Oncology Clinical Pathways

Prostate Cancer

March 2024 – V2.2024

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Prostate Cancer – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Vietnam Veterans – Agent Orange Exposure or Specified Locations

- Prostate cancer

Gulf War and Post 9/11 Veterans

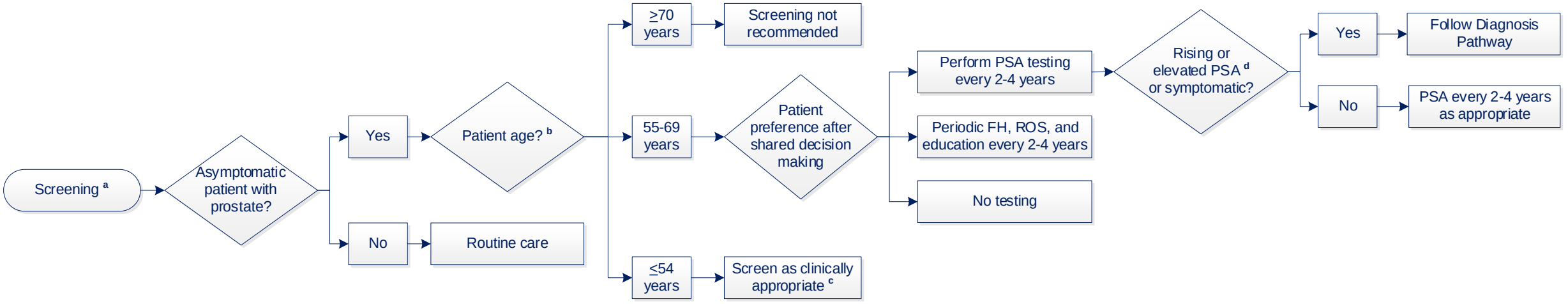
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Reproductive cancers of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

Prostate Cancer – Screening



[a] **Screening** in an average risk patient; refers to PSA testing of a individual without symptoms for prostate cancer and without a prior diagnosis of prostate cancer; use of PSA for symptoms or prior diagnosis of prostate cancer is considered diagnostic testing, surveillance, or monitoring, rather than screening

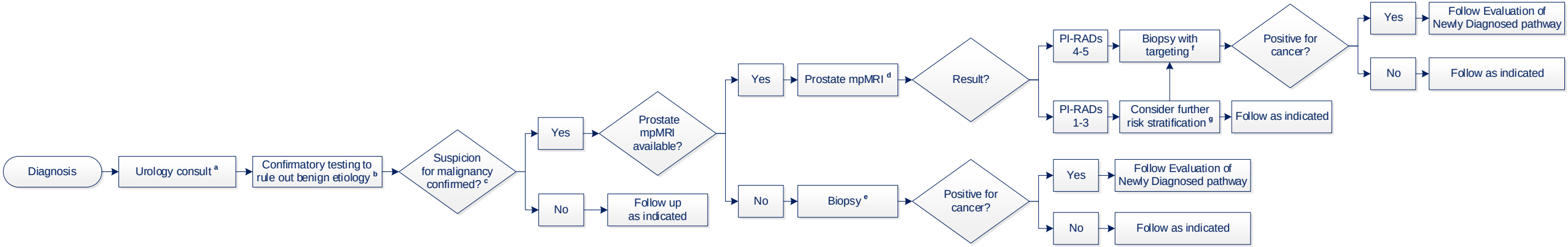
[b] **Patient Age** should be taken into consideration whether to screen patients of any age because benefits are not expected to outweigh harms when life expectancy is <10 years and/or patient would not tolerate additional evaluation or treatment (if the screen was positive)

[c] **Clinically Appropriate** is defined as individuals who may be at increased risk for prostate cancer include African Americans, family history of prostate cancer, known germline mutation associated with an increased risk in prostate cancer, and potentially, Agent Orange exposure; despite this increased risk, there is insufficient evidence as to whether the balance of benefits and harms of screening for prostate cancer is different in these individuals when compared to others of similar age; may offer or provide this service for *selected* patients depending on individual circumstances; if screening is requested by the patient after a discussion with his provider, screening may be done; clinicians should not screen anyone who does not express a preference for screening

[d] **Rising or Elevated PSA** evidence is inadequate to make formal guidance on determining concerning vs. non concerning PSA levels; consider the following parameters for making a referral to Urology: PSA >3 in the absence of UTI or other benign etiology, 0.75ng/ml rise in PSA over a year

PSA Prostate-Specific Antigen
FH Family History
ROS Review of Systems

Prostate Cancer – Diagnosis



[a] **Urology Consult** within 28 days or as clinically appropriate; timelines are suggestive clinical recommendations and do not account for patient-specific conditions and/or illnesses

[b] **Confirmatory Testing** consider repeat PSA, perform DRE, obtain urinalysis, post void residual, and consider use of biomarkers

[c] **Suspicion for Malignancy Confirmed** consider patient age, comorbidities, and preferences

[d] **Prostate mpMRI** prostate specific test; perform 1-3 months after initial urology consult; timelines are suggestive clinical recommendations and do not account for patient-specific conditions and/or illnesses

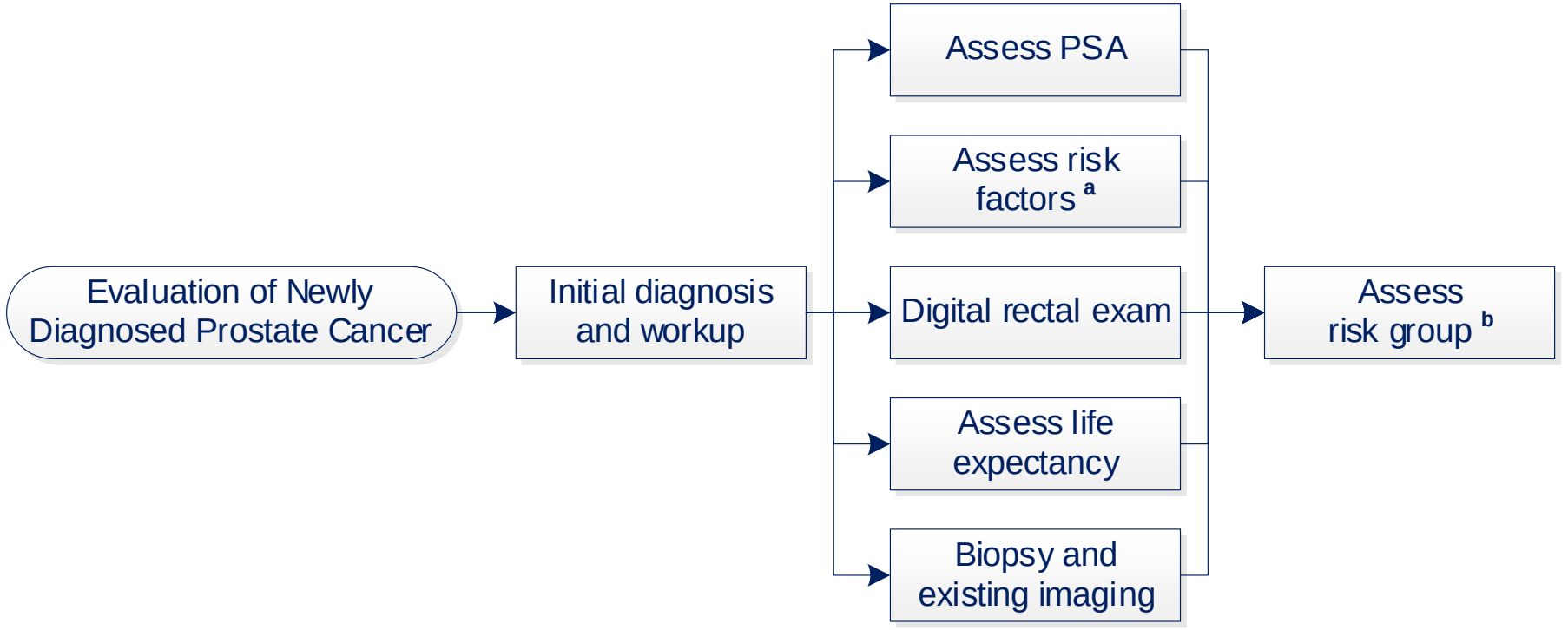
[e] **Biopsy** if prostate mpMRI unavailable, prostate biopsy should not be delayed when indicated; not all patients will need mpMRI; perform 1-3 months after initial urology consult; timelines are suggestive clinical recommendations and do not account for patient-specific conditions and/or illnesses

[f] **Biopsy with Targeting** should not exclude template biopsy unless indicated

[g] **Risk Stratification** if prostate PI-RADS 1-3 consider further risk stratification, such as PSA density, other markers, and PSMA PET/CT, if not already performed

PI-RADS Prostate Imaging Reporting and Data System
mpMRI Multiparametric Magnetic Resonance Imaging

Prostate Cancer – Evaluation of Newly Diagnosed



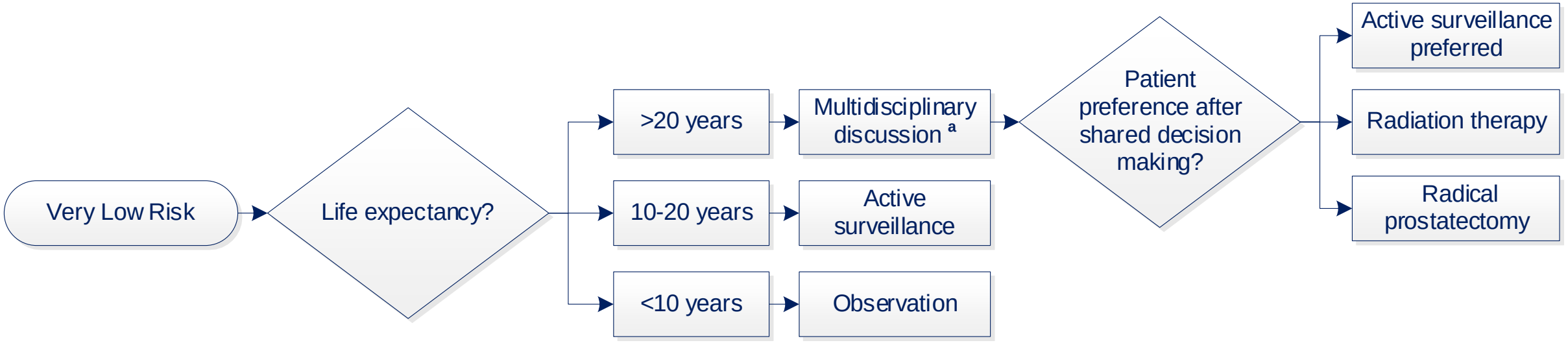
[a] **Risk Factors** Race, Agent Orange exposure, family history, known germline mutation

[b] **Risk Groups** Refer to risk stratification and corresponding pathways

Prostate Cancer – Risk Stratification

Risk Group	Defined by Clinical/ Pathologic Features			Imaging for Nodal or Metastatic Disease	Germline Testing	Initial Therapy
Very low	All the following: • T1c • Grade group 1 • PSA < 10 ng/ml • < 3 prostate biopsy fragments/ cores positive; ≤ 50% cancer in each fragment/core • PSA density < 0.15 ng/ml/g			Not indicated	Recommended for any of the following: • Ashkenazi Jewish ancestry • Family history of high-risk germline mutations • Strong family history of cancer	Follow **Very Low Risk** pathway
Low	All the following: • T1-T2a • Grade Group 1 • PSA < 10 ng/ml					Follow **Low Risk** pathway
Intermediate	All the following: • No high-risk group features • No very high-risk group features • One or more intermediate risk factors (IRF) ○ T2b-T2c ○ Grade Group 2 or 3 ○ PSA 10-20 ng/ml	***Favorable Intermediate***	All the following: • One IRF • Grade Group 1 or 2 • < 50% positive biopsy cores	• Bone imaging not recommended for staging • Pelvic ± abdominal imaging recommended if nomogram predicts >10% probability of pelvic LN involvement		Follow **Favorable Intermediate Risk** pathway
		Unfavorable Intermediate	At least one of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% positive biopsy cores	• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings		Follow **Unfavorable Intermediate Risk** pathway
High	At least one high-risk feature: • T3a • Grade Group 4 or 5 • PSA > 20 ng/ml			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings	Recommended	Follow **High or Very High-Risk** pathway
Very High	At least one of the following: • T3b-T4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • > 4 cores with Grade Group 4 or 5			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings	Recommended	
Regional	Any T, N1, M0: Consider testing tumor for HRRm and MSI or dMMR				Recommended	Follow **Regional Risk** pathway
Metastatic	Any T, Any N, M1: Recommend testing tumor for HRRm and MSI or dMMR				Recommended	Follow CSPC **M1** pathway

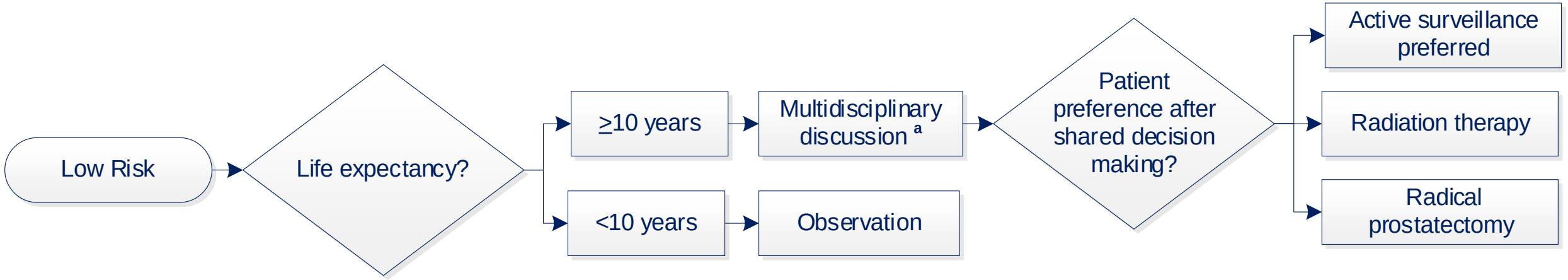
Prostate Cancer – Very Low Risk Group



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology

Prostate Cancer – Low Risk Group



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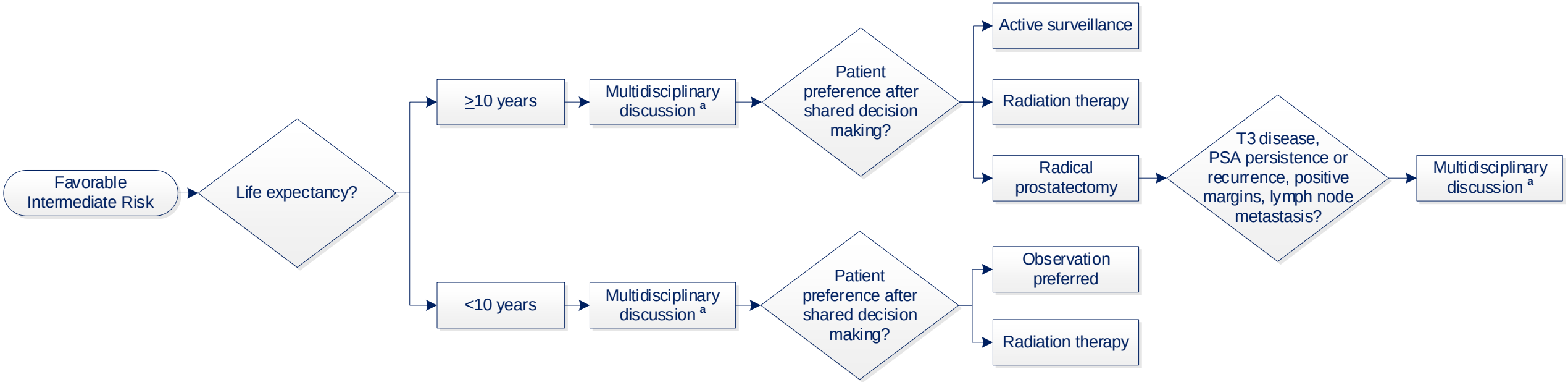
[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology

Prostate Cancer – Favorable Intermediate Risk Group



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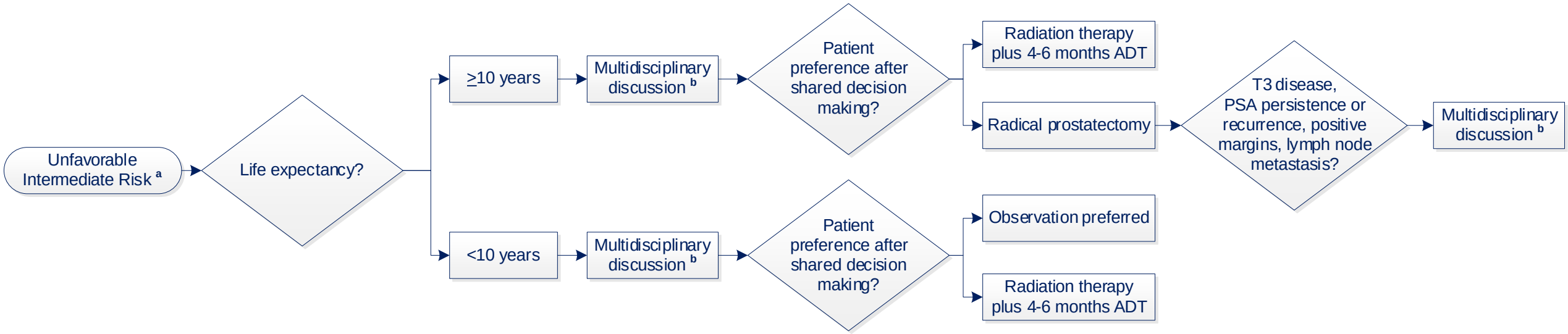
[a] **Multidisciplinary discussion** to include Radiation Oncology, and Urology

Prostate Cancer – Unfavorable Intermediate Risk Group

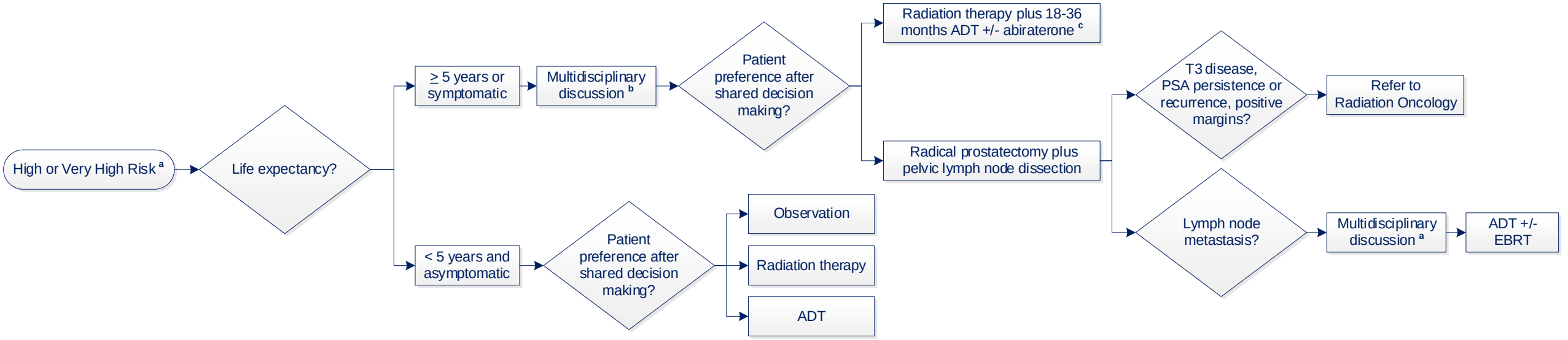


Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Imaging** PSMA PET/CT or PET/MRI preferred if available or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) and soft tissue imaging (with CT, MRI, F18-fluciclovine PET)

[b] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, and Medical Oncology

Prostate Cancer – High or Very High Risk Group



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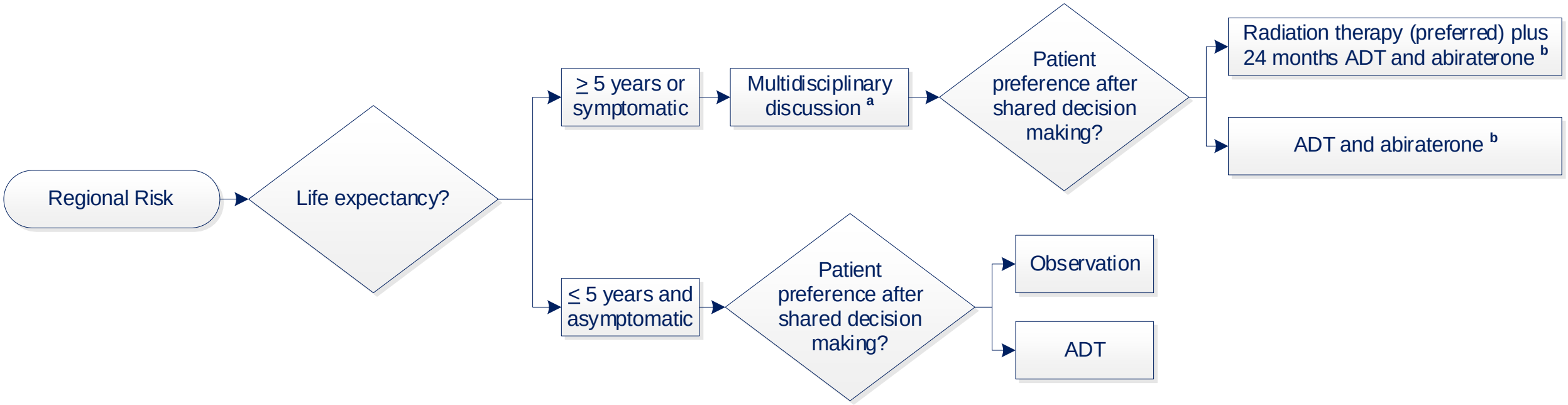
[a] **Imaging** PSMA PET/CT or PET/MRI preferred if available or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) and soft tissue imaging (with CT, MRI, F18-fluciclovine PET)

[b] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

[c] **Abiraterone** prescribe only for very high risk group patients; duration for maximum of 2 years

Prostate Cancer – Regional Risk Group

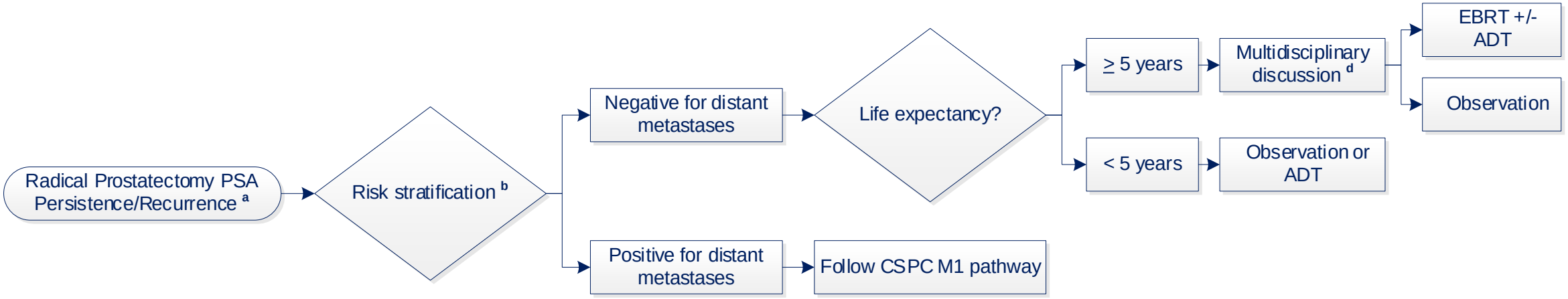


Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

[b] **Abiraterone** contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

Prostate Cancer – Radical Prostatectomy PSA Persistence/Recurrence



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

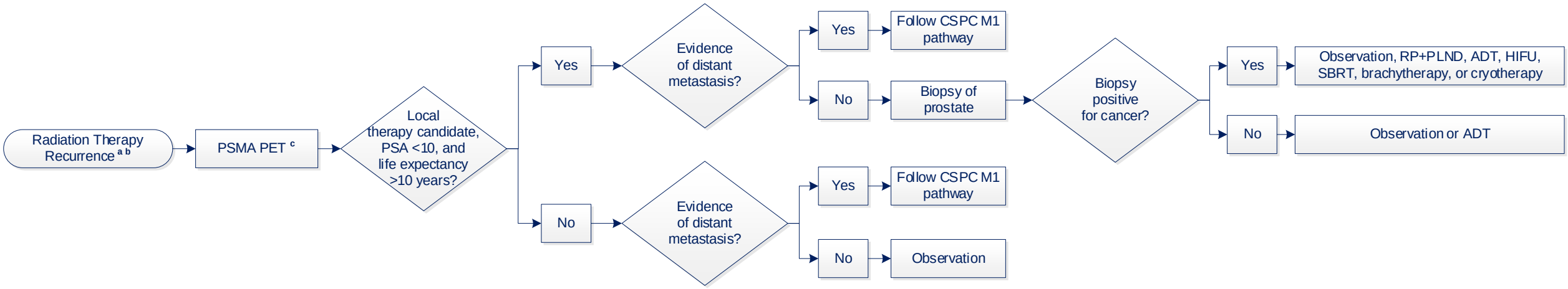
[a] **PSA Persistence/Recurrence** defined as rising, detectable PSA based on at least two determinations; PSA≥0.2 is considered of value for biochemical recurrence in a post-prostatectomy setting

[b] **Risk Stratification** PSADT; pathology report: PSMA PET imaging, if not available: fluciclovine PET/CT; CT chest/abdomen/pelvis; bone imaging with Tc99m-MDP/HDP SPECT/CT or F18 sodium fluoride PET/CT (or PET/MRI); MRI prostate/pelvis; provider appropriateness review and consideration should be made for imaging evaluation in the setting of early recurrence with low PSA values (<0.5 ng/ml)

[c] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, and Medical Oncology

EBRT External Beam Radiation Therapy

Prostate Cancer – Radiation Therapy Recurrence



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

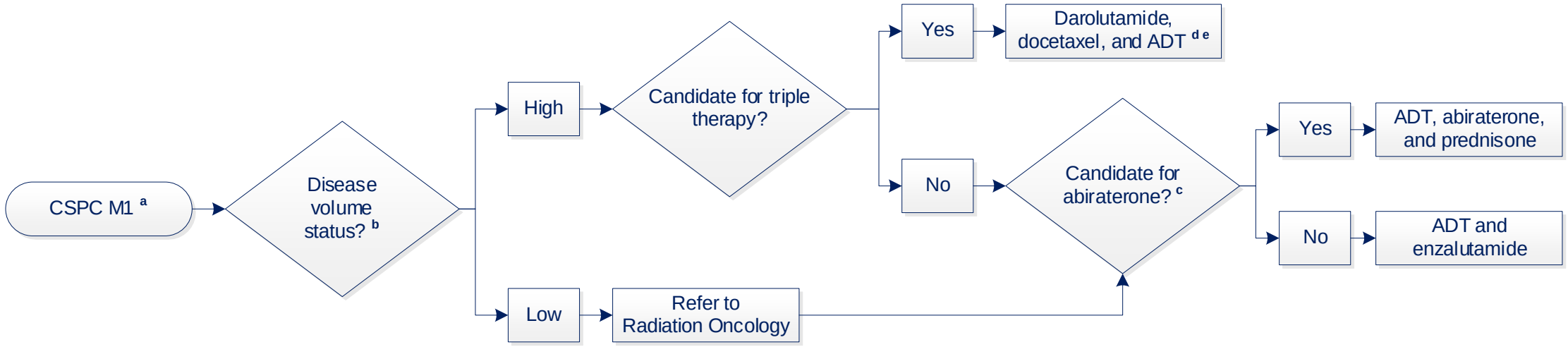
[a] **Recurrence** defined as rising PSA >2 above Nadir or positive DRE post-curative intent radiation

[b] **PSA Bounce** defined as a transient rise in PSA, at a median of 12-18 months after treatment; PSA bounce may occur in the absence of recurrent disease and does not necessarily signify a treatment failure or constitute an indication for intervention

[c] **PSMA PET** if not available, recommend prostate MRI and fluciclovine PET/CT or CT chest/abdomen/pelvis and bone imaging (technetium bone scan or F-18 sodium fluoride PET)

RP Radical Prostatectomy
PLND Pelvic Lymph Node Dissection
HIFU High Intensity Focused Ultrasound

Prostate Cancer – Castrate Sensitive Prostate Cancer (CSPC) M1



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **First Generation Antiandrogens** not recommended for long-term use however short course may be administered to block testosterone flare

[b] **Low-volume disease** defined as no visceral metastases and four or less bone metastases; **high volume disease** is differentiated from low-volume disease by visceral metastases and/or more than four bone metastases

[c] **Abiraterone** contraindications include hepatic dysfunction [f], significant cardiovascular disease [g], uncontrolled hypertension, or the inability to tolerate prednisone

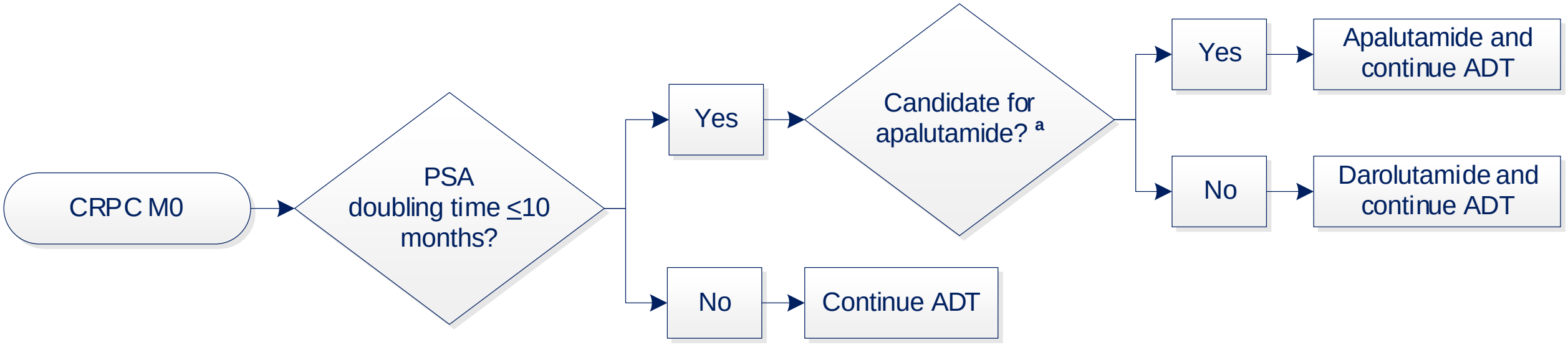
[d] **Inclusion Criteria** includes ECOG 0-1 and distant metastasis (M1) detected on imaging

[e] **Exclusion Criteria** includes CVA, MI, unstable angina, CHF (NYHA class III or IV) in the prior 6 months and/or uncontrolled HTN

[f] **Hepatic Dysfunction** defined as baseline Tbili ≥ 1.5 x ULN (except in Gilbert's Disease), AST or ALT ≥ 2.5 x ULN (AST or ALT ≤ 5x ULN allowed in known liver metastases), and/or Child-Pugh Class C

[g] **Significant CV disease** defined as MI or ATE in past 6 months, severe or unstable angina, NYHA Class III or IV heart failure, and/or EF < 50% at baseline

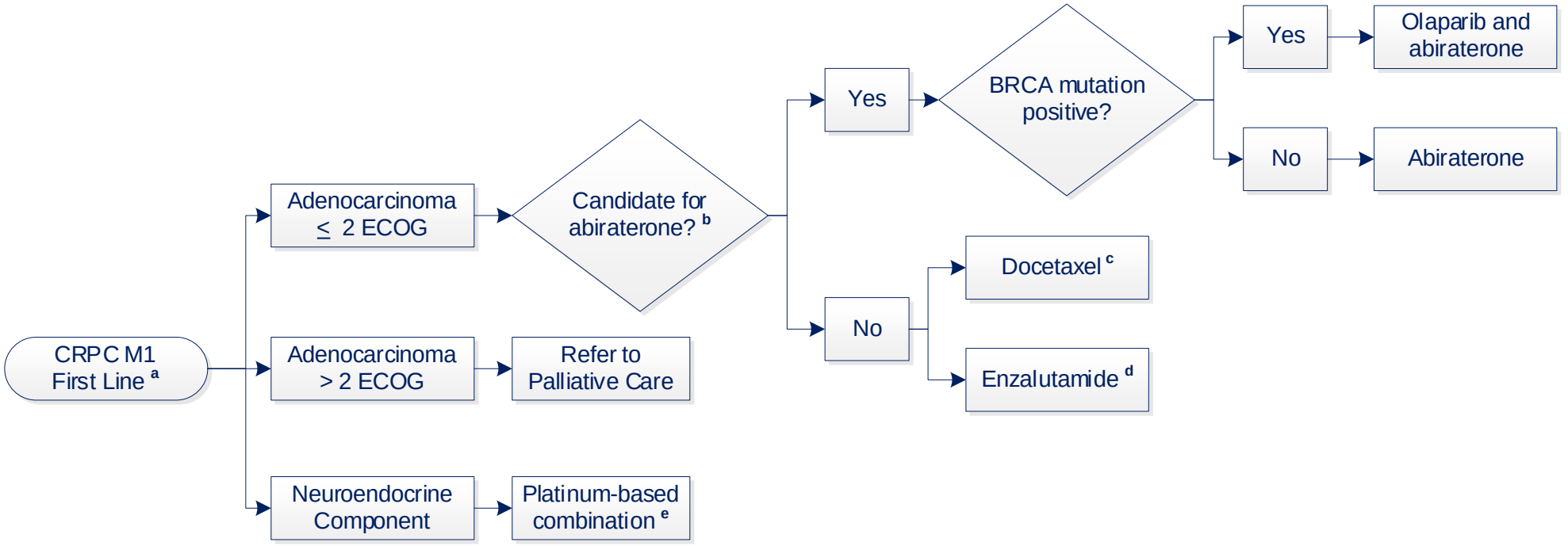
Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M0



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Apalutamide** contraindications include history of severe renal or hepatic dysfunction, cardiovascular or cerebrovascular event in prior 6 months, high fall risk, or seizure history

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, First Line



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Consider Biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

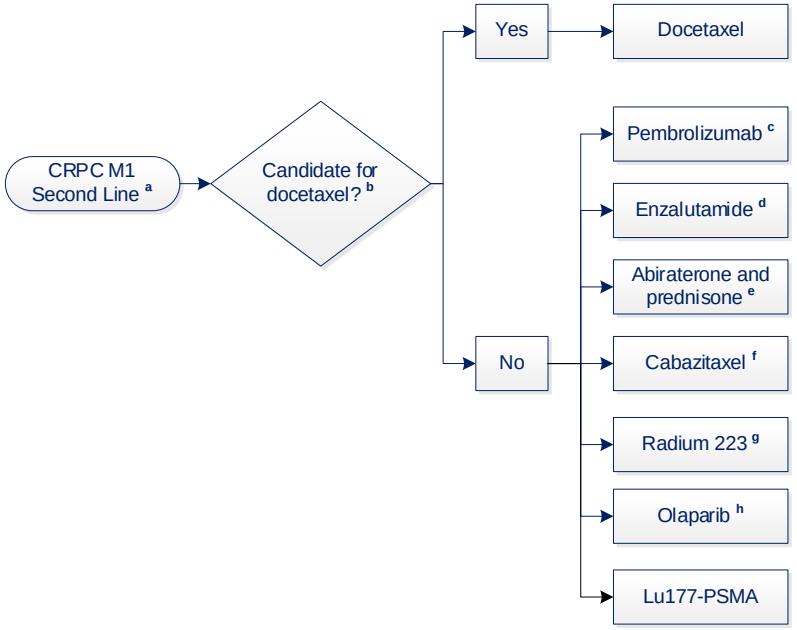
[b] **Abiraterone** contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[c] **Docetaxel** prescribe for relatively rapidly progressing symptomatic disease

[d] **Enzalutamide** contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[e] **Platinum-Based Combination** No regimen is proven more effective than another

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, Second Line



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Consider Biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

[b] **Docetaxel** prescribe for relatively rapidly progressing symptomatic disease

[c] **Pembrolizumab** prescribe if patient has MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair) or TMB high in tumor agnostic fashion

[d] **Enzalutamide** prescribe if not previously received (response unlikely if previously progressed on abiraterone); contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[e] **Abiraterone** prescribe if not previously received (response unlikely if previously progressed on enzalutamide or other androgen receptor antagonist); contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

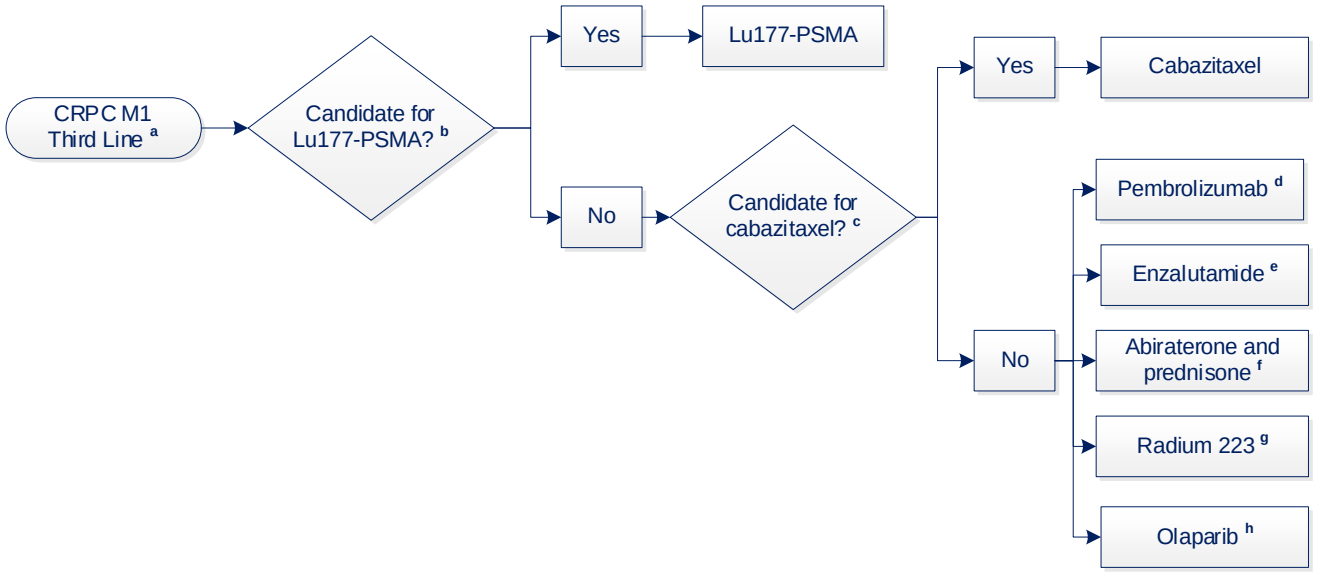
[f] **Cabazitaxel** favored for use after previous failure of one ART (enzalutamide/abiraterone); avoid repeat of previously used therapies

[g] **Radium 223** prescribe if patient has symptomatic bone metastases and no visceral disease

[h] **Olaparib** prescribe if not previously received and patient has HRRm (Homologous Recombination Repair mutation)

[i] **Lu177-PSMA** contraindications cannot be given with radium 223, cabazitaxel, or investigational product; patient can continue standard care i.e., AR-directed therapy

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, Third Line



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Consider biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

[b] **Lu177-PSMA** contraindications cannot be given with radium 223, cabazitaxel, or investigational product; patient can continue standard care i.e., AR-directed therapy

[c] **Cabazitaxel** favored for use after previous failure of one ART (enzalutamide/abiraterone); avoid repeat of previously used therapies

[d] **Pembrolizumab** prescribe if patient has MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair) or TMB high in tumor agnostic fashion

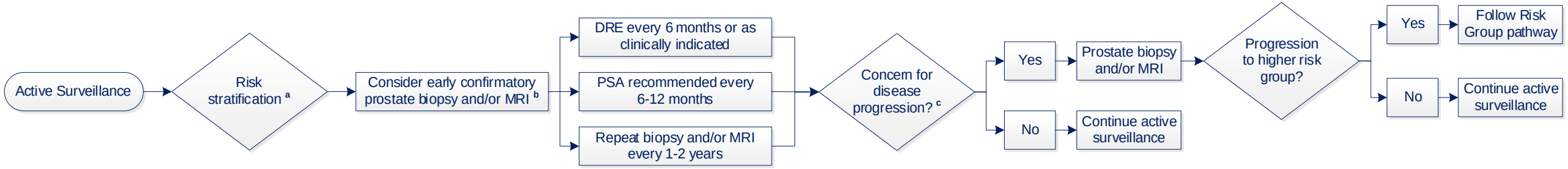
[e] **Enzalutamide** prescribe if not previously received (response unlikely if previously progressed on abiraterone);contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[f] **Abiraterone** prescribe if not previously received (response unlikely if previously progressed on enzalutamide or other androgen receptor antagonist); contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[g] **Radium 223** prescribe if patient has symptomatic bone metastases and no visceral disease

[h] **Olaparib** prescribe if not previously received and patient has HRRm (Homologous Recombination Repair mutation)

Prostate Cancer – Active Surveillance

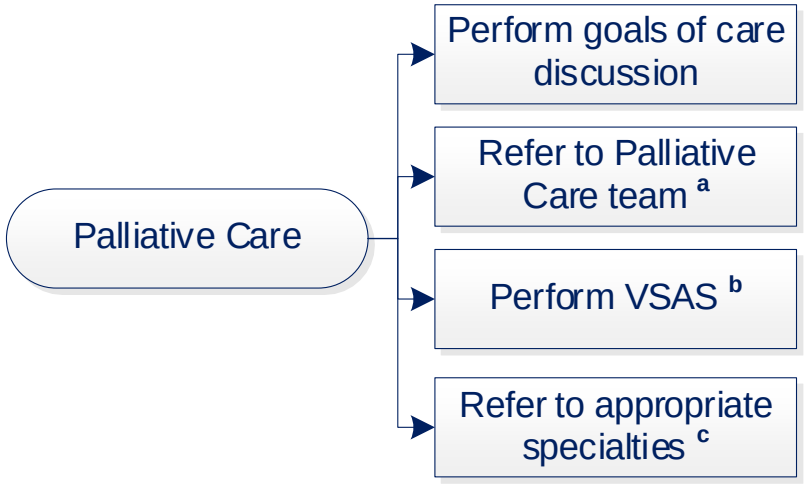


[a] **Risk Stratification** based on a combination of factors that would impact the likelihood of clinically relevant disease progression including: life expectancy (reassess every 1-2 years; if limited life expectancy consider observation), risk group, PSA velocity, DRE, MRI findings, clinical concordance, and patient preference

[b] **Confirmatory Prostate Biopsy** consider if there is a discordance between pathologic and clinical findings or if initial biopsy is determined to be inadequate

[c] **Concern for Disease Progression** based on DRE, PSA, and/or MRI results

Prostate Cancer – Palliative Care



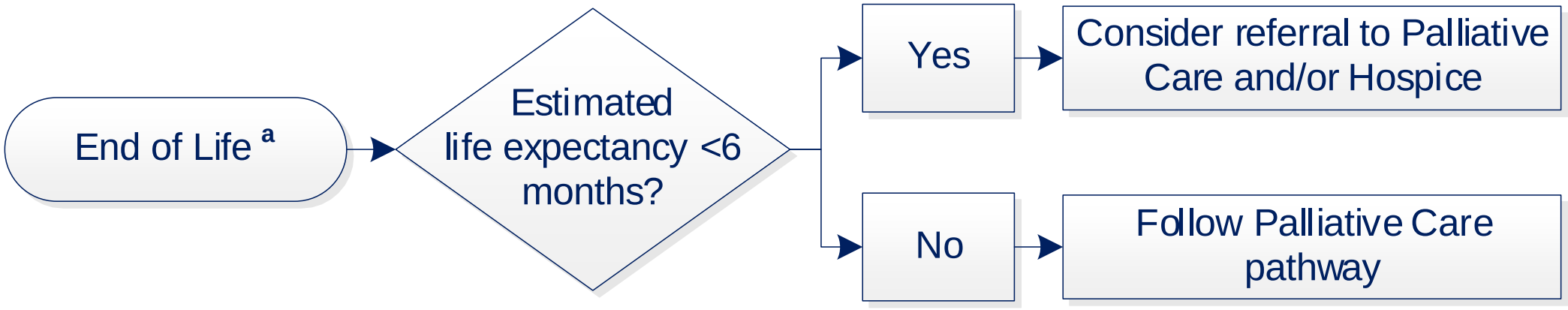
[a] **Palliative Care** can be utilized at any time for curative and non-curative situations for Veterans with advanced cancer; consultations related to palliative care should be completed within 28 days or as clinically appropriate; timelines are suggestive clinical recommendations and do not account for patient-specific conditions and/or illnesses

[b] **VSAS** VA Oncology Symptom Assessment Scale is a tool for documentation of symptoms in Veterans with cancer; the tool uses a 10-point symptom scale for assessment of symptoms

[c] **Appropriate Specialties** includes Mental Health, Pain Management, Social Work, Chaplain, Nutrition, and/or Radiation Oncology

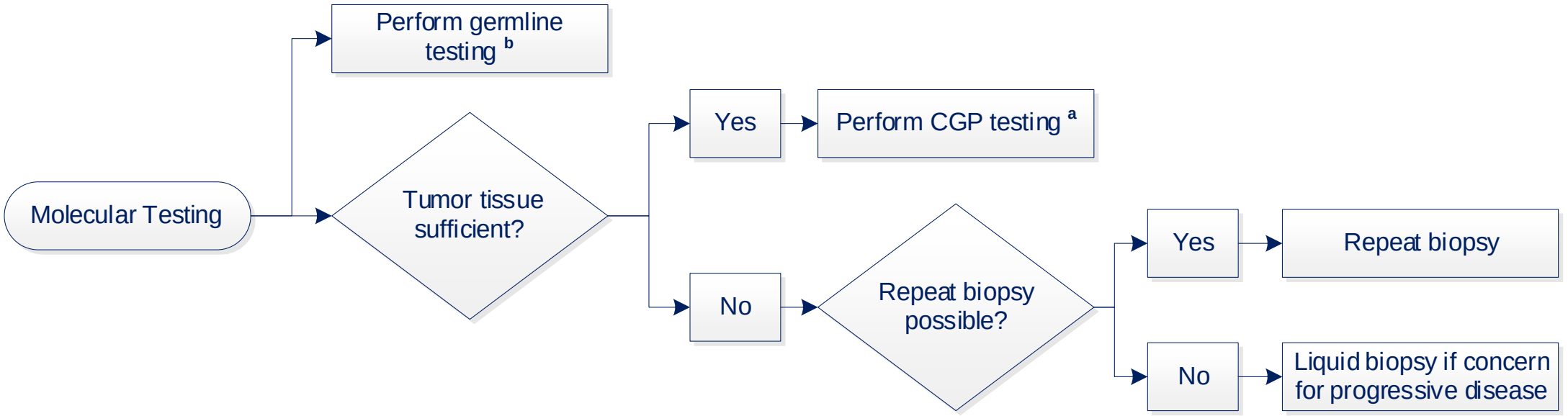
VSAS VA Symptom Assessment Scale

Prostate Cancer – End of Life



[a] **End of Life** perform goals of care discussion if not already performed; consultations related to end of life care should be completed within 28 days or as clinically appropriate; timelines are suggestive clinical recommendations and do not account for patient-specific conditions and/or illnesses

Prostate Cancer – Molecular Testing



[a] **CGP Testing** for metastatic disease

[b] **Germline Testing** for high risk, very high risk, regional risk, and metastatic disease

CGP Comprehensive Genomic Profiling

Prostate Cancer – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Very Low, Low, or Intermediate Risk Prostate Cancer with: 1.) Ashkenazi Jewish Ancestry (non-metastatic, T1 or T2); 2.) Family History of High-Risk Germline Mutations (non-metastatic, T1 or T2); or 3.) Strong Family History of Cancer (non-metastatic, T1 or T2)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS	Fulgent Prevention Genetics	Yes Yes	Blood, Saliva
High risk or Very High Risk Prostate Cancer (non-metastatic, T3 or T4)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS	Fulgent Prevention Genetics	Yes Yes	Blood, Saliva
Regional Risk Prostate Cancer (any T, N1) Non-Metastatic	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS	Fulgent Prevention Genetics	Yes Yes	Blood, Saliva
	Somatic NGS***	Comprehensive genomic profiling (CGP)	Tempus Foundation Medicine	Yes Yes	Tumor Tissue****, Blood
	IHC	MLH1, MSH2, MSH6, PMS2	Tempus (MMR)	Yes (When ordered with CGP)	Tumor Tissue
Metastatic Prostate Cancer (any T, any N, M1)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS	Fulgent Prevention Genetics	Yes Yes	Blood, Saliva
	Somatic NGS***	Comprehensive genomic profiling (CGP)	Tempus Foundation Medicine	Yes Yes	Tumor Tissue****, Blood
	IHC	MLH1, MSH2, MSH6, PMS2	Tempus (MMR)	Yes (When ordered with CGP)	Tumor Tissue

* Germline NGS test should include at a minimum BRCA1/2, ATM, CHEK2, EPCAM (deletion), HOXB13, MLH1, MSH2, MSH6, PMS2, NBN, TP53

** POC: Point of Care (Providers ordering Germline genetic test); For genetic online ordering, refer to CCGS page for further details

*** Somatic NGS test should include analysis of mutations in homologous recombination repair (HRR) genes

****Tissue preferred, but liquid acceptable if tissue insufficient