annually** + when goals change	99497/ 99498	**Document**: directives, surrogate, code status; relevant when life expectancy shapes AS vs. surgery decision in elderly patients with SRM and competing comorbidities[21]

ABBREVIATIONS: CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System; RBC/HPF = red blood cells per high-power field; UA = urinalysis; AUA = American Urological Association; SUFU = Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction; MH = microscopic hematuria; US = ultrasound; NPV = negative predictive value; CT = computed tomography; RCC = renal cell carcinoma; MRI = magnetic resonance imaging; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; AS = active surveillance; SRM = small renal mass; ACP = advance care planning; AWV = Annual Wellness Visit
† ACP is covered with no patient copay when performed during the AWV; 99497 covers the first 30 minutes, 99498 each additional 30 minutes.

Subtle Early Signs in Older Adults (>65)

SIGN/SYMPTOM[1,4,22,23]	CLINICAL SIGNIFICANCE[1,4,22,24]
Painless gross hematuria	Often intermittent and attributed to BPH, anticoagulation, or UTI in older adults, **delaying imaging**; any gross hematuria at age ≥60 warrants cross-sectional imaging + urology referral, **not repeat urinalysis**; ~1.3% of gross hematuria patients are diagnosed with RCC
Incidental renal mass on unrelated imaging	Reported deep in a radiology study ordered for another reason and easily lost in the problem list; **>60%** of RCC is **detected incidentally**; flag and act on any solid enhancing mass ≥1 cm with dedicated renal-protocol imaging within 1–2 weeks
Prodromal laboratory drift (falling Hgb, rising ESR/CRP, abnormal LFTs or creatinine)	Inflammatory markers, hemoglobin, and renal/liver indices can shift **6–8 months before diagnosis** but are read as age-related; abnormal trends appear in 25–40% of patients before RCC diagnosis → **consider RCC** in unexplained anemia or rising inflammatory markers
Unexplained weight loss, anemia, or elevated ESR/CRP	Frequently ascribed to frailty or chronic disease in the elderly; in a patient with a **known renal mass**, these may signal **progression or paraneoplastic syndrome** (present in 10–40% of RCC) → escalate imaging
Paraneoplastic findings (new hypertension, hypercalcemia, erythrocytosis, Stauffer syndrome)	Paraneoplastic syndromes occur in **10–40%** of RCC and are **not consistently stage-dependent**; new-onset hypertension (**3–18%**), hypercalcemia (**1–30%**), or unexplained erythrocytosis (**2–4%**) in an older adult should prompt renal imaging

SIGN/SYMPTOM[1,4,22,23]	CLINICAL SIGNIFICANCE[1,4,22,24]
Bosniak III–IV cystic mass on a report	PCPs may not recognize the **malignancy implication of a Bosniak category**; **Bosniak III** carries **~80%** malignancy rate and **IV ~88%** (v2019 meta-analysis) → both require **urology referral**
Microscopic hematuria in a high-risk patient†	**AUA/SUFU 2025 high-risk criteria**: age ≥60 (men), >25 RBC/HPF, >30 pack-years, or prior gross hematuria → cystoscopy + CT urography; **do not** defer as "benign" in older adults

ABBREVIATIONS: BPH = benign prostatic hyperplasia; UTI = urinary tract infection; RCC = renal cell carcinoma; Hgb = hemoglobin; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; LFTs = liver function tests; PCP = primary care physician; RBC/HPF = red blood cells per high-power field; CT = computed tomography; AUA = American Urological Association; SUFU = Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
† AUA/SUFU 2025 update: women should not be classified as high-risk based on age alone; women age <60 are now classified as low/negligible-risk (changed from <50 in 2020 version)

Geriatric Risk Factors

RISK FACTOR	SIGNAL STRENGTH	NOTES
Kidney disease/ dialysis	RR up to **12.3** (dialysis); HR **2.58** non-dialysis[1,25]	**The strongest signal**; eGFR monitoring and nephrology coordination are already core to Medicare care[1,25]
Obesity (BMI >=30)	RR **1.9** (BMI ≥30); HR **1.71** (BMI ≥35 vs 25)[1,25]	**Strongest modifiable factor**; weight management aligns with existing BMI quality measures[1,25]
Hypertension	HR **1.70**; diastolic RR **2.3**[1]	Both an RCC risk factor and a **TKI toxicity** → BP optimization is doubly relevant[1,2]
Smoking	RR **1.6**; HR **1.58** (>37.5 pack-years)[1,25]	**Cessation counseling** and pharmacotherapy tie to tobacco quality measures[1,2]
Diabetes mellitus	HR **1.83** (age/sex-adjusted; attenuated multivariable)[2]	Influences **surgical risk** and **systemic-therapy selection** (mTOR-inhibitor hyperglycemia)[2]
Age 65-74	**Peak incidence age group**; **49%** of diagnoses at ≥65[4]	Aligns the highest-risk window with the Medicare population[1,4]
Hereditary syndromes (VHL, Birt-Hogg-Dube, HLRCC)	**6-9%** of kidney cancers carry germline mutations[4]	Refer for **genetic evaluation if diagnosis ≤46**, bilateral/multifocal, or family history[4]

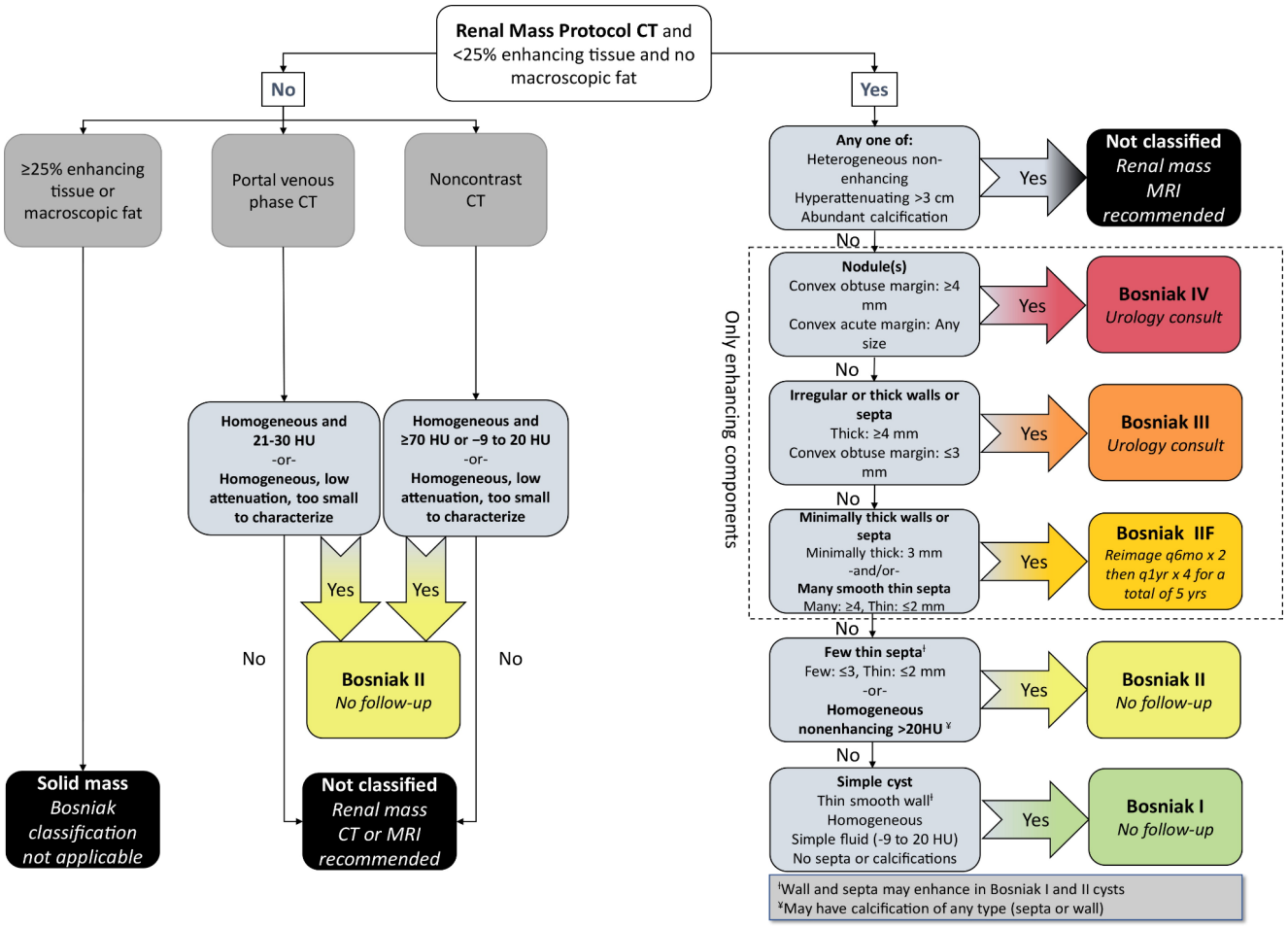
RISK FACTOR	SIGNAL STRENGTH	NOTES
Trichloroethylene (TCE) exposure	Meta-analysis RR 1.32 (95% CI 1.17–1.50); **highest-exposure RR 1.58**; case-control **OR 1.63**[26,27]	**IARC Group 1 carcinogen**; used in metal degreasing and industrial solvents; dose-response with cumulative exposure demonstrated[26,27]
Benzene, petrochemicals, PAHs, and other industrial solvents	Benzene meta-analysis **RR 1.20** (95% CI 1.03–1.39); organic solvents **OR 1.6**; benzene case-control **OR 1.8**[28]	Exposures span petroleum refining, chemical manufacturing, and rubber industries; risk strongest in **chemical-industry workers**; occupational history screening recommended[1]

ABBREVIATIONS: RR = relative risk; HR = hazard ratio; eGFR = estimated glomerular filtration rate; BMI = body mass index; RCC = renal cell carcinoma; TKI = tyrosine kinase inhibitor; BP = blood pressure; mTOR = mechanistic target of rapamycin; VHL = von Hippel–Lindau; HLRCC = hereditary leiomyomatosis and renal cell carcinoma

Diagnostic Thresholds

Renal cell carcinoma evaluation follows a **stepwise sequence**: **clinical detection** (incidental imaging finding, hematuria evaluation, or symptomatic presentation), cross-sectional imaging characterization (renal-protocol CT or MRI), **risk stratification of cystic masses** (**Bosniak classification**) or solid masses (size, enhancement pattern), **tissue diagnosis** when indicated (core needle biopsy, FNA is **not adequate**), and **histopathologic classification** with grading to guide surgical planning and systemic therapy selection.[4,29] **The critical branch point is the imaging phenotype**: solid enhancing masses **≥1 cm** are **presumed malignant** until proven otherwise and proceed directly to urologic evaluation, while **cystic masses are risk-stratified** using the Bosniak classification to determine whether surveillance or intervention is warranted.[22,30] For metastatic disease, the **IMDC** (**Heng**) criteria provide the primary risk stratification that directs first-line systemic therapy selection.[1,4] This **imaging-first approach**, combined with histologic subtyping, WHO/ISUP grading, and AJCC TNM staging after resection, forms the framework for **all subsequent treatment decisions**.

Initial Imaging: Bosniak Classification of Cystic Renal Masses (v2019)



Histopathologic Grading: WHO/ISUP Nucleolar Grade

The **WHO/ISUP grading system** replaced the Fuhrman system and is validated for clear cell and papillary RCC (**chromophobe RCC** is not graded).[31,32] Grade is based on the **single highest-grade field** and correlates with recurrence and survival. WHO/ISUP grading demonstrates superior predictive accuracy compared to Fuhrman grading (C-index 0.817 vs. 0.737).[33] **Grade 4** (sarcomatoid/rhabdoid differentiation) is a key trigger for **adjuvant pembrolizumab consideration** per NCCN guidelines.[4]

WHO/ISUP GRADE	DEFINITION	CLINICAL SIGNIFICANCE
G1	Nucleoli absent or inconspicuous and basophilic at 400x magnification	**Low risk**; favorable prognosis
G2	Nucleoli conspicuous and eosinophilic at 400× magnification, visible but not prominent at 100×	**Low-intermediate risk**; most common grade at diagnosis

WHO/ISUP GRADE	DEFINITION	CLINICAL SIGNIFICANCE
G3	Nucleoli conspicuous and eosinophilic at 100× magnification	**Intermediate-high risk**; significant separation in outcomes from G2
G4	Marked nuclear pleomorphism and/or multinucleate giant cells and/or sarcomatoid and/or rhabdoid differentiation	**High risk**; consider adjuvant therapy; independent predictor of poor survival

ABBREVIATIONS: WHO/ISUP = World Health Organization/International Society of Urological Pathology

Staging Systems

AJCC 8th Edition TNM (2017) is the standard pathologic staging system for renal cell carcinoma in all current U.S. guidelines.[4,34] **Key changes** from the 7th edition **include**: pelvicalyceal system invasion is now classified as **pT3a** (previously not specified), and the qualifier "**grossly**" was **removed** from renal vein invasion criteria.[34] At diagnosis, approximately **70%** of cases are **Stage I** and **11%** are **Stage IV**.[1] The **NCCN Kidney Cancer Guidelines** adopt the complete AJCC 8th Edition staging system for kidney cancer:

AJCC 8th Edition Prognostic Stage Groups: Renal Cell Carcinoma

STAGE	T	N	M
I	**T1** (≤7 cm, limited to kidney)	N0	M0
II	**T2** (>7 cm, limited to kidney)	N0	M0
I	**T1–T2**	N1	M0
II	**T3** (extends into major veins or perinephric tissues, not beyond Gerota's fascia)	NX, N0, or N1	M0
II	**T4** (invades beyond Gerota's fascia, including ipsilateral adrenal)	Any N	M0
III	**Any T**	Any N	M1
IVA	**T1** (≤7 cm, limited to kidney)	N0	M0
IVB	**T2** (>7 cm, limited to kidney)	N0	M0

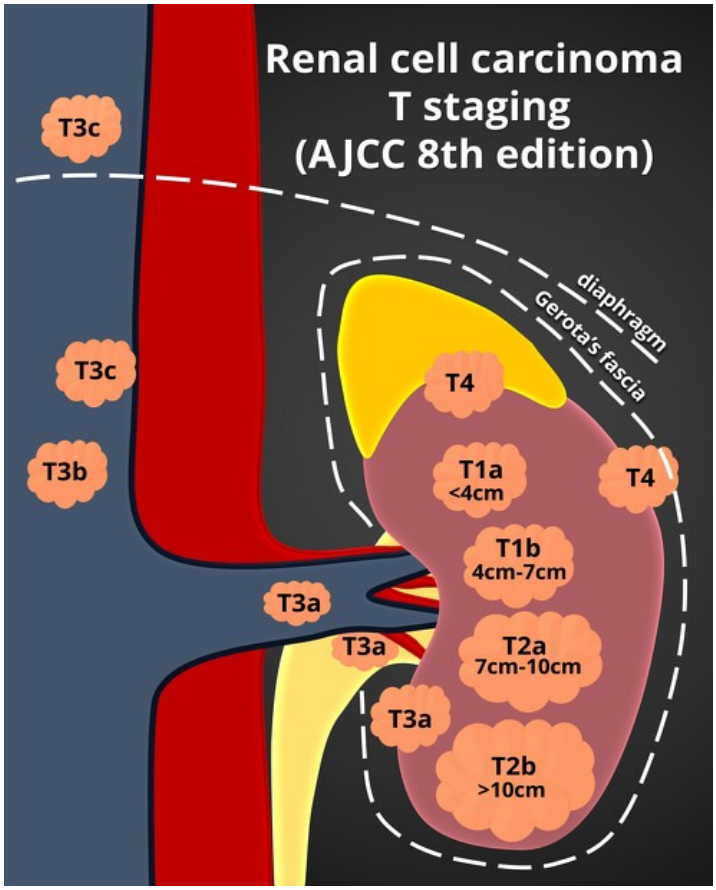
ABBREVIATIONS: T = tumor; N = node; M = metastasis; AJCC = American Joint Committee on Cancer
Adapted from: Amin MB, Edge SB, Greene FL, *et al.*, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017

T Definitions - Renal Cell Carcinoma

T CATEGORY	DEFINITION
T1a	≤4 cm, limited to kidney
T1b	>4 cm but ≤7 cm, limited to kidney
T2a	>7 cm but ≤10 cm, limited to kidney
T2b	>10 cm, limited to kidney
T3a	Extends into renal vein or segmental branches, invades pelvicalyceal system, or invades perirenal/renal sinus fat (not beyond Gerota's fascia)
T3b	Extends into vena cava below diaphragm
T3c	Extends into vena cava above diaphragm or invades wall of vena cava
T4	Invades beyond Gerota's fascia (including contiguous extension into ipsilateral adrenal gland)

ABBREVIATIONS: T = tumor; AJCC = American Joint Committee on Cancer
Adapted from: Amin MB, Edge SB, Greene FL, *et al.*, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017

Graphical depiction of AJCC 8th Edition RCC Stage Groups



Risk Stratification for Metastatic Disease: IMDC (Heng) Criteria

The **IMDC model** is the primary risk stratification system for metastatic RCC and directs first-line systemic therapy selection per NCCN guidelines.[4] It has been **validated in both first-line and second-line settings** with a concordance index of **0.70**.[35] An updated analysis of 728 patients treated with modern IO-based combinations reported **18-month OS of 90–93%** for favorable risk, **78–83%** for intermediate risk, and **50–74%** for poor risk.[36] The **NCCN Guidelines** integrate the complete IMDC and MSKCC risk models:[4]

IMDC PROGNOSTIC FACTOR	THRESHOLD	RISK FACTOR WEIGHT*
Time from diagnosis to systemic therapy	<1 year	**1 point**
Karnofsky performance status	<80%	**1 point**
Hemoglobin	Below lower limit of normal (typically <12 g/dL)	**1 point**
Corrected serum calcium	Above upper limit of normal (typically >10.2 mg/dL)	**1 point**

IMDC PROGNOSTIC FACTOR	THRESHOLD	RISK FACTOR WEIGHT*
Absolute neutrophil count	Above upper limit of normal (typically >7.0 × 10^9/L)	**1 point**
Platelet count	Above upper limit of normal (typically >400,000/µL)	**1 point**

RISK GROUP	RISK FACTORS*	MEDIAN OS (MODERN IO ERA)
Favorable	0	18-month OS **90–93%**
Intermediate	1–2	18-month OS **78–83%**
Poor	3–6	18-month OS **50–74%**

ABBREVIATIONS: IMDC = International Metastatic RCC Database Consortium; OS = overall survival; IO = immuno-oncology; RCC = renal cell carcinoma
***Risk factor scores are equally weighted and total score is cumulative**
Adapted from: Amin MB, Edge SB, Greene FL, *et al.*, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017

Other Relevant Staging and Classification Systems

SYSTEM	BASIS	KEY FEATURES	PRIMARY USE	KEY DISTINCTIONS
WHO 5th Edition Classification (2022)[37]	Histologic type, molecular markers	**Six categories of epithelial renal tumors**; introduces molecularly defined RCC category (TFE3, TFEB, FH-deficient, SDH-deficient, ALK-rearranged, ELOC-mutated, SMARCB1-deficient); **eliminates papillary type 1/2 subcategorization**; >20 recognized malignant subtypes	**Pathologic diagnosis**; determines histologic subtype input for AJCC staging, WHO/ISUP grading, and systemic therapy selection	**Not a staging system**; complements staging by defining tumor biology; clear cell (75–80%), papillary (10–15%), chromophobe (5%) remain dominant subtypes
Leibovich Score (2003/2018)[38,39]	pT stage, regional LN status, tumor size, nuclear grade, histologic necrosis	**2003 model**: 0–11 point score for ccRCC; **2018 update**: separate models for ccRCC, papillary, and chromophobe; C-index 0.78–0.87 across validations	Predicts **recurrence-free** and **cancer-specific survival** after nephrectomy; guides surveillance intensity and adjuvant trial eligibility	**Better predictor of recurrence** than AJCC staging alone (C-index 0.78–0.87 vs. 0.60–0.77 for TNM)

SYSTEM	BASIS	KEY FEATURES	PRIMARY USE	KEY DISTINCTIONS
SSIGN Score[40,41]	Stage, size, grade, necrosis	Integrates AJCC stage, tumor size, WHO/ISUP grade, and necrosis into a **composite score**; C-index 0.82–0.89	Predicts cancer-specific survival after nephrectomy for ccRCC	Comparable to Leibovich; validated in ASSURE trial;[42] performs best **within first 2 years** post-nephrectomy
R.E.N.A.L. Nephrometry Score[43]	Imaging-based anatomical features	**5 components**: (**R**)adius, (**E**)xophytic/endophytic, (**N**)earness to collecting system, (**A**)nterior/posterior, (**L**)ocation relative to polar lines; sum 4–6 = **low** complexity, 7–9 = **moderate**, 10–12 = **high**	**Pre-operative surgical planning**; predicts partial vs. radical nephrectomy feasibility and perioperative outcomes	**Not a prognostic staging system**; quantifies surgical complexity; interobserver correlation 0.92; guides nephron-sparing surgery decisions
MSKCC (Motzer) Criteria[44]	5 clinical/laboratory factors	KPS <80%, LDH >1.5× ULN, hemoglobin < LLN, corrected calcium > ULN, time from diagnosis to treatment <1 year	Risk stratification for **metastatic RCC**; historical standard **preceding IMDC**	Predecessor to IMDC; uses **LDH** instead of neutrophils/platelets; C-index 0.65–0.66 vs. 0.70 for IMDC; **IMDC now preferred**

ABBREVIATIONS: WHO = World Health Organization; RCC = renal cell carcinoma; TFE3 = transcription factor E3; TFEB = transcription factor EB; FH = fumarate hydratase; SDH = succinate dehydrogenase; ALK = anaplastic lymphoma kinase; ELOC = elongin C; SMARCB1 = SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1; AJCC = American Joint Committee on Cancer; WHO/ISUP = World Health Organization/International Society of Urological Pathology; ccRCC = clear cell renal cell carcinoma; LN = lymph node; pT = pathologic tumor; TNM = Tumor, Node, Metastasis; SSIGN = Stage, Size, Grade, and Necrosis; R.E.N.A.L. = Radius, Exophytic/Endophytic, Nearness to collecting system, Anterior/Posterior, Location relative to polar lines; MSKCC = Memorial Sloan Kettering Cancer Center; KPS = Karnofsky Performance Status; LDH = lactate dehydrogenase; ULN = upper limit of normal; LLN = lower limit of normal; IMDC = International Metastatic RCC Database Consortium; CT = computed tomography; MRI = magnetic resonance imaging

Clues to Dig Deeper

CLINICAL CLUE	WHY IT MATTERS	NEXT DIAGNOSTIC STEP
Microscopic hematuria, asymptomatic	Cancer probability **0.5–5.0%** overall, **7–20%** in high-risk subgroups; repeat urinalysis delays workup[18]	Apply AUA/SUFU 2025 risk tiers; triage to cystoscopy ± imaging by risk category[18]
Simple-appearing renal cyst on imaging	Bosniak IIF carries **~26%** malignancy risk; can be under-triaged without formal classification[45]	**Confirm Bosniak category** on renal-protocol imaging; urology referral for **IIF and above**[4,45]
Stable small renal mass on active surveillance	Mean growth **~0.3 cm/year**; rapid growth (>0.5 cm/year) is an **intervention trigger** easily missed[4]	**Verify surveillance interval**; document growth-rate trend at each imaging time point[4]
"History of kidney cancer" on problem list	May represent active disease under adjuvant therapy **or** surveillance, mis-coded as resolved[4,9]	Confirm treatment/ surveillance status **before accepting history-only framing**
Unexplained anemia or rising inflammatory markers, age ≥60	Lab drift (hemoglobin, ESR/CRP, LFTs) may **predate RCC diagnosis by 6–8 months** in 25–40% of patients[1]	Consider abdominal imaging (CT or ultrasound) when otherwise unexplained[1]
Incidental renal mass on unrelated imaging	>60% of RCC found **incidentally**; findings can be buried in reports ordered for other indications[1]	Dedicated r**enal-protocol imaging** and **urology referral** within 1–2 weeks for any solid enhancing mass ≥1 cm[4]

ABBREVIATIONS: AUA = American Urological Association; SUFU = Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction; IIF = Bosniak category IIF; RCC = renal cell carcinoma; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; LFTs = liver function tests; CT = computed tomography

Key Differentials in Elderly

PRESENTATION	DIFFERENTIAL DIAGNOSIS[1,4,19,46]	KEY DISTINGUISHING FEATURES/ NEXT STEPS[15,24,45,47]
Solid enhancing renal mass ≥1 cm	**Clear cell RCC** (most common, ~70% of RCC); papillary RCC; chromophobe RCC	**Renal-protocol CT or MRI**; presumed malignant until proven otherwise; urology referral within 1–2 weeks

PRESENTATION	DIFFERENTIAL DIAGNOSIS[1,4,19,46]	KEY DISTINGUISHING FEATURES/ NEXT STEPS[15,24,45,47]
Fat-containing renal mass	**Angiomyolipoma** (macroscopic fat on CT is virtually diagnostic); **up to 20%** of SRMs are **benign**	Confirm macroscopic fat on thin-section unenhanced CT; if fat-poor, **biopsy to differentiate from RCC**
Homogeneous mass with central scar	**Oncocytoma** (benign); cannot be reliably distinguished from chromophobe RCC **on imaging alone**	Core needle biopsy **if it would change management**; segmental enhancement inversion on MRI suggestive but not definitive
Mass centered in collecting system	**Upper-tract urothelial carcinoma** (renal pelvis, **C65**); distinct histology and treatment from RCC	Urine cytology + ureteroscopy with biopsy; CT urography (sensitivity 88–100%); **do not code or manage as RCC**
Non-enhancing, thin-walled cystic lesion	Benign simple cyst (**Bosniak I–II**); ~0–9% malignancy risk	Confirm Bosniak category on dedicated imaging; **no referral** required for Bosniak I–II
Complex cystic mass with thick septa or nodularity	**Cystic RCC** (Bosniak III ~80%, IV ~88% malignant)	**Urology referral** for Bosniak III–IV; **do not manage as simple cyst**
Gross hematuria, painless, age ≥60	**Bladder cancer** (16.5% probability); **RCC** (~1.3%); **UTUC** (~5% of urothelial cancers)	Cross-sectional imaging + cystoscopy on first episode; do not attribute to BPH, anticoagulation, or UTI **without workup**
Multiple renal lesions or known extrarenal primary	**Metastasis to kidney** from another primary malignancy	Correlate with oncologic history; code as **C79.0-** with primary site; biopsy if it would alter management
Unexplained anemia, elevated ESR/CRP, weight loss in patient ≥60	**Paraneoplastic syndrome of RCC**; may predate diagnosis by 6–8 months	**Abdominal imaging** (CT or ultrasound) when laboratory abnormalities are otherwise unexplained

ABBREVIATIONS: RCC = renal cell carcinoma; CT = computed tomography; MRI = magnetic resonance imaging; SRM = small renal mass; UTUC = upper tract urothelial carcinoma; BPH = benign prostatic hyperplasia; UTI = urinary tract infection; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein

Comorbidity Screening

COMORBIDITY	PREVALENCE/ASSOCIATION[1,13,24]	SCREENING/PCP ACTION[21,48,49]
Chronic kidney disease (N18.30–N18.5)	**25% higher prevalence at RCC diagnosis** vs general population; CKD is both a **risk factor** (HR 2.28 for eGFR <30) and a **consequence** of nephrectomy (eGFR <60 in 38–59% post-surgery)	**Annual eGFR** (CKD-EPI or cystatin C); advocate partial nephrectomy when feasible; **nephrology referral** if eGFR <45; **adjust TKI dosing** to measured renal function
Hypertension (I10)	**Established RCC risk factor** (diastolic RR 2.3); TKI-induced HTN occurs in **21–40%** of first-time users; HTN is a biomarker of TKI efficacy	**BP at every visit**; ACEi/ARB first-line (renoprotective + possible survival benefit); add dihydropyridine CCB if needed; hold TKI if BP ≥180/110; avoid non-DHP CCBs (CYP3A4 interaction)
Type 2 diabetes mellitus (E11.-)	**18.4%** prevalence in mRCC cohorts; mTOR inhibitors cause hyperglycemia in up to 50% (all-grade); influences surgical risk	**Fasting glucose** at each visit during mTOR inhibitor therapy; **A1C every 3 months**; metformin is first-line for mTOR inhibitor–induced hyperglycemia per ADA 2026; avoid mTOR inhibitors in difficult-to-manage diabetes if alternatives exist
Heart failure/ cardiovascular disease (I50.-)	**Strongest competing mortality risk** in elderly RCC; TKI cardiotoxicity includes LVSD and HF; comorbidity burden independently worsens OS (HR 1.98 for high CCI)	Baseline cardiac assessment (echocardiogram, ECG) before TKI/ICI; monitor LVEF during VEGFR-TKI therapy; coordinate with cardio-oncology for pre-existing CVD
Cognitive impairment/ dementia (F03.-, G30.-)	Patients with MCI/dementia are **half as likely to initiate oral anticancer agents** (HR 0.53); VEGFR-TKI treatment itself impairs learning, memory, and executive function	**Screen cognition** (Mini-Cog or MMSE) **before** oral TKI initiation; simplify regimens; involve caregivers in adherence support; consider IV-based regimens if adherence is at risk
Malnutrition/ sarcopenia (E46, R63.0)	Significantly increased mortality **from targeted drugs in mRCC**; malnutrition linked to systemic inflammation and increased drug toxicity via altered pharmacokinetics	**Nutritional screening** within CGA (MNA or G8); **dietitian referral**; prehabilitation before systemic therapy; monitor weight and albumin at each visit

COMORBIDITY	PREVALENCE/ASSOCIATION[1,13,24]	SCREENING/PCP ACTION[21,48,49]

ABBREVIATIONS: RCC = renal cell carcinoma; CKD = chronic kidney disease; HR = hazard ratio; eGFR = estimated glomerular filtration rate; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; TKI = tyrosine kinase inhibitor; RR = relative risk; HTN = hypertension; BP = blood pressure; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; DHP = dihydropyridine; CYP3A4 = cytochrome P450 3A4; mRCC = metastatic renal cell carcinoma; mTOR = mechanistic target of rapamycin; A1C = glycated hemoglobin; ADA = American Diabetes Association; LVSD = left ventricular systolic dysfunction; HF = heart failure; OS = overall survival; CCI = Charlson Comorbidity Index; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; VEGFR = vascular endothelial growth factor receptor; ICI = immune checkpoint inhibitor; CVD = cardiovascular disease; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; MNA = Mini Nutritional Assessment; CGA = comprehensive geriatric assessment; PCP = primary care physician

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

These emergency conditions require **immediate intervention** in patients with known or suspected RCC:

- **Massive gross hematuria with hemodynamic instability**: suggests tumor hemorrhage or renal vein invasion[50,51]
  - → **Emergent CT angiography**; TAE or surgical exploration
- **Acute flank pain with retroperitoneal hemorrhage** (Wünderlich syndrome): RCC underlies **~17%** of spontaneous perirenal hemorrhage[50,51]
  - → **Emergent CT**; TAE if stabilized; nephrectomy if unstable
- **Acute neurological deficits (seizures, focal weakness, altered mental status)**: brain metastases in 8% of mRCC; high hemorrhage propensity[52]
  - → **Emergent CT head**; dexamethasone 10 mg IV; neurosurgery/radiation oncology
- **Grade 3–4 immune-related adverse events (colitis, pneumonitis, myocarditis, hepatitis)**[53]
  - → **Hold ICI immediately**; IV methylprednisolone 1–2 mg/kg/day; escalate if steroid-refractory within 48 hr
- **Hypercalcemia crisis** (corrected Ca >14 mg/dL with AMS)[54]
  - → **Aggressive IV saline**; calcitonin 4–8 IU/kg SQ q8–12h; zoledronic acid 4 mg IV

⚠ RED FLAG — URGENT (24-72 HOURS)

Expedited workup required = **do not** refer to routine follow-up:

- **New painless gross hematuria, age ≥60**: pretest cancer probability >10%[1]
  - → Cross-sectional imaging + urology referral on first episode; do not repeat urinalysis
- **New pathologic fracture or severe bone pain**: bone metastases in **32%** of mRCC; 71% experience ≥1 SRE[55]
  - → **Orthopedic/oncology consultation**; initiate bone-protective agent
- **Rapidly enlarging mass on surveillance** (>5 mm/year or doubling): triggers intervention[4]
  - → **Expedited urology referral**
- **New IVC or tumor thrombus on imaging**[4]
  - → **Refer to high-volume urologic oncology center**; thrombus level determines operative approach
- **AKI on TKI or immunotherapy**[56]
  - → **Hold offending agent**; urinalysis, urine protein/creatinine, renal ultrasound; same-day **nephrology consultation**

3 MEAT DOCUMENTATION ESSENTIALS

Renal cell carcinoma documentation translates clinical complexity into **a record that supports continuity**, **quality measurement**, and **accurate risk adjustment**. The most frequent pitfalls: unspecified laterality defaulting to **C64.9**, premature **Z85.528** during active adjuvant therapy, missed metastatic site coding, and reliance on serum creatinine alone in low-muscle-mass patients. The MEAT framework below ties **each element into appropriate clinical action**:

*A 71-year-old male presents for follow-up. He underwent left radical nephrectomy for clear cell RCC 4 months ago and is on adjuvant pembrolizumab cycle 4. The encounter note previously read only "history of kidney cancer, doing well." Because he is on active adjuvant therapy, the accurate code is **C64.2** (active left RCC), **not Z85.528** — and the note should reflect the full clinical picture.*

MONITOR: "Weight: 78 kg, stable. Functional status: independent ADLs; G-8 = 15 → **no geriatric vulnerability flagged**. Blood pressure: 138/82 mmHg (baseline pre-nephrectomy 128/78). **eGFR by CKD-EPI**: 52 mL/min (pre-nephrectomy 68). **TSH**: 2.4 mIU/L (checkpoint inhibitor thyroid surveillance). **No immune-related adverse events**: no rash, colitis, hepatitis, or pneumonitis symptoms. Surveillance CT chest/abdomen/pelvis (date): no evidence of recurrence or metastatic disease. Next imaging per protocol in 3 months."

EVALUATE: "Surgical pathology: clear cell RCC, **WHO/ISUP grade 2**, left kidney. AJCC stage III (**pT3aN0M0**); 14 lymph nodes examined, all negative. Margins negative. No sarcomatoid or rhabdoid features. **IMDC risk group**: not applicable (adjuvant setting). Pembrolizumab cycle 4 of 17 planned; tolerating without dose modification. **Apixaban interaction review**: no contraindication with current regimen; pharmacist documented."

ASSESS: "Active clear cell renal cell carcinoma, left kidney, on adjuvant pembrolizumab (**C64.2**). **Associated**: CKD stage 3a (**N18.31**), eGFR 52 by CKD-EPI; essential hypertension (**I10**), suboptimally controlled post-nephrectomy; anemia in neoplastic disease (**D63.0**), Hgb 11.2. G-8 15 = no formal CGA indicated; functional monitoring continues. **PHQ-2 screened**: negative."

TREAT: "Adjuvant pembrolizumab 200 mg IV q3 weeks, cycle 4 of 17 (**KEYNOTE-564 protocol**). **Hypertension**: lisinopril increased 10 → 20 mg; recheck BP in 2 weeks. **CKD monitoring**: eGFR by CKD-EPI at each visit; avoid nephrotoxins; **pharmacy-verified apixaban dose-appropriate** for renal function. **Immune-related AE plan**: TSH q6 weeks, LFTs each cycle, urinalysis for nephritis. **Surveillance imaging**: CT chest/abdomen/pelvis q3 months during adjuvant therapy. **Shared decision-making documented**: patient understands adjuvant intent, expected duration, and stopping criteria. **ACP documented** (CPT 99497): surrogate named, code status discussed. Return in 3 weeks for cycle 5 or sooner for new symptoms."

Clinical Documentation Elements

- **Document laterality of the primary tumor** (right **C64.1** or left **C64.2**), confirmed against imaging and operative reports; avoid **C64.9** unless laterality is truly unknown[3]
- **Document active-disease status vs personal history**:[4] Use **Z85.528** only when treatment is complete with **no evidence of disease**; patients on adjuvant therapy or active surveillance **retain C64.x**
- **Document histologic subtype explicitly** (clear cell, papillary, chromophobe) and **WHO/ISUP grade**;[1,4] subtype drives systemic therapy selection: clear cell vs non-clear cell follow entirely different NCCN treatment algorithms
- **Document AJCC 8th Edition TNM stage** and, for metastatic disease, the **IMDC risk group** (favorable/intermediate/poor);[4] IMDC risk directs first-line systemic therapy selection
- **Code each confirmed metastatic site separately** (e.g., **C78.00** lung, **C79.51** bone, **C79.31** brain) alongside the primary;[1] each documented site supports **clinical complexity and care coordination**
- **Document renal function by Cockcroft-Gault or CKD-EPI** for TKI dosing decisions;[29] serum creatinine alone **overestimates function** in low-muscle-mass elders
- **Document advance care planning discussion** for elderly patients facing active surveillance vs surgery, particularly those with significant comorbidities or limited life expectancy[21]

Reframing Common Documentation Shortcuts

INSTEAD OF...	DOCUMENT...*[1,3,4,29]
"Kidney cancer"	"**Active clear cell RCC, left kidney** (**C64.2**), **pT1aN0M0**, **WHO/ISUP grade 2**; on active surveillance with CT q6 months"

INSTEAD OF...	DOCUMENT...*[1,3,4,29]
"History of kidney cancer"	Use **Z85.528 ONLY after** definitive treatment with **no evidence of disease**; patients on adjuvant therapy or active surveillance **retain C64.x**
"Metastatic RCC"	"Clear cell RCC (**C64.1**) with right lung metastasis (**C78.01**), bone metastasis (**C79.51**), **IMDC intermediate risk**; on cabozantinib + nivolumab" → code each site separately
"Renal mass, stable"	"**T1a SRM**, **2.3 cm**, **Bosniak II**, **growth rate 0.4 cm/year**, renal-protocol CT q6 months on active surveillance; intervention trigger >5 mm/year"
"Cr stable"	"eGFR 48 mL/min **by CKD-EPI** (CKD stage 3b, **N18.32**); TKI dose adjusted per renal function" → serum creatinine alone **overestimates function** in low-muscle-mass elders
"On immunotherapy"	"**Pembrolizumab 400 mg IV q6 weeks** (adjuvant, cycle 4/17); irAE monitoring: TSH q6 wk, LFTs and glucose q3 wk; last echocardiogram [date]"

ABBREVIATIONS: RCC = renal cell carcinoma; WHO/ISUP = World Health Organization/International Society of Urological Pathology; CT = computed tomography; SRM = small renal mass; eGFR = estimated glomerular filtration rate; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CKD = chronic kidney disease; TKI = tyrosine kinase inhibitor; IMDC = International Metastatic RCC Database Consortium; irAE = immune-related adverse event; TSH = thyroid-stimulating hormone; LFTs = liver function tests
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

DOCUMENTATION IS COMPREHENSIVE DOCUMENTATION

Documentation that names laterality, active-disease status, and every metastatic site lets the record carry the patient's **true clinical complexity** so the care team, and the next clinician, see the whole picture. **Specify laterality and metastatic sites at every qualifying encounter**.[1]

4 TREATMENT AND REFERRAL QUICK GUIDE

Treatment in renal cell carcinoma is driven by: AJCC 8th Edition TNM stage, histologic subtype (clear cell, papillary, chromophobe), WHO/ISUP nucleolar grade, IMDC risk group (for metastatic disease), biomarker and molecular features (sarcomatoid/rhabdoid differentiation, VHL status), and functional/geriatric assessment — **not chronological age alone**.[4,29,57,58] A fit 80-year-old may tolerate definitive surgery or IO-TKI combination therapy similarly to a younger patient; a frail 65-year-old may not.[13,21] Clear cell and non-clear cell histologies follow **entirely separate NCCN treatment algorithms**, and within clear cell metastatic disease, **IMDC risk group** (favorable vs intermediate/poor) determines the preferred first-line systemic regimen.[4,21]

The PCP's highest-value contributions are: ensuring timely urology referral for incidental renal masses, advocating for nephron-sparing surgery and active surveillance in appropriate elderly patients with small renal masses, proactively managing comorbidities (CKD, hypertension, diabetes) that affect surgical candidacy and drug tolerability, co-monitoring TKI and

immunotherapy toxicities, performing geriatric screening (G8) before treatment decisions, and coordinating long-term post-treatment surveillance — which the NCCN Guidelines explicitly state may be performed by a primary care physician.[4,21,29,57]

Regimens and surgical strategies outlined in the tables below follow the NCCN Kidney Cancer Guidelines (v2.2026) and the ASCO metastatic clear cell RCC guideline (2022).[4,58] The AUA Renal Mass and Localized Renal Cancer Guideline (2021) provides additional evidence for **localized disease management**, active surveillance, and follow-up.[29,57]

Therapy Escalation Snapshot

TRIGGER[4,13,29,57,58]	ACTION*[4,21,56,58]
SRM growth >5 mm/year or doubling on active surveillance	**Urology reassessment** for intervention (partial nephrectomy, ablation); restage with renal-protocol CT/MRI
New hematuria, flank pain, or size progression in known renal mass	**Cross-sectional restaging**; oncology/urology referral; **do not** attribute to benign cause without imaging
Radiographic progression on first-line systemic therapy	**Switch therapy line** per NCCN/ASCO algorithm: **VEGFR TKI monotherapy** (cabozantinib preferred) **after IO-based combination**; nivolumab monotherapy **if prior VEGFR TKI**
Grade 3–4 immune-related adverse event (colitis, hepatitis, pneumonitis, myocarditis)	**Hold immunotherapy**; initiate corticosteroids per NCCN irAE guidelines; oncology contact **same day**
Grade 3–4 TKI toxicity (uncontrolled HTN, hand-foot syndrome, hepatotoxicity)	**Hold TKI**; manage toxicity; consider dose reduction or alternative schedule (e.g., sunitinib 2 weeks on/1 week off)
G-8 score ≤14 or clinical frailty identified	**Full CGA before any treatment decision**; favor lower-toxicity strategies, active surveillance, or dose-modified regimens
Confirmed sarcomatoid/rhabdoid differentiation on pathology	Escalate to **IO-based combination regardless of IMDC risk**; these features predict aggressive biology and IO responsiveness
New brain, bone, or visceral metastasis on surveillance imaging	Multidisciplinary oncology review; **consider SRS for oligometastatic brain disease**; systemic therapy initiation or change

ABBREVIATIONS: SRM = small renal mass; CT = computed tomography; MRI = magnetic resonance imaging; NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; IO = immuno-oncology; irAE = immune-related adverse event; HTN = hypertension; G-8 = Geriatric 8 screening; CGA = comprehensive geriatric assessment; IMDC = International Metastatic RCC Database Consortium; RCC = renal cell carcinoma; SRS = stereotactic radiosurgery
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

NCCN/ASCO/AUA-Aligned Treatment by Stage and Patient Profile

SUBTYPE/ SETTING	PREFERRED REGIMEN(S)*[4,21,29,57,58]	KEY PCP NOTES[4,21,29,57,58]
Stage I, T1a (≤4 cm)	**Partial nephrectomy** (preferred); ablation; SBRT; AS; radical nephrectomy (select)	AS appropriate for **<2 cm** or **significant competing mortality**; CSS comparable to intervention at 4 years
Stage I, T1b (>4–7 cm)	**Partial or radical nephrectomy**; AS (select); ablation (2B); SBRT (select)	**Nephron-sparing** preserves eGFR and reduces CKD risk
Stage II–III (localized/locally advanced)	**Radical nephrectomy**; partial if indicated; SBRT (select)	**Clear cell**: adjuvant pembrolizumab (category 1) or surveillance; **non-clear cell**: surveillance
Adjuvant (clear cell, high recurrence risk)	**Pembrolizumab** 200 mg IV Q3W × ~1 year; SC formulation available	**KEYNOTE-564**:[59] OS HR 0.62, 5-year OS 87.7% vs 82.3%; grade 4/ sarcomatoid derives particular benefit
Stage IV, clear cell, first-line (all category 1)	**Axitinib + pembrolizumab**; cabozantinib + nivolumab; ipilimumab + nivolumab; lenvatinib + pembrolizumab	**IMDC risk directs selection**; ipi/nivo 9-year OS HR 0.69 (int/poor); cabozantinib monotherapy if IO contraindicated
Stage IV, clear cell, favorable risk	**Same four IO combinations**; also axitinib + avelumab, pazopanib, sunitinib; AS (select)	**IO-TKI** preferred when rapid control needed; ipi/nivo: lower ORR but higher CR rate vs sunitinib
Stage IV, non-clear cell	**Clinical trial** (preferred); cabozantinib; cabozantinib + nivolumab; lenvatinib + pembrolizumab	**Less IO-responsive**; collecting duct/ medullary may respond to platinum chemotherapy
Subsequent-line (prior IO)	**Cabozantinib**; axitinib; belzutifan (after IO + VEGF-TKI); lenvatinib/ everolimus; tivozanib	**VEGFR TKI** after IO combination per ASCO; cabozantinib has most robust second-line data
Cytoreductive nephrectomy	**Consider if resectable primary**; systemic therapy preferred for poor-risk	**CARMENA**:[60] sunitinib alone noninferior to CN + sunitinib; CN no longer standard for most
Oligometastatic disease	Metastasectomy, SBRT, or ablation	Adjuvant pembrolizumab an option if NED post-metastasectomy **within 1 year** of nephrectomy
G-8 ≤14 or frailty	**CGA**; reduced-intensity strategies; favor AS for SRM; **dose-modified regimens**	Functional status, not age, guides decisions; GA-guided care reduces toxicity

SUBTYPE/ SETTING	PREFERRED REGIMEN(S)*[4,21,29,57,58]	KEY PCP NOTES[4,21,29,57,58]

ABBREVIATIONS: NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology; AUA = American Urological Association; PCP = primary care physician; AS = active surveillance; SBRT = stereotactic body radiation therapy; CSS = cancer-specific survival; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; SC = subcutaneous; OS = overall survival; HR = hazard ratio; IMDC = International Metastatic RCC Database Consortium; RCC = renal cell carcinoma; IO = immuno-oncology; TKI = tyrosine kinase inhibitor; ORR = overall response rate; CR = complete response; VEGF = vascular endothelial growth factor; VEGFR = vascular endothelial growth factor receptor; CN = cytoreductive nephrectomy; NED = no evidence of disease; G-8 = Geriatric 8 screening; CGA = comprehensive geriatric assessment; GA = geriatric assessment; SRM = small renal mass; IV = intravenous; Q3W = every 3 weeks

CLINICAL PEARL - FUNCTION AND COMORBIDITY > CHRONOLOGIC AGE

In older adults, **function predicts tolerance and survival better than age**: CGA-defined fit patients had a median OS of **35.5** months versus **10.9** months in frail patients on first-line TKIs ($p<0.001$).[61] **Screen with G8 and let function, not the calendar, guide intensity**; [13,21] up to **30%** of elderly RCC patients die of competing causes before the tumor becomes clinically relevant.[1]

Non-Pharmacologic Care and Supportive Interventions

INTERVENTION[4,13,21,]	TARGET/ RECOMMENDATION[21,63–65]	NOTES[21,29,57,58,64]
Prehabilitation (pre-surgery or pre-systemic therapy)	Address malnutrition, pain, deconditioning, and social isolation before treatment	**SIOG four-stage strategy**: (**1**) multidisciplinary assessment, (**2**) prehabilitation, (**3**) toxicity minimization, (**4**) rehabilitation/end-of-life care
Physical activity/ exercise prescription	≥150 min/wk moderate or 75 min/ wk vigorous aerobic + resistance training 2–3×/wk; goal 6,000–8,000 steps/day for adults ≥60	**Category 1 for fatigue reduction**; ≥7 hrs/wk moderate-vigorous activity associated with 40% lower all-cause mortality in RCC survivors; refer to trained personnel if impairments present
Nutritional assessment and support	**Integrate into CGA**; dietitian referral for weight loss or anorexia during systemic therapy	**Malnutrition increases mortality** risk from targeted drugs; close relationship between malnutrition, systemic inflammation, and drug toxicity in elderly mRCC
Daily home BP monitoring (on TKI)	**Begin at TKI initiation**; log readings for every visit	HTN occurs in **35–55%** on VEGFR-TKIs; ACEi/ARB may reduce proteinuria and dose interruptions; early detection prevents grade 3+ events

INTERVENTION[4,13,21,]	TARGET/ RECOMMENDATION[21,63–65]	NOTES[21,29,57,58,64]
Early palliative care	**Early in treatment process** for advanced/metastatic disease; concurrent with oncology	ASCO recommends **early referral** (not waiting until cessation of antineoplastic therapy); improves QoL, symptom control, and prognostic awareness; only 9.1% of RCC hospitalizations receive PC
Advance care planning	**Annually** and when goals change; during AWV	Especially relevant when functional status shapes **AS vs surgery decisions**; document directives, surrogate, code status
Smoking cessation	**Quitline**; pharmacotherapy if appropriate	**Modifiable RCC risk factor**; supports treatment tolerance and overall outcomes

ABBREVIATIONS: SIOG = International Society of Geriatric Oncology; CGA = comprehensive geriatric assessment; RCC = renal cell carcinoma; mRCC = metastatic RCC; CBT = cognitive behavioral therapy; RCT = randomized controlled trial; NCCN = National Comprehensive Cancer Network; BP = blood pressure; TKI = tyrosine kinase inhibitor; HTN = hypertension; VEGFR = vascular endothelial growth factor receptor; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ASCO = American Society of Clinical Oncology; QoL = quality of life; PC = palliative care; AWV = Annual Wellness Visit; AS = active surveillance; SRM = small renal mass

Medication Safety and Key Interactions

DRUG/CLASS	INTERACTION/TOXICITY*[13,53,66,67]	CLINICAL ACTION*[4,13,66,68]
Pembrolizumab (anti-PD-1)	**irAEs**: colitis, pneumonitis, hepatitis, endocrinopathies (hypothyroidism most common); AKI ~1% monotherapy, ~5% with ipi/nivo; **caution with active autoimmune disease**	**sCr before every dose**; TSH q6 wk; LFTs q cycle; hold for grade ≥2 organ toxicity; high-dose steroids for grade ≥3
Nivolumab (anti-PD-1)	**Similar irAE profile**; higher toxicity when combined with ipilimumab (grade ≥3 irAEs ~46%); myocarditis rare but **potentially fatal**	**Same monitoring as pembrolizumab**; baseline ECG and troponin if ipi/nivo combination; urgent cardiology for suspected myocarditis
Ipilimumab (anti-CTLA-4)	**Used only in combination with nivolumab**; colitis and hepatitis more frequent than with anti-PD-1 alone	**Diarrhea diary**; LFTs before each dose; early steroids for grade ≥2 colitis
Sunitinib (VEGFR TKI)	HTN, fatigue, HFS, thrombocytopenia, LV dysfunction; CYP3A4 substrate	2/1 schedule reduces grade ≥3 AEs from ~46% to ~8% with comparable efficacy; **avoid strong CYP3A4 inhibitors/inducers**; home BP monitoring

DRUG/CLASS	INTERACTION/TOXICITY*[13,53,66,67]	CLINICAL ACTION*[4,13,66,68]
Cabozantinib (VEGFR/MET TKI)	HTN, diarrhea, fatigue, HFS, proteinuria; **CYP3A4 substrate**; take on empty stomach	**Reduce dose 20 mg with strong CYP3A4 inhibitors**; increase 20 mg with strong/moderate inducers; baseline cardiac assessment
Axitinib (VEGFR TKI)	HTN, proteinuria, thyroid dysfunction; **CYP3A4 substrate**; short half-life (2.5–6 h)	**Reduce dose ~50% with strong CYP3A4 inhibitors**; avoid strong inducers; BP and TSH monitoring
Lenvatinib (VEGFR TKI)	HTN, proteinuria, diarrhea, hepatotoxicity; used with pembrolizumab or everolimus	**BP and renal function monitoring**; LFTs; dose reductions common in elderly
Belzutifan (HIF-2α inhibitor)	Anemia (83%), hypoxia (14.5% any grade, 10.5% grade ≥3); **distinct from TKI/IO toxicity profile**	**Hgb before each dose**; pulse oximetry; ESA or transfusion for anemia; supplemental O_2 for hypoxia; **fewer discontinuations vs everolimus**
Everolimus (mTOR inhibitor)	Hyperglycemia (15%), stomatitis (38%), pneumonitis (14%), hyperlipidemia; **avoid in poorly controlled diabetes**	**Fasting glucose and lipids q4–6 wk**; chest imaging if new cough/dyspnea; oral care for stomatitis prevention
Temsirolimus (mTOR inhibitor)	**Similar class effects**; IV administration weekly; infusion reactions; interstitial lung disease	**Premedicate with antihistamine**; monitor glucose, lipids, CBC; reduce dose with strong CYP3A4 inhibitors

ABBREVIATIONS: PD-1 = programmed death-1; irAE = immune-related adverse event; AKI = acute kidney injury; sCr = serum creatinine; TSH = thyroid-stimulating hormone; LFT = liver function test; ECG = electrocardiogram; CTLA-4 = cytotoxic T-lymphocyte-associated protein 4; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; HTN = hypertension; HFS = hand-foot syndrome; LV = left ventricular; AE = adverse event; BP = blood pressure; CYP3A4 = cytochrome P450 3A4; MET = mesenchymal-epithelial transition factor; HIF-2α = hypoxia-inducible factor 2-alpha; IO = immuno-oncology; Hgb = hemoglobin; ESA = erythropoiesis-stimulating agent; mTOR = mechanistic target of rapamycin; IV = intravenous; CBC = complete blood count
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

When to Refer

CRITERION[4,13,18,57]	SPECIALIST[4,13,21,57]	URGENCY[4,13,21,57]
Acute airway/hemodynamic compromise from tumor hemorrhage or IVC thrombus	Emergency department/surgical team	**Emergent**
Acute neurologic deficit suggesting brain metastasis	Emergency department/ neurosurgery	**Emergent**

CRITERION[4,13,18,57]	SPECIALIST[4,13,21,57]	URGENCY[4,13,21,57]
Grade ≥3 irAE on checkpoint inhibitor (colitis, pneumonitis, myocarditis, hepatitis)	Oncology (**same day**); subspecialty per organ	**Emergent**
Gross hematuria in any patient ≥60	Urology (with cross-sectional imaging)	**Urgent** (within 1–2 weeks)
High-risk microhematuria (≥60, >25 RBC/HPF, >30 pack-years, or prior gross hematuria)	Urology for cystoscopy + CT urography	**Urgent** (within 2 weeks)
Incidental solid enhancing renal mass ≥1 cm	Urology	**Urgent** (dedicated imaging + referral within 1–2 weeks)
Bosniak III–IV cystic mass	Urology	**Urgent** (80–88% malignant)
Confirmed or suspected metastatic RCC	Medical oncology	**Urgent** (systemic therapy planning)
IVC or tumor thrombus on imaging	High-volume surgical center	**Urgent**
Rapid growth on surveillance (>5 mm/year or doubling)	Urology/medical oncology	**Urgent**
New pathologic fracture or severe bone pain suggesting bone metastasis	Medical oncology + orthopedics/radiation oncology	**Urgent**
AKI on TKI or immunotherapy	Oncology + nephrology	**Urgent** (same day to next day)
Hereditary-syndrome features (≤46 y, bilateral, multifocal, family history)	Genetics/genetic counseling	**Routine** (do not omit)
Intermediate-risk microhematuria (age 40–59 M/50–59 F, 11–25 RBC/HPF, 10–30 pack-years)	Urology for cystoscopy + renal ultrasound	**Routine** (within 4–6 weeks)
G-8 ≤14 or established frailty before treatment	Geriatric oncology/CGA	Before treatment cycle 1
Hospice-eligible with end-stage metastatic disease	Hospice (Medicare Hospice Benefit)	When goals align

ABBREVIATIONS: IVC = inferior vena cava; irAE = immune-related adverse event; RBC/HPF = red blood cells per high-power field; CT = computed tomography; RCC = renal cell carcinoma; AKI = acute kidney injury; TKI = tyrosine kinase inhibitor; G-8 = Geriatric 8 screening; CGA = comprehensive geriatric assessment

Follow-Up Timing

STAGE/PHASE[4,57,58]	FREQUENCY[4,57,69]	LABS/MONITORING[4,57,68]
Active surveillance (T1a SRM)	Abdomen CT/MRI **within 6 mo** of initiation, then CT/MRI/US at least annually; CXR or CT at baseline and annually	**Labs annually**; consider biopsy at initiation or follow-up; intervention trigger: growth >5 mm/yr or doubling
Post-ablation, Stage I	Abdomen CT/MRI or CEUS at **1–3 mo**, **6 mo**, **12 mo**, then **annually**; chest CT annually × 5 yr	**Labs annually**; biopsy if imaging concern for residual/recurrent disease
Post-SBRT, Stage I	Abdomen/chest CT **q3 mo yr 1**, **q6 mo yr 2**, **q9 mo yr 3–4**, **annually yr 5**	Renal function
Post-nephrectomy, Stage I	Baseline abdomen CT/MRI within **3–12 mo**, then **annually × 5 yr**; chest CT **annually × 5 yr**	**Labs annually**; intensify if positive margins or grade 3/4/sarcomatoid
Post-nephrectomy, Stage II	Abdomen/pelvis CT/MRI **q6 mo × 2 yr**, then **annually × 5 yr**; chest CT annually × 5 yr	**Labs annually**; restage **before** adjuvant therapy if considered
Post-nephrectomy, Stage III/T4 N×M0	H&P **q3–6 mo × 3 yr**, then **annually × 5 yr**; abdomen/pelvis + chest CT q**3–6 mo × 3 yr**, then **annually × 5 yr**	CMP q3–6 mo × 3 yr, then annually; **bone scan/brain MRI** as symptoms warrant
On adjuvant pembrolizumab	Follow-up as for Stage III disease	**irAE monitoring** per agent label: TSH, LFTs, sCr each cycle
On systemic therapy (Stage IV/relapsed)	H&P **q6–16 wk**; chest/abdomen/pelvis imaging **q6–16 wk**; brain MRI at baseline and as indicated	**Labs per therapeutic agent**; imaging interval adjusted to rate of disease change
Long-term survivorship (>5 yr, NED)	**H&P annually**; abdomen imaging at increasing intervals; chest imaging for higher-stage disease	**Annual labs including eGFR**; ~30% of recurrences occur after 5 yr; Z85.528 appropriate only at this phase

ABBREVIATIONS: SRM = small renal mass; CT = computed tomography; MRI = magnetic resonance imaging; US = ultrasound; CXR = chest X-ray; CEUS = contrast-enhanced ultrasound; SBRT = stereotactic body radiation therapy; CMP = comprehensive metabolic panel; H&P = history and physical; irAE = immune-related adverse event; TSH = thyroid-stimulating hormone; LFT = liver function test; sCr = serum creatinine; NED = no evidence of disease; eGFR = estimated glomerular filtration rate

Comorbidity Management – Primary Care Role

COMORBIDITY	APPROACH*[13,66,67]	CAUTION*[4,13,66]
Hypertension (I10)	**Optimize BP before TKI**; daily home monitoring after initiation; ACEi/ARB first-line for TKI-induced HTN	**HTN in 21–40%** on VEGF-TKIs; **avoid non-DHP CCBs** (verapamil, diltiazem) due to CYP3A4 interaction; hold TKI if BP ≥180/110
Chronic kidney disease (N18.x)	**Monitor eGFR at baseline and during TKI**; **nephrology referral** if eGFR <45 or proteinuria; advocate for nephron-sparing surgery	**CKD is both an RCC risk factor and a driver of surgical choice**; partial nephrectomy preserves eGFR (80% vs 35% freedom from eGFR <60 at 3 yr)
Diabetes mellitus (E11.x)	**Glycemic optimization before treatment**; fasting glucose at each visit during mTOR inhibitor therapy; A1C q3 mo	mTOR inhibitors cause **hyperglycemia** in **13–50%**; consider alternative agent class if diabetes is poorly controlled
Heart failure/CV disease (I50.x, I25.x)	**Baseline echocardiogram and troponin before ICI combination**; cardio-oncology consult if preexisting CV disease	**TKI-induced LV dysfunction**; ICI-associated myocarditis (rare but potentially fatal); serial ECG for QTc-prolonging agents
Cognitive impairment (F03.x, G30.x)	**Document functional capacity**; engage caregiver for oral TKI adherence; simplify regimen	**Impairs adherence** to twice-daily dosing and home BP monitoring protocols
Polypharmacy	Pharmacist-led reconciliation **before TKI initiation** and at each dose change	**CYP3A4 interactions**: strong inhibitors increase sunitinib AUC ~51%; **avoid grapefruit**; review statins, azoles, anticoagulants
Frailty/sarcopenia (R54, E46)	**G8 screening**; full CGA if ≤14; nutritional assessment and prehabilitation before treatment	**Function predicts toxicity and survival more than age**; malnutrition increases mortality risk from targeted drugs

ABBREVIATIONS: BP = blood pressure; TKI = tyrosine kinase inhibitor; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; HTN = hypertension; VEGF = vascular endothelial growth factor; DHP = dihydropyridine; CCB = calcium channel blocker; CYP3A4 = cytochrome P450 3A4; eGFR = estimated glomerular filtration rate; RCC = renal cell carcinoma; CKD = chronic kidney disease; mTOR = mechanistic target of rapamycin; CV = cardiovascular; ICI = immune checkpoint inhibitor; LV = left ventricular; ECG = electrocardiogram; QTc = corrected QT interval; AUC = area under the curve; G-8 = Geriatric 8 screening; CGA = comprehensive geriatric assessment
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Cost-Smart Options

BRAND (EST. COST)*[70–72]	GENERIC/ ALTERNATIVE (EST. COST)*[73,74]	EST. SAVINGS	COST-SMART TIP[4,58,75]
Active surveillance (serial imaging ~$2,000–$4,000/ yr)	No alternative needed: AS is the **lowest-cost strategy** when appropriate	Avoids **$6,000–$26,000** procedural cost	**Most cost-effective management for T1a SRM** in 65-year-old at $100K/QALY threshold; CSS **comparable to intervention** (0.19% vs 0.68% at 4 yr); appropriate for **<2 cm** or significant competing mortality
Percutaneous cryoablation (~$6,000–$20,500 total episode; 2018 Medicare reimbursement ~$481)	vs robot-assisted partial nephrectomy (**~$19,400–$26,500 total episode**; 2018 Medicare **reimbursement ~$1,553**)	**~$6,000–$13,000** per episode	Comparable QALYs at lower cost; dominant strategy in 85% of Monte Carlo simulations; suitable for T1a ≤3 cm with CKD, anticoagulation, or surgical risk
Sutent (sunitinib) 50 mg/d (~$8,000–$14,000/mo TKI; ~$358K–$656K lifetime)	**Generic** sunitinib available; pazopanib has equivalent efficacy at **~$1,500/mo lower PPPM cost**	**~$1,500/mo PPPM** vs sunitinib	Generic sunitinib available; pazopanib equivalent PFS/OS with fewer dose reductions and lower PPPM; 2/1 schedule cuts grade ≥3 toxicity from 45.7% to 8.2% with comparable efficacy — reduces downstream hospitalization costs

BRAND (EST. COST)*[70–72]	GENERIC/ ALTERNATIVE (EST. COST)*[73,74]	EST. SAVINGS	COST-SMART TIP[4,58,75]
Keytruda + Inlyta (pembrolizumab + axitinib; ~$960K–$1.4M lifetime; ~$834K 3-yr total)	vs Opdivo + Yervoy (ipilimumab + nivolumab; **~$284K–$720K 3-yr total**)	**~$114K–$400K** over 3 yr	**Ipi/nivo**: most cost-effective IO combination (ICER $34K–$52K/QALY per OS month gained); **higher initial 3-month cost but lower subsequent monthly costs**; time-limited induction (4 cycles) then nivo maintenance vs continuous IO-TKI
Lenvima + Keytruda (lenvatinib + pembrolizumab; ~$960K–$1.4M lifetime)	No generic available; highest OS cost per month gained (~$293K/ OS month)	—	**Highest PFS gain** (10.07 mo dRMST) but **highest cost** and highest symptomatic grade ≥3 AEs per OS month gained (6%); **consider ipi/nivo or cabo/nivo** for better cost-efficacy balance
Welireg (belzutifan) (single-source brand)	No generic available	—	FDA-approved after PD-1/PD-L1 + VEGF-TKI; PFS HR 0.75 vs everolimus; favorable toxicity profile; manufacturer assistance may be available
Afinitor (everolimus) 10 mg/d	**Generic** everolimus available	Significant	**Generic available**; use in lenvatinib/ everolimus combination or as monotherapy in subsequent lines; **monitor hyperglycemia** in diabetic patients

BRAND (EST. COST)*[70–72]	GENERIC/ ALTERNATIVE (EST. COST)*[73,74]	EST. SAVINGS	COST-SMART TIP[4,58,75]
Partial nephrectomy (robotic: ~$11,800–$19,400 total episode)	**Lobectomy equivalent**: open partial nephrectomy (**~$11,400**; declining volume)	Variable	**Robotic now dominant surgical approach** (141% volume increase 2010–2018); open PN declining; comparable oncologic outcomes; choose based on surgeon volume and tumor complexity
Adjuvant pembrolizumab (~$13,000–$17,000/mo × 12 mo)	**Surveillance alone** (no drug cost)	**~$156K–$204K**	**KEYNOTE-564**: OS HR 0.62 favors pembrolizumab; NNT ~19 for OS benefit at 5 yr; reserve for high-risk clear cell (pT2 grade 4, pT3+, N+, or M1 NED); surveillance is reasonable **for lower-risk resected disease**

ABBREVIATIONS: AS = active surveillance; SRM = small renal mass; CSS = cancer-specific survival; QALY = quality-adjusted life year; CKD = chronic kidney disease; TKI = tyrosine kinase inhibitor; PPPM = per patient per month; PFS = progression-free survival; OS = overall survival; IO = immuno-oncology; ICER = incremental cost-effectiveness ratio; VEGF = vascular endothelial growth factor; PD-1 = programmed death-1; PD-L1 = programmed death-ligand 1; HR = hazard ratio; AE = adverse event; dRMST = difference in restricted mean survival time; FDA = US Food and Drug Administration; PN = partial nephrectomy; NNT = number needed to treat; NED = no evidence of disease; RCC = renal cell carcinoma; NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology
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Patient Education and Adherence

RCC patient education is distinguished by the high proportion of **incidentally detected disease** (37–61%), the **complexity of oral TKI regimens** requiring daily adherence and home BP monitoring, the **emerging role of active surveillance** as a guideline-endorsed alternative to surgery for small renal masses, and the need to recognize **immune-related adverse events** (**irAEs**) that can occur during or after immunotherapy — a concept unfamiliar to most patients who associate cancer treatment only with chemotherapy.[1,29] **Education should emphasize**: what symptoms to report **urgently** (new gross hematuria, severe fatigue, rash, shortness of breath, diarrhea, or signs of AKI), why **TKI dosing consistency and home BP monitoring matter**, and how treatment decisions in older adults are **guided by function and comorbidity** rather than age alone.

DOCUMENTATION — PATIENT EDUCATION

Document the following education topics, the patient and caregiver(s) present, materials provided, and patient understanding (**teach-back method**):

- **Diagnosis in plain language**:[1] Document that the patient understands **histologic subtype** (clear cell, papillary, chromophobe), **tumor laterality**, **stage**, and **prognosis**; clarify that early-stage RCC carries **excellent long-term survival** (>94% cancer-specific survival for T1a)
- **Treatment plan options**:[29] Document modalities discussed (active surveillance vs partial nephrectomy vs radical nephrectomy vs ablation for localized disease; IO-based combinations for metastatic disease); **patient questions and preferences recorded**
- **Active surveillance protocol** (when applicable):[4] Document counseling that **AS is guideline-endorsed for T1a masses**, especially <2 cm or with significant competing mortality; imaging schedule (q3–6 mo initially, then individualized); **triggers for intervention** (growth >5 mm/yr, new symptoms)
- **Oral TKI adherence and home monitoring** (when applicable):[76] Document counseling on consistent daily dosing, home BP checks **starting Day 1 of TKI therapy**, when to contact clinic (SBP >160 or DBP >100), and common toxicities to report (hand-foot syndrome, diarrhea, fatigue); mean adherence to TKIs is **85–91%** in trials but lower in real-world settings**
- **What to report between visits on immunotherapy**:[53,68] Document counseling on **irAE recognition**: new rash, diarrhea ≥4 stools/day, shortness of breath, severe fatigue, vision changes, joint pain, or signs of AKI (edema, decreased urine output); irAEs can occur after treatment completion and **patients should monitor for at least 2 years**
- **Advance care planning**: Surrogate designation, code status, goals of care; CPT 99497/99498 billable during AWV with no patient copay; particularly relevant when life expectancy shapes AS vs surgery decisions in elderly patients
- **Caregiver assessment**: Document caregiver present, their understanding of medication schedule and surveillance plan, and burden screening; oral TKI adherence requires caregiver engagement when cognitive impairment is present

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Quality Metrics Tie-In

No RCC-specific HEDIS measures or MIPS measures are currently active in MY2026, but RCC management intersects multiple **cross-cutting quality measurement domains**: blood pressure control (**TKI-induced hypertension**), depression screening (PHQ-9), geriatric safety (fall risk, medication reconciliation), care transitions (post-nephrectomy follow-up), and advance care planning.[4,21,69] **RCC's combination of** TKI-induced hypertension requiring daily home monitoring, oral agent adherence challenges, post-nephrectomy readmission risk (**~5–6%**), high psychological

distress (**up to 46%** report psychiatric symptoms), and polypharmacy in elderly patients on IO-TKI combinations means that cross-cutting national measures **apply across the care trajectory** and can **anchor quality reporting for any PCP managing an RCC patient** in a value-based program.

MEASURE	STANDARD	APPLICABILITY TO RCC
HEDIS CBP: Controlling High Blood Pressure	**Denominator**: adults 18–85 with hypertension **Numerator**: BP 140/90 mmHg; **Exclusions**: hospice, ESRD, inpatient palliative care	Directly relevant **during TKI therapy**: all-grade HTN incidence **20–50%** with VEGFR TKIs;[77] onset within days of initiation; **PCP-led BP management** with daily home monitoring is the **standard of care**
HEDIS COA: Care for Older Adults- Medication Review	**Denominator**: MA enrollees ≥66, continuously enrolled **Numerator**: 2 sub-measures documented annually: (**1**) functional status assessment, (**2**) medication review, **Exclusions**: hospice, ESRD	TKI regimens require **CYP3A4 interaction screening** (statins, anticoagulants, antihypertensives); **medication reconciliation at every visit** per NCCN Older Adult Oncology guidelines[21]
HEDIS COA: Care for Older Adults- Functional Status Assessment	**Denominator**: MA/SNP enrollees ≥66 **Numerator**: functional status assessment documented annually **Exclusions**: hospice, ESRD	ECOG performance status and G-8 geriatric screening **directly satisfy this sub-measure**; document at every visit to guide **AS vs surgery decisions** in elderly low-risk patients
HEDIS TRC: Transitions of Care Patient	**Denominator:** enrollees ≥18 with inpatient discharge **Numerator:** 4 sub-measures within 30 days: (**1**) notification of inpatient admission, (**2**) receipt of discharge information, (**3**) patient engagement after discharge, (**4**) medication reconciliation post-discharge; **Exclusions:** hospice	Post-nephrectomy 30-day readmission rate is **4.5–7.8%** depending on approach; **renal/ genitourinary complications** and **VTE** are the most common readmission drivers; PCP post-discharge **follow-up within 7 days** reduces readmission risk[78]
HEDIS DMS-E: Utilization of the PHQ-9 to Monitor Depression Symptoms for Adolescents and Adults	**Denominator:** enrollees ≥12 with diagnosis of major depression or dysthymia AND elevated PHQ-9 ≥10 **Numerator:** follow-up PHQ-9 documented within 4–8 months of index elevated score **Exclusions:** hospice	Kidney cancer survivors have **1.92x** hazard of depression in the first year; up to **46%** report psychiatric symptoms; depression predicts survival in **metastatic RCC**[79,80]

MEASURE	STANDARD	APPLICABILITY TO RCC
HEDIS ACP: Advance Care Planning	**Denominator:** enrollees ≥66; **Numerator:** advance care plan or surrogate decision-maker documented, **OR** documentation that ACP was discussed but patient declined **Exclusions:** hospice	ACP should be addressed when life expectancy shapes **AS vs surgery** in elderly patients with **T1a SRM** and **significant competing mortality**
HEDIS PCR: Plan All-Cause Readmission	**Denominator:** enrollees ≥18 with acute inpatient discharge; **Numerator:** unplanned readmission within 30 days (lower is better) **Exclusions:** planned readmissions (maintenance chemotherapy, transplant), hospice, psychiatric	Nephrectomy readmission driven by **VTE** (OR 10.96), **organ space infection** (OR 15.23), and return to OR (OR 8.46); minimally invasive approach **reduces readmission** odds vs open (OR 0.40–0.65)[78]

ABBREVIATIONS: HEDIS = Healthcare Effectiveness Data and Information Set; BP = blood pressure; ESRD = end-stage renal disease; TKI = tyrosine kinase inhibitor; HTN = hypertension; VEGFR = vascular endothelial growth factor receptor; PCP = primary care physician; MA = Medicare Advantage; CYP3A4 = cytochrome P450 3A4; NCCN = National Comprehensive Cancer Network; ECOG = Eastern Cooperative Oncology Group; G-8 = Geriatric 8 screening; AS = active surveillance; VTE = venous thromboembolism; PHQ-9 = Patient Health Questionnaire-9; RCC = renal cell carcinoma; ACP = advance care planning; SRM = small renal mass; OR = odds ratio; AWV = Annual Wellness Visit; CPT = Current Procedural Terminology; SDoH = social determinants of health
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5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

ELEMENT	DOCUMENTATION REQUIREMENT[3,4,58]
Primary RCC with laterality (C64.1/C64.2)	State 'malignant neoplasm' or 'carcinoma' **explicitly**; confirm laterality (right = **C64.1**, left = **C64.2**) against imaging and operative reports; **C64.9** only when laterality is **genuinely undocumented** after chart review
Histologic subtype and WHO/ISUP grade	**Document subtype** (clear cell, papillary, chromophobe) and **grade** (G1–G4); **C64** is the only primary code, but **subtype drives**: treatment selection, IMDC risk stratification, and systemic therapy eligibility

ELEMENT	DOCUMENTATION REQUIREMENT[3,4,58]
AJCC 8th Edition stage and TNM	**Document cTNM** (clinical) or **pTNM** (pathologic) **explicitly**; include **T substage** (T1a vs T1b vs T3a–c) as this determines surgical approach and adjuvant eligibility
IMDC risk group (metastatic disease)	**Document favorable/intermediate/poor risk** with the 6 component factors; risk group directs first-line systemic therapy selection per NCCN and ASCO guidelines
Each metastatic site coded separately	**C78.00/01/02** (lung, with laterality); **C79.51** (bone); **C78.7** (liver); **C79.31** (brain); **C79.70/71/72** (adrenal); each documented site **supports clinical complexity** and accurate HCC mapping
Sequencing: C64.x first, then metastatic sites	Primary site code **C64.1** or **C64.2** sequenced first, followed by secondary site code(s); document method of confirmation (imaging, biopsy) for **each metastatic site**
Renal pelvis urothelial carcinoma (C65.1/C65.2)	**Distinct from C64**; document renal pelvis origin and urothelial histology; **do not code or manage as RCC**
Active surveillance status	**Document** '**C64.x**, active surveillance' **explicitly** with imaging interval and growth-rate trend; **do not transition to Z85.528** while on AS
Post-treatment, no active disease	Use **Z85.528 ONLY after** definitive treatment with no evidence of disease and no ongoing adjuvant therapy; patients on adjuvant pembrolizumab or active surveillance **retain C64.x**
Comorbidities = frequently undercoded	CKD (**N18.x**), hypertension (**I10**), diabetes (**E11.x**), heart failure (**I50.x**), depression (**F32.x/F33.x**); each maps to additional HCCs reflecting true disease burden

ABBREVIATIONS: RCC = renal cell carcinoma; WHO/ISUP = World Health Organization/International Society of Urological Pathology; IMDC = International Metastatic RCC Database Consortium; AJCC = American Joint Committee on Cancer; TNM = tumor, node, metastasis; cTNM = clinical tumor-node-metastasis stage; pTNM = pathologic tumor-node-metastasis stage; HCC = Hierarchical Condition Category; NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology; AS = active surveillance; CKD = chronic kidney disease; ICD-10 = International Classification of Diseases, 10th Revision

Annual Clinical Review and Confirmation

- **Annual review**:[4] Active RCC must be **reassessed annually** with MEAT documented; patients on active surveillance, adjuvant therapy, or under post-treatment surveillance for known disease **retain an active diagnosis** requiring ongoing documentation each encounter
- **Laterality Confirmation**:[3] Before accepting **C64.9** (unspecified), review imaging and operative reports; laterality is **almost always documented** there even when missing from the problem list; **C64.1** (right) or **C64.2** (left) should be used in the vast majority of cases

- **Active Disease Vs. History**:[3] **Z85.528** (personal history) applies only **after treatment is complete** with no evidence of disease; a patient on adjuvant pembrolizumab or under surveillance imaging has active disease and is coded **C64.x**
- **Metastatic site documentation**:[58] For metastatic disease, document the primary (**C64.x**) and code each confirmed metastatic site separately (**C78.00** lung, **C79.51** bone, **C78.7** liver, **C79.31** brain); each site reflects the patient's **true clinical complexity** and **care coordination burden**
- **Visit modality**: Face-to-face **or** synchronous audio-video telehealth qualifies when it supports meaningful clinical evaluation; chart updates without an encounter **do not satisfy MEAT**
- **Avoid rollover**: **Do not** copy forward last year's note **without updating**: treatment status, current line of therapy and cycle if on systemic therapy, IMDC risk group for metastatic disease, surveillance imaging results and growth-rate trend, and the comorbidity burden

Good Documentation — EHR Tips

- **EHR TIP — Smartphrase]** Build a **.rcc_visit dot phrase** that **auto-populates**: laterality-specific **C64.x** code (**C64.1** right, **C64.2** left), histology (clear cell/papillary/chromophobe), AJCC TNM stage, treatment status (active surveillance/post-nephrectomy/systemic therapy with regimen and cycle), eGFR by CKD-EPI, complication codes (**D63.0** anemia, **N18.x** CKD stage), and imaging interval. Separate **.rcc_surveillance phrase**: laterality, last imaging date/result, growth rate (cm/year), eGFR trend, and follow-up interval with return criteria. **Eliminates unspecified C64.9 coding** and supports MEAT in a single paste
- **[EHR TIP — Alert]** "**Laterality Hard-Stop**" = problem-list prompt requiring right/left before **C64** is saved; prevents default **C64.9** when **laterality is documented elsewhere**. "**Active vs. History Guard**" = flags **Z85.528** while adjuvant therapy or active surveillance remains documented; confirms **C64.x** vs. **Z85.528** alignment. "**Metastatic-Site Check**" = flags active **C64.x** without secondary-neoplasm codes (**C78.00** lung, **C79.51** bone, **C78.7** liver, **C79.31** brain) when metastatic disease is noted in clinical text; maps to **HCC 17**
- **[EHR TIP — Best Practice]** Pin laterality-specific **C64.x** with histology and stage (e.g., "Clear cell RCC, left kidney, C64.2, AJCC stage I, on active surveillance"), **not** "kidney cancer." Require structured laterality and active-vs-history fields **before C64.x or Z85.528 selection**. Code comorbidities **individually** (**N18.x** CKD, **I10** HTN, **D63.0** anemia). Reserve **Z85.528** only after confirmed remission with no active treatment or surveillance
- **[EHR TIP — Workflow] Fire BPA when**: surveillance imaging overdue per documented interval (q6 months for active surveillance, per protocol post-resection); eGFR not recalculated at visit; laterality-unspecified **C64.9** persisting >30 days; **Z85.528** coded with active systemic therapy on medication list; no MEAT encounter in 6 months for active-surveillance patients. Display Cockcroft-Gault/CKD-EPI alongside creatinine to support **safe dosing in low-muscle-mass patients**

- **[EHR TIP — Order Set]** "**RCC Active Surveillance**": renal-protocol CT or MRI per interval, CMP with eGFR, CBC, blood pressure check, growth-rate calculation, advance care planning prompt. "**RCC Post-Nephrectomy Surveillance**": CT chest/abdomen per protocol, CMP with eGFR, CBC, LDH, hepatic panel. "**RCC Systemic Therapy**": CBC with differential, CMP, TSH (immunotherapy), urinalysis, blood pressure (TKI), hepatic panel, immune-related AE assessment

Brief Case Examples

SUCCESS: LATERALITY-SPECIFIC CODING WITH SURVEILLANCE TRACKED

SCENARIO

A 71-year-old male with an incidentally discovered 2 cm left renal mass (Bosniak II, clear cell-favored on imaging), HTN, CKD stage 3a (eGFR 52 mL/min by CKD-EPI), on apixaban. Lives independently; **G8 score 15**. On active surveillance per shared decision-making with urology. Presents for scheduled 6-month renal-protocol CT follow-up and **annual primary care review**.

Documentation: "**C64.2**: Clear cell–favored renal mass, left kidney, T1a (active disease); **Bosniak II**; on active surveillance with renal-protocol CT every 6 months. eGFR by CKD-EPI 52 mL/min (**N18.31**: CKD stage 3a). **I10**: HTN, optimized. Apixaban interactions reviewed by pharmacist before any future systemic therapy. Growth rate 0.3 cm/year over 18 months → no intervention threshold met. Shared decision-making and imaging interval documented. Advance care planning addressed. Return 6 months with CT or sooner for new symptoms."

Outcome: C64.2 (HCC 22) + N18.31 + I10 mapped with full surveillance loop documented. **Every MEAT element present**: laterality-specific diagnosis with imaging classification, active surveillance plan with defined imaging interval and growth kinetics, renal function staging, medication safety review, functional status (G8), shared decision-making, care coordination with urology, and follow-up interval with return criteria. No avoidable procedure-related morbidity.

PITFALL: UNSPECIFIED LATERALITY AND OMITTED METASTATIC COMPLEXITY

SCENARIO

A patient with prior left nephrectomy for RCC, now on adjuvant pembrolizumab for clear cell RCC with known pulmonary metastasis. Presents for routine follow-up.

Documentation as written: "History of kidney cancer, on treatment, doing well. Kidney cancer (**C64.9**)."

Consequence: (**1**) Laterality omitted: **C64.9** used despite documented left nephrectomy; correct code is **C64.2**. (**2**) "History" framing conflicts with **active adjuvant pembrolizumab → Z85.528 would be incorrect** and understates active disease. (**3**) Known pulmonary metastasis uncoded: **C78.00** (HCC 17, CNA RAF 4.209) entirely missing from the record. (**4**) No treatment details, renal function, immune-related toxicity monitoring, or functional assessment documented. **No MEAT elements present** beyond a bare, inaccurate diagnosis label.

RAF Impact: Coding only **C64.9** captured HCC 22 (CNA RAF 0.363) while the secondary pulmonary metastasis code (**C78.00**, HCC 17, CNA RAF 4.209) was missing = a significant **under-representation of true clinical complexity**.

Fix: Document active disease with laterality; code metastatic site; include treatment, monitoring, and clinical detail. **Corrected documentation**: "**C64.2**: Active clear cell RCC, left kidney (status post left nephrectomy [date]); on adjuvant pembrolizumab cycle [X]. **C78.00**: Pulmonary metastasis = HCC 17. eGFR by CKD-EPI [value] mL/min. Blood pressure [value]; immune-related toxicity screening [status]. Imaging surveillance [status/interval]. Return [interval] or sooner for new symptoms." **Coding after fix**: **C64.2** (HCC 22) + **C78.00** (HCC 17) replaces **C64.9** (HCC 22 alone) = laterality-accurate, metastatic-complete coding with **full clinical picture preserved**.

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