Roadmap for Management of

Men With Favorable-Risk Prostate Cancer

Version 1

MUSIC
Michigan Urological Surgery Improvement Collaborative

Making Michigan #1 in Prostate Cancer Care

In our efforts to continuously improve quality of care for men in Michigan with prostate cancer, the Michigan Urological Surgery Improvement Collaborative (MUSIC) has developed a systematic approach for management of men with **favorable-risk, early-stage prostate cancer.*** *We define men with favorable-risk prostate cancer as patients with early-stage tumors with a Gleason Score of 6 or less, as well as select patients with low-volume Gleason Score 3+4=7 cancer. After diagnosis, these men should consider Active Surveillance (AS) as one management option.*

This roadmap outlines an approach to management of patients with favorable-risk prostate cancer that was developed in the MUSIC collaborative. This approach divides care into two distinct phases that begin at the time of diagnosis:

1) Consideration Phase: Steps to take while considering AS
2) Surveillance Phase: A roadmap for how to perform AS

*This document is not intended for men with higher-risk prostate cancer (i.e., high-volume Gleason 3+4=7 or greater). For these men, definitive local treatment is most commonly recommended, but individual discussions will be necessary to determine the best course of action for an individual patient.

Introduction

Management Phases for Men with Favorable-Risk Prostate Cancer

MUSIC's roadmap for men with favorable-risk prostate cancer divides the management process into two distinct phases: The **Consideration Phase** and the **Surveillance Phase**.

Consideration Phase

Steps to take while considering AS

Step 1: Estimate life expectancy
Step 2: Determine appropriateness for AS
Step 3: Obtain confirmatory testing
Step 4: Engage in shared-decision making

Surveillance Phase

How to perform surveillance

Step 1: Select surveillance plan
Step 2: Monitor disease longitudinally
Step 3: Assess need for transition to other treatment(s)

Management Phases for Men with Favorable-Risk Prostate Cancer

Consideration Phase

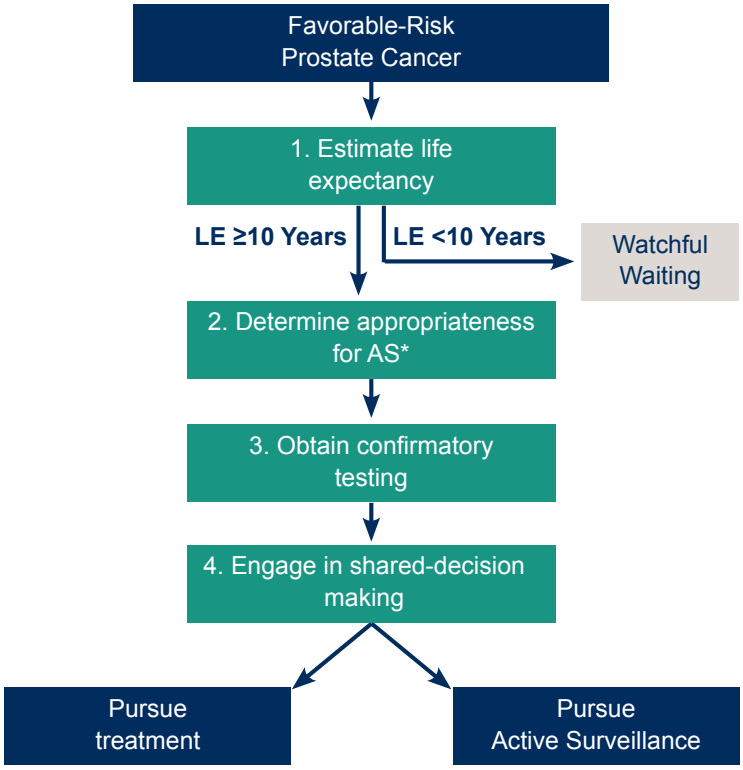
The Consideration Phase involves four important steps in determining who is appropriate for Active Surveillance:

Step 1: Estimate life expectancy

Step 2: Determine appropriateness for AS based on MUSIC criteria*

Step 3: Obtain confirmatory testing to further evaluate appropriateness

Step 4: Engage in shared-decision making to make a management decision

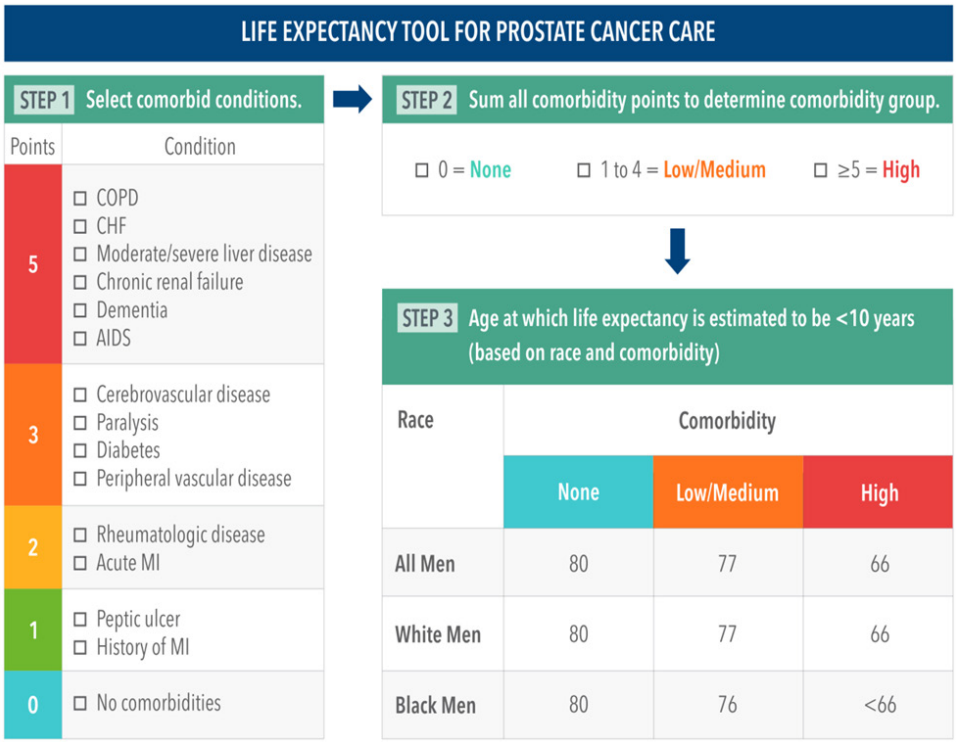


*Some men will choose treatment at this point based on preference or uncertainty around appropriateness for AS.

Consideration Phase: Steps to Take While Considering Active Surveillance

Step 1: Estimate Life Expectancy

This instrument allows you to determine the average age at which a patient has 10 years of life remaining, accounting for common comorbidities.



LIFE EXPECTANCY TOOL FOR PROSTATE CANCER CARE

STEP 1 Select comorbid conditions.

Points	Condition
5	☐ COPD ☐ CHF ☐ Moderate/severe liver disease ☐ Chronic renal failure ☐ Dementia ☐ AIDS
3	☐ Cerebrovascular disease ☐ Paralysis ☐ Diabetes ☐ Peripheral vascular disease
2	☐ Rheumatologic disease ☐ Acute MI
1	☐ Peptic ulcer ☐ History of MI
0	☐ No comorbidities

STEP 2 Sum all comorbidity points to determine comorbidity group.

☐ 0 = None ☐ 1 to 4 = Low/Medium ☐ ≥5 = High

STEP 3 Age at which life expectancy is estimated to be <10 years (based on race and comorbidity)

Race	Comorbidity		
	None	Low/Medium	High
All Men	80	77	66
White Men	80	77	66
Black Men	80	76	<66

If a favorable-risk prostate cancer patient is older than the age listed for their comorbidity group and race, then estimated life expectancy is less than 10 years and Watchful Waiting is often recommended.

Consideration Phase: Estimate Life Expectancy

Alternative Tools for Estimating Life Expectancy

1) Social Security actuarial estimate accounting for typical health of prostate cancer patients*

Age at which average man has 20 years of life remaining:	64-65
Age at which average man has 10 years of life remaining:	79-80

If a favorable-risk prostate cancer patient is older than 80, then life expectancy is less than 10 years and Watchful Waiting is often recommended. This age may be younger in men with significant comorbidities as this tool does not account for other medical conditions.

**Adapted from Kent M, et al. BMC Med 14:25, 2016*

2) Web-based tool evaluating competing risks of death from prostate cancer and other comorbid conditions available at: **https://www.mskcc.org/nomograms/prostate**

Step 2: Determine Appropriateness for AS Based on MUSIC Criteria

Using initial biopsy results, evaluate a patient's appropriateness for Active Surveillance as established by the MUSIC Consensus Panel.

Gleason Grade and Tumor Volume	Panel Recommendation(s)
Low Volume Gleason 6 *Definition: 1-2 cores positive and no cores >50% cancer*	Strongly Consider Surveillance
Intermediate Volume Gleason 6 *Definition: 1-2 cores positive and any core >50% cancer OR 3-5 cores positive no more than 2 cores with >50% cancer*	Strongly Consider Surveillance **OR** Consider Surveillance*
High Volume Gleason 6 *Definition: 3-5 cores positive and 3 or more with >50% cancer OR 6 or more cores positive*	Consider Surveillance **OR** Uncertain*
Low Volume Gleason 3+4 *Definition: 1-3 cores positive and no cores containing 3+4 with >50% cancer*	Consider Surveillance **OR** Uncertain*

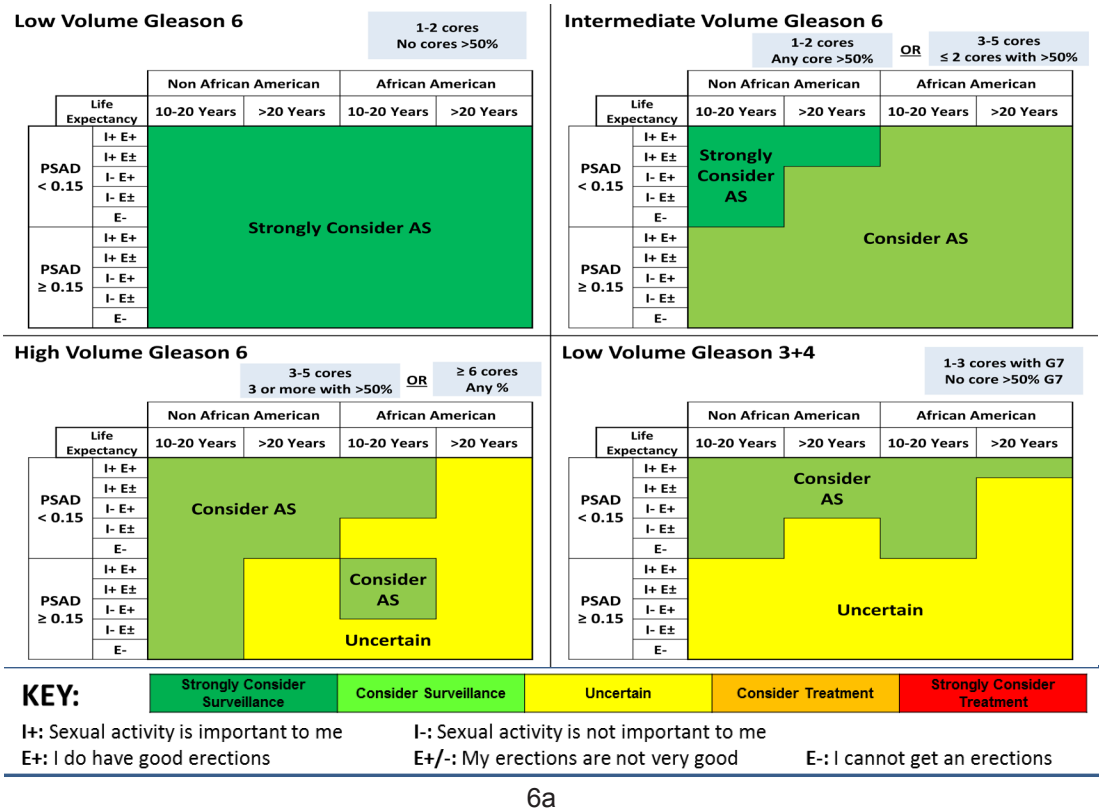
*Dependent upon other patient characteristics such as PSA density, sexual interest, and race/ethnicity. (See placard on flip-side for more specific detail).

Consideration Phase: Determine Appropriateness Based on MUSIC Criteria

Additional Details on Evaluating Appropriateness for AS Based on MUSIC Criteria

This placard is used to present the MUSIC appropriateness panel recommendations for Active Surveillance for 160 different clinical scenarios considered by the panel. Scenarios differed based on Gleason score, tumor volume, PSA density, race, life expectancy, and sexual function/interest.

Directions for use: 1) Select a quadrant on this chart based on a patient's Gleason score and tumor volume. 2) Within that quadrant locate the appropriate PSA density and sexual function row. 3) Move horizontally across row to the location that matches patient's life expectancy and race as indicated at the top of table. That location will provide the specific recommendation for a patient meeting all of the criteria.



Step 3: Confirmatory Testing

A very important consideration for men diagnosed with favorable-risk prostate cancer is the possibility of underestimating the true grade and/or volume of the tumor. Previous work from MUSIC, and elsewhere, has determined that information available at the time of diagnosis (e.g., PSA, results of diagnostic biopsy, clinical T stage) underestimates the true volume and grade of cancer in 30-50% of patients.

Thus, confirmatory testing is recommended to increase confidence that Active Surveillance is an appropriate form of management. Results from such tests may indicate that definitive local treatment is more appropriate.

Recommended Confirmatory Tests

(At least one should be obtained within 6 months of diagnosis)

Repeat Prostate Biopsy

and/or

Multi-Parametric MRI

and/or

Genomic Testing

Consideration Phase: Obtain Confirmatory Test

Interpretation of Confirmatory Test Results

One or more of the recommended Confirmatory Tests should be performed within 6 months of diagnosis to increase confidence around appropriate cancer risk-stratification.

Test Options	Reassuring Confirmatory Test Result	Recommended Response to Non-Reassuring Test Result
Repeat Prostate Biopsy*	Biopsy grade and volume remain consistent with AS appropriateness criteria	Shared-decision making to consider treatment more strongly
Multi-Parametric MRI**	Absence of PIRADS 4 or 5 lesion	Proceed to targeted biopsy or shared-decision making to consider treatment more strongly
Genomic Testing***	**Prolaris** – <3% probability of CaP mortality **Oncotype Dx** – >80% freedom from primary Gleason 4 **Decipher Score** – <0.2	Shared-decision making to consider treatment more strongly

*Should be at least 12 cores, consider anterior sampling or saturation biopsy.
**Obtain at least 6 weeks but no more than 6 months from biopsy. Must involve: 3T magnet, multi-parametric imaging with appropriate sequences (DWI,T2), appropriate radiologic expertise.
***With diagnostic biopsy or repeat biopsy.

Step 4: Once results of Confirmatory Tests are available, engage again in shared-decision making. At this point, the conversation should reconsider the merits of definitive treatment versus Active Surveillance based on the full set of information from estimation of life expectancy, evaluation of appropriateness, and interpretation of Confirmatory Test results.

Surveillance Phase

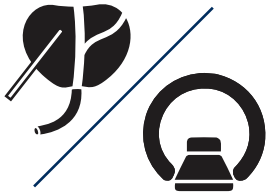
After the Consideration Phase many patients will decide to pursue Active Surveillance. At this point, patients enter the surveillance phase, a period that involves regular follow-up evaluations and testing to monitor for changes in the risk of the cancer. The specific evaluations include PSA testing, clinical examinations, and reassessments of tumor burden via repeat biopsy and MRI imaging.

The goal of this section is to provide a **roadmap for how to perform surveillance**.

Surveillance Phase Components

Office Visits

PSA Testing



Tumor Burden Reassessment

This document outlines two separate surveillance plans (High-intensity and Low-Intensity) that vary with respect to the frequency of follow-up testing. The decision to pursue one pathway or another is based on clinical parameters and patient preferences, guided by the urologist's opinion and experience. Both surveillance plans are distinctly different from Watchful Waiting, which only involves PSA and clinical examinations.

Surveillance Phase

Surveillance Phase

MUSIC recommends that patients choose between surveillance plans that vary in the frequency of planned follow-up. These plans were modelled on established protocols from centers with extensive experience in Active Surveillance[1,2]. In the absence of evidence that one plan is clearly superior, the decision for which to pursue should be made between patient and provider after considering risks, benefits and pragmatic aspects of both plans.

High-Intensity Surveillance Plan

Diagnosis	Confirmatory Test	Surveillance Phase	
PSA		Obtain every 6 months	Continue until deterioration in health or age or change in patient preferences
DRE		Obtain every 6 months	
Tumor Burden Reassessment*+ (Biopsy or MRI)	Obtain test(s) within 6 months of Diagnosis	Obtain every 12 months	

Low-Intensity Surveillance Plan

Diagnosis	Confirmatory Test	Surveillance Phase	
PSA		Obtain every 12 months	Continue until deterioration in health or age or change in patient preferences
DRE		Obtain every 12 months	
Tumor Burden Reassessment* (Biopsy or MRI)	Obtain test(s) within 6 months of Diagnosis	Obtain at least once every 3 years	

* Biopsy should occur at least every 2 years.
+ Genomic testing can be obtained on initial or subsequent biopsy at provider discretion. Consider likelihood of non-reimbursement for repeat genomic testing since this is not yet an established process.

Surveillance Phase: How to Perform Surveillance

Watchful Waiting Plan

Watchful Waiting is typically reserved for men with an estimated life expectancy of less than 10 years.

Diagnosis	Surveillance Phase	
PSA	Obtain every 12 months	Consider imaging or systemic therapy (ADT) for suspicion of metastases
DRE	Obtain every 12 months	
Tumor Burden Reassessment (Biopsy or MRI)	Not performed	
Genomics	Not performed	

[1] High-Intensity Surveillance Plan most consistent with Johns Hopkins protocol — Tosoian JJ, et al., Eur Urol 69:576-81, 2016.

[2] Low-Intensity Surveillance Plan most consistent with Toronto protocol — Klotz L, et al., J Clin Oncol 33:272-7, 2015.

When to Perform Additional Testing While on Surveillance

Scenarios That Should Prompt Further Investigation	Recommended Response
New and Concerning DRE Findings	Early tumor burden reassessment
Rapid PSA Kinetics *Definition: PSA doubling time <3 years*	Shorter interval repeat PSA testing for significant single PSA rise Early tumor burden reassessment for confirmed and sustained velocity increase
Other Clinical Suspicion for Disease Progression	Early tumor burden reassessment
Patient Preference	Modify intensity of surveillance or transition to treatment, if sustained changes in patient preferences

Surveillance Phase: When to Perform Additional Test(s)

Transitioning to Treatment

If at some point in follow-up a patient's clinical profile or preferences change, a transition to an alternative management strategy may be warranted.

Transitioning to more aggressive management: Clinical results obtained in follow-up suggesting cancer progression or changing patient preferences may prompt a transition to more aggressive treatment, such as surgery or radiation. In the event that any of the following test results occur, another round of shared-decision making to consider a transition to more definitive treatment is recommended.

Surveillance Test	Result to Prompt Discussion Regarding Transition to Definitive Treatment
Biopsy	Progression of tumor burden to a higher risk category *Consider results in context of MUSIC Appropriateness Criteria*
MRI	New PI-RADS 4 OR 5 lesion or significant change in known lesion *MRI changes may prompt further evaluation with biopsy or direct transition to definitive treatment based on patient/provider preference*
Genomic Test	Reclassification into a higher genomic risk category
Patient Preference	Desire of patient to forego continued surveillance in favor of treatment

Transitioning to Watchful Waiting: Should be considered if new health conditions suggest a patient's life expectancy drops below 10 years.

Transitioning to Treatment: Deciding When to Stop Surveillance

For questions about the Michigan Urological Surgery Improvement Collaborative please contact us at musicurology@umich.edu

A nonprofit corporation and independent licensee of the Blue Cross and Blue Shield Association