GPS mdx
for Localized Prostate Cancer

NCCN Prostate Cancer Guideline Update November 7, 2025, Version 3. 2026

Highlights

- **Artera AI is no longer listed as a predictive tool for ST-ADT** due to a lack of prospective, biomarker directed, randomized trial of the treatment of interest. The NCCN panel recommends further validation prior to using Artera AI to guide treatment decisions
- **Decipher and Artera AI are no longer listed for Low-risk prostate cancer**. They are only listed as prognostic tools in NCCN High-risk and Very High-risk Prostate Cancer. No test is indicated for Low-risk prostate cancer.
- **Negative GPS language removed** "A comprehensive list of advanced tools that do not reach the threshold of level I evidence is outside the scope of this guideline, but examples of such tests include gene expression tests (i.e., 31-gene assay [Prolaris] and 17-gene assay [Genomic Prostate Score])." Has been deleted
- **GPS' Clinical Utility Study and Canary PASS study is criticized** in the discussion of section the guidelines

GPS in the discussion section

The GPS test was 7-fold less likely to choose active surveillance compared to controls.

Excerpt from guidelines

"The Panel notes that there are risks to using tools that lack robust validation to change management decisions, as they may drive patients or providers to choose inappropriate options. For example, in one trial, 200 patients with very low to favorable intermediate. risk prostate cancer (excluding those with grade group 2 and >3 positive cores and limiting inclusion of those with PSA 10–20 ng/mL to only those with PSA density <0.15) were randomized to standard counseling with or without the 17-gene genomic prostate score (GPS) assay.**143 Patients with lower health literacy who received the GPS test were 7-fold less likely to choose active surveillance compared to controls. Therefore, if advanced tools are used, the Panel recommends only tools that have high-quality, long-term clinical trial data, ideally across multiple clinical trials."**

Talking points:

- The objective of this study is to gain insight on how GPS results impact decision making in African American men in the real world. This is not a validation study that measure performance.
- The study clearly shows GPS results effect urologists and patients decisions
- The study does not indicate if the GPS results in the arm with a 7-fold increase had a higher GPS result then the control. The objective of the study is not to measure performance but, how the urologists and patient react to it.
- ~70 to 80% of the 191 patients decided on AS. The conclusion of 7-fold increase in treatment compared to control group is not well powered and doesn't represent a large proportion of urologist and AA men.

- AA and those that are not sufficient health literate are more likely to have more anxiety and fear when discussing the GPS endpoints (AP, Death, Mets etc.…).

Excerpt from guidelines

"While multiple gene expression tests have made claims to improve the safety and/or efficacy of active surveillance, such an improvement has not been born out in prospective studies. For example, evaluation of diagnostic biopsy tissue from patients enrolled in the Canary PASS multicenter active surveillance cohort suggested that results of a molecular assay were not associated with adverse pathology in combination with clinical variables nor was there an association with upgrading in surveillance biopsies.[149] While this study utilized GPS, no other gene expression or digital pathology-based tool has positive prospective validation in this setting…

…Multiple retrospective studies suggest that the 17-gene GPS tool (previously called Oncotype Dx) may be prognostic for patients with localized prostate cancer.[154,155] GPS was also studied in the prospective Canary PASS active surveillance cohort with post-hoc biomarker analysis.[149] GPS results were obtained from 432 patients, 101 of whom underwent radical prostatectomy after an initial period of active surveillance. The authors concluded that adding GPS to a model containing PSA density and diagnostic grade group did not significantly improve adverse pathology stratification over the clinical variables alone (HR, 1.17; 95% CI, 1.00–1.43; P = .066). Additionally, there was no association observed between GPS and subsequent biopsy upgrade (P = 0.48). Event rates and sample size may have impacted the results. Additionally, as previously referenced, the GPS test was evaluated in a randomized trial and demonstrated that it decreased the relative odds of choosing active surveillance by approximately 50% with variable statistical significance depending on analysis method (P = .029 when excluding participants with inadequate biopsy specimens who did not receive a planned GPS result; P = .067 for all patients in an intention-to-treat analysis).[143]"

Talking points

NCCN Acknowledges the Canary Pass study is not properly powered.

- The lack of association of GPS result with adverse pathology at delayed surgery reported in the multivariable analysis "**may be related to the relatively small sample size for the adverse pathology endpoint in this study (N=101 men with delayed radical prostatectomy, with 52 events), as a higher number of events was expected when the study was designed (the pre-specified protocol target was 65 events for adequate power).**"

The Canary PASS patients are not in our intended use population

- Canary Pass cohort population is patient currently on AS. GPS intended use population is for newly diagnosed prostate cancer patients considering which treatment (AS or definitive treatment)
- GPS is extensively validated to predict risk of adverse pathology in patients who are **candidates for Active Surveillance** (not for upgrading in surveillance biopsies).

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Prostate Cancer

Version 3.2026 — November 7, 2025

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.

NCCN Guidelines for Patients® available at www.nccn.org/patients

PRINCIPLES OF RISK STRATIFICATION AND BIOMARKERS

General Principles:

- Currently, the primary method for personalization of treatment from localized to advanced prostate cancer is based on prognostic risk stratification, rather than the use of predictive tools.
- NCCN uses multiple categories and subgroupings to capture prognostic risk to personalize treatment recommendations.
- The purpose of the NCCN categories and subgroupings are to provide a method for risk stratification to allow standardized treatment recommendations to be provided.
  - It is acknowledged that there are methods of risk stratification with superior prognostic performance to NCCN risk groups. However, they have not been routinely reported in clinical trials. This limits the ability to provide evidence-based guideline treatment recommendations using these methods. Thus, the NCCN Guidelines continue to use NCCN categories and subgroups of risk as a framework.
  - Clinical trials have established the benefit of various treatments in prostate cancer and have commonly enrolled patients across a spectrum of risk. Subgroup analyses, absolute benefit estimates, and expert opinion are used to provide treatment recommendations for each NCCN risk group or disease state.
  - There is intrinsic heterogeneity in prognosis within a given NCCN category and subgroup. Thus, treatment recommendations for adjacent subgroups or categories of risk may be appropriate when using additional risk stratification methods.
  - The Panel acknowledges the ability to personalize treatment decisions through additional tools and have created this section to assist.
- Tools that are prognostic or predictive in one disease state may not be in other disease states, or they may have other forms of clinical utility beyond prognostication and prediction of treatment benefit.
  - For example, germline homologous recombination deficiency (HRD) mutations do not have an established prognostic or predictive role in localized prostate cancer, but specific HRD mutations have been demonstrated to have a prognostic and predictive role in advanced disease. Additionally, the utility of germline testing extends to inform screening recommendations for other cancers and cascade germline testing for family members.
- Imaging is also a biomarker (ie, MRI, PSMA-PET/CT) and can aid in risk stratification. See Principles of Imaging (PROS-E).

Note: All recommendations are category 2A unless otherwise indicated.

PRINCIPLES OF RISK STRATIFICATION AND BIOMARKERS

Biomarker Categories:

- **Biomarkers and risk stratification methods are tools that may assist in personalization of treatment. For clarity these tools are separated by type and category:**

Type:

- **Standard Tools: These include clinical and/or pathologic variables routinely collected to assign a patient to an NCCN category and/or subgroup. Examples include TNM stage, Grade Group, PSA, and metastatic volume of disease.**
- **Clinical and Pathologic Tools: These include clinical and/or pathologic tools that are generally derived from standard tools. Examples include multivariable models or nomograms, histologic variants, and PSA kinetics.**
- **Advanced Tools: These involve an additional test above what is collected to assign an NCCN category or subgroup. These may include, but are not limited to, germline or somatic tests, gene expression tests, digital histopathology-based tests, additional imaging, and circulating markers.**

Category:

- **Prognostic: Discriminates the risk of developing an oncologic endpoint (eg, distant metastasis). The relative benefit of a treatment (ie, the treatment effect or hazard ratio) is generally similar across a prognostic spectrum, although the absolute benefit of an intervention may vary by risk (ie, number needed to treat [NNT]).**
  - **Ideally, prognostic biomarkers independently discriminate and are associated with a clinically meaningful endpoint above and beyond standard tools relevant to that disease setting that ultimately helps guide a therapeutic decision.**
- **Predictive: Discriminates a difference in the relative benefit of a specific treatment for an oncologic endpoint.**
  - **Ideally, predictive biomarkers have been demonstrated to measure differential treatment effects that ultimately help guide a therapeutic decision in the context of a randomized trial, specifically randomizing the treatment of interest.**

Note: All recommendations are category 2A unless otherwise indicated.

PRINCIPLES OF RISK STRATIFICATION AND BIOMARKERS

Clinical and Pathologic Tools:

- An extensive number of prognostic clinical or pathologic tools have been reported based on highly variable evidence quality (retrospective or registry study vs. randomized trial), validation rigor, strength of endpoint (adverse pathology or BCR vs. distant metastasis), and univariable versus multivariable association with an outcome. Thus, while some of these tools may have value, these limitations hinder the ability to accurately provide guidance to specific treatment recommendations with confidence.
- A comprehensive list of these tools is outside the scope of this guideline.
  - Examples of such prognostic tools include multivariable models and nomograms (eg, CAPRA,[1] STAR-CAP,[2] MSKCC nomograms[3]), histopathology (ie, cribriform, intraductal carcinoma, absolute and percent Gleason pattern 4, total mm of cancer), and clinical variables (ie, PSA density, PSA velocity, PSA level, PSADT).

Advanced Tools:

- Advanced risk stratification tools generally offer either superior prognostic performance beyond clinical and pathologic tools AND/OR serve as predictive biomarkers for identifying patient groups that differentially benefit from a specific treatment. In general, these tools are only recommended when they have the potential ability to change management and should not be ordered reflexively.
  - Prognostic tools: Generally, the Panel recommends the use of prognostic tests that are validated in well-designed prospective studies with clinically meaningful endpoints based on disease settings that guide a specific treatment indication based on a specific score or result. These studies can be either prospective integral or integrated clinical trial(s) or post-hoc correlative analyses of prospective trials.
  - Predictive tools: Generally, the Panel recommends the use of predictive tests that are validated in a prospective, biomarker-directed, randomized clinical trial of the treatment of interest. Alternatively, if validation is post-hoc in a trial not designed to test the tool, it should be performed in more than one independent randomized trial of the treatment of interest.
- The Panel recognizes that there is an extensive number of advanced tools created with substantial variability in quality of reporting and model design, endpoint selection, and quality and caliber of validation. There are risks in using advanced tools to change management without robust validation, as they may drive patients or providers to inappropriate treatment options. If advanced tools are used, it is recommended to use tests that have robust validation, ideally with high-quality, long-term clinical trial data and across multiple clinical trials.
- Only advanced tools with high evidence quality are shown in Table 1. Other prognostic tools that are commonly used are described in the Discussion.

Note: All recommendations are category 2A unless otherwise indicated.

PRINCIPLES OF RISK STRATIFICATION AND BIOMARKERS

Table 1. Advanced Prognostic Tools[a]

Intermediate-Risk Prostate Cancer		
Tool	**Category**	**Discussion**
22-gene genomic classifier (GC) (Decipher)[4-6]	Gene Expression	NRG/RTOG 0126 phase III randomized trial was profiled post-hoc with a prespecified analysis plan.[4] The study demonstrated the independent prognostic effect of GC on biochemical failure, secondary therapy, DM, PCSM, MFS, and OS. Patients receiving RT alone with low GC scores had 10-year DM rates of 4%, compared with 16% for GC high risk. These results suggest that the benefit of short-term ADT in NCCN intermediate-risk prostate cancer is likely to be smaller in patients with low GC scores (≤0.45) than in patients with high GC scores (≥0.60). A breakdown of outcomes between patients with favorable vs. unfavorable intermediate-risk disease was not provided.
Multimodal artificial intelligence (MMAI) (ArteraAI Prostate)[b,7-11]	AI-Pathology	A post-hoc meta-analysis of eight phase III randomized trials (NRG/RTOG 9202, 9408, 9413, 9902, 9910, 0126, 0415, and 0521) with MMAI scores have been reported.[7,8] There were a total of 630 patients with NCCN intermediate-risk disease who primarily received RT alone or RT+ST-ADT. Among patients with NCCN intermediate-risk disease, those with MMAI low-risk disease had 5-year and 10-year DM rates of 1% and 4%, respectively. In contrast, those with MMAI intermediate- and high-risk tumors had 5-and 10-year DM rates of 7% and 40%. MMAI was independently prognostic for DM, PCSM, and death after DM. These results suggest that the benefit of short-term ADT in NCCN intermediate-risk prostate cancer is likely to be smaller in patients with MMAI low-risk disease than in patients with MMAI intermediate- or high-risk disease. Neither a breakdown of favorable vs. unfavorable intermediate risk, nor a breakdown of outcomes after RT alone vs. RT+ST-ADT were provided.

DM = distant metastases; MFS = metastasis-free survival; PCSM = prostate cancer-specific mortality; ST-ADT = short-term ADT

[a] In the absence of prospective trials, caution is warranted if using these prognostic tools to influence treatment decisions. The Panel awaits future trials that confirm the initial results described here.

[b] There is also an MMAI predictive biomarker that was validated post-hoc in RTOG 9408 to predict benefit of ST-ADT added to RT in patients with intermediate-risk prostate cancer. While promising, due to differences in tissue sampling, grading, staging, and treatment, the Panel recommends further validation prior to using this predictive biomarker to guide treatment decisions in isolation.

Note: All recommendations are category 2A unless otherwise indicated.

References

PRINCIPLES OF RISK STRATIFICATION AND BIOMARKERS

Table 1. Advanced Prognostic Tools[a]

Tool	Category	Discussion
High-Risk and Very-High-Risk Prostate Cancer		
22-gene GC[4-6]	Gene Expression	A meta-analysis of three phase III randomized trials (NRG/RTOG 9202, 9413, and 9902) that included patients with high-/very-high-risk prostate cancer were profiled post-hoc with a prespecified analysis plan.[5] The study demonstrated the independent prognostic effect of GC on biochemical failure, DM, MFS, PCSM, and OS. Patients with low GC scores had 10-year DM rates of 6%, compared with 26% for GC high risk. The absolute benefit of LT-ADT over ST-ADT was 11% for patients with high GC scores (NNT of 9), and 3% for patients with low GC scores (NNT of 33). These results suggest that the benefit of long-term ADT in NCCN high- and very-high-risk prostate cancer is likely to be smaller in patients with low GC scores (≤0.45) than in patients with high GC scores (≥0.60). A breakdown of outcomes between patients with high- vs. very high-risk disease was not provided.
MMAI[b,7-12]	AI-Pathology	Multiple post-hoc meta-analyses of patients with NCCN high- or very-high-risk disease from six randomized phase III randomized trials (NRG/RTOG 9202, 9408, 9413, 9902, 9910, and 0521) with MMAI scores have been reported.[8,10] A total of 1090 patients had NCCN high-/very-high-risk disease and were treated predominately with RT+LT-ADT (with or without chemotherapy; 68%) or RT+ST-ADT (30%), and a small number with RT alone (2%). Among patients with NCCN high-/very-high-risk disease, those with MMAI low-risk disease had 5-year rates of DM of 0% and 10-year rates of 3%. In contrast, those with MMAI intermediate- and high-risk tumors had 8% and 26% risk of metastasis at 10 years post-treatment, respectively. MMAI was independently prognostic for DM, PCSM, and death after DM. These results suggest that the benefit of ADT in NCCN high- and very-high-risk prostate cancer is likely to be smaller in patients with MMAI low-risk disease than in patients with MMAI intermediate- or high-risk disease. Neither a breakdown of high- vs. very high-risk, nor a breakdown of outcomes between cohorts receiving RT+ST-ADT vs. RT+LT-ADT, were provided. Published results from four phase III randomized trials from the STAMPEDE platform, which included 1575 patients with locally advanced, M0 disease (ie, NCCN very-high-risk disease), with post-hoc derivation of MMAI scores have been reported.[12] Overall, patients with locally advanced N0M0 disease had a 5% PCSM event rate, but when divided by MMAI quartile, there was a significant difference between the lower three quartiles (3%) vs. the highest quartile (11%). When restricting to patients receiving abiraterone, these rates were 2% vs. 5%. These results suggest that the benefit of abiraterone in NCCN very-high-risk prostate cancer is likely to be smaller in patients with MMAI low-risk disease than in patients with MMAI high-risk disease.
BCR Post-RP		
Tool	**Category**	**Discussion**
22-gene GC[13,14]	Gene Expression	Two phase III randomized trials post-RP were profiled post-hoc with prespecified analysis plans. NRG/RTOG 9601 demonstrated the independent prognostic effect of GC on DM, PCSM, and OS, and found that for patients with lower entry PSAs (<0.7 ng/mL), the 12-year DM rate benefit from hormone therapy for patients with GC lower risk vs. GC higher risk was 0.4% vs. 11.2%.[13] The SAKK 09/10 phase III trial tested post-RP lower vs. higher dose RT alone. The study demonstrated the independent prognostic effect of GC on biochemical progression, clinical progression, secondary hormone therapy, DM, and MFS.[c,14] These results suggest that the benefit of ADT added to RT for patients with RP recurrence planned for early secondary RT is likely to be smaller in those with low or intermediate GC scores (<0.6) than in those with high GC scores (≥0.60).

DM = distant metastases; LT-ADT = long-term ADT; MFS = metastasis-free survival; NNT = number needed to treat; PCSM = prostate cancer-specific mortality; ST-ADT = short-term ADT

[a] In the absence of prospective trials, caution is warranted if using these prognostic tools to influence treatment decisions. The Panel awaits future trials that confirm the initial results described here.

[b] There is also an MMAI predictive biomarker that was validated post-hoc in RTOG 9408 to predict benefit of ST-ADT added to RT in patients with intermediate-risk prostate cancer. While promising, due to differences in tissue sampling, grading, staging, and treatment, the Panel recommends further validation prior to using this predictive biomarker to guide treatment decisions in isolation.

[c] SAKK 09/10 combined GC low and intermediate risk due to relatively similar prognosis. NRG/RTOG 9601 dichotomized patients by GC low versus intermediate and high risk. However, due to the age of the tissue from NRG/RTOG 9601 (>20 years old), there is a known shifting of GC scores, and a more contemporary distribution of score distribution would approximate closer to combining GC low and intermediate risk together.

Note: All recommendations are category 2A unless otherwise indicated.

References

Advanced Risk Stratification Tools

The Panel strongly advocates the maximum utilization of all routine clinical, pathologic, and patient information to risk stratify patients. This includes the information that forms the basis of the NCCN risk groups, as well as other routine information that can be derived from standard tests, such as PSA density, PSA velocity, percentage or absolute pattern 4, and intraductal and cribriform architecture. Other tools have been developed that, variably, have been shown to be superior to standard clinical tools at estimating prognosis, and these are referred to as advanced risk stratification tools. These currently include multigene expression tests and digital pathology-based artificial intelligence tests, as discussed in more detail below.

These advanced risk stratification tools should only be considered when they have the potential ability to change disease management; they should not be ordered reflexively. Importantly, the Panel notes that there are risks to using tools that lack robust validation to change management decisions, as they may drive patients or providers to choose inappropriate options. For example, in one trial, 200 patients with very low to favorable-intermediate risk prostate cancer (excluding those with grade group 2 and >3 positive cores and limiting inclusion of those with PSA 10–20 ng/mL to only those with PSA density <0.15) were randomized to standard counseling with or without the 17-gene genomic prostate score (GPS) assay.[143] Patients with lower health literacy who received the GPS test were 7-fold less likely to choose active surveillance compared to controls. Therefore, if advanced tools are used, the Panel recommends only tools that have high-quality, long-term clinical trial data, ideally across multiple clinical trials.

Currently, the Panel recommends using tests with high-quality, prospective validation. For predictive tools, ideally this validation is from dedicated prospective biomarker-focused trials (eg, NRG GU006). Alternatively, this can be from post-hoc assessment of the biomarker in completed prospective trials, ideally multiple such trials. For prognostic tools, the Panel generally recommends the use of prognostic tests that are validated in well-designed prospective studies with clinically meaningful endpoints based on disease settings that guide a specific treatment indication based on a specific score or result. These studies can be either prospective integral or integrated clinical trial(s) (eg, NRG GU009, NRG GU010) or post-hoc correlative analyses of prospective trials.

Tumor Multigene Expression Testing

Gene testing of a tumor offers the potential of added insight into the biologic behavior of a cancer that could thereby aid in clinical decision-making.

Several tissue-based molecular assays have been developed to improve risk stratification. The 22-gene genomic classifier (GC; Decipher) is discussed in more detail in the *Principles of Risk Stratification* in the algorithm above; others are discussed below. The training and development of each assay is distinct, the genes analyzed are unique, and there is heterogeneity in the robustness of validation. It is important to understand that companies may make invalid or inaccurate claims about these tests, which can create confusion for patients and providers. Furthermore, the resulting test score, such as low or high risk, may be discordant between different tests due to multiple factors.

It is clear that use of tissue-based molecular assays will often change decisions about disease management.[144-147] However, what is unclear from such studies is if the change in management improved patient outcomes or was appropriate. Furthermore, it is increasingly clear that each assay should be evaluated independently because they do not capture the same biology. For example, a study of over 50,000 patients was performed to compare three commonly used gene expression

signatures via creation of derived signatures for each test, and the correlation between the signatures was poor (R2, 0.32–0.36).[148]

While multiple gene expression tests have made claims to improve the safety and/or efficacy of active surveillance, such an improvement has not been born out in prospective studies. For example, evaluation of diagnostic biopsy tissue from patients enrolled in the Canary PASS multicenter active surveillance cohort suggested that results of a molecular assay were not associated with adverse pathology in combination with clinical variables nor was there an association with upgrading in surveillance biopsies.[149] While this study utilized GPS, no other gene expression or digital pathology-based tool has positive prospective validation in this setting.

Currently, the above-mentioned validation criteria for prognostic biomarker tests has been reached by the 22-gene GC prognostic assay, which has reported outcomes from multiple post-hoc analyses of randomized trials.[150-153] The relevant disease settings and more details for this tool are available in the *Principles of Risk Stratification* in the algorithm above. There are multiple biomarker-directed randomized trials utilizing the 22-gene GC assay that have completed enrollment or are ongoing (eg, NRG GU006, 009, 010).

Multiple retrospective studies suggest that the 17-gene GPS tool (previously called Oncotype Dx) may be prognostic for patients with localized prostate cancer.[154,155] GPS was also studied in the prospective Canary PASS active surveillance cohort with post-hoc biomarker analysis.[149] GPS results were obtained from 432 patients, 101 of whom underwent radical prostatectomy after an initial period of active surveillance. The authors concluded that adding GPS to a model containing PSA density and diagnostic grade group did not significantly improve adverse pathology stratification over the clinical variables alone (HR, 1.17; 95% CI, 1.00–1.43; P = .066). Additionally, there was no association observed between GPS and subsequent biopsy upgrade (P = 0.48). Event rates and sample size may have impacted the results. Additionally, as previously referenced, the GPS test was evaluated in a randomized trial and demonstrated that it decreased the relative odds of choosing active surveillance by approximately 50% with variable statistical significance depending on analysis method (P = .029 when excluding participants with inadequate biopsy specimens who did not receive a planned GPS result; P = .067 for all patients in an intention-to-treat analysis).[143]

Similarly, multiple retrospective institutional and tumor registry studies suggest that the 31-gene cell cycle progression test (CCP; Prolaris) may have prognostic value for patients with localized prostate cancer.[156-158] No prospective trials have been published to date.

Numerous other tests have been developed with variable evidence quality that are currently outside of the Discussion presented here.

Digital Pathology-Based Tools

More recently a new class of advanced risk stratification tool has been developed that utilizes artificial intelligence (AI) to analyze digital pathology slides from a patient's prostate biopsy or prostatectomy specimen. Analogous to the multigene prognostic assays, these tools are primarily focused to improve risk stratification. The multimodal AI (MMAI) test (ArteraAI Prostate) is one such test, which gained FDA approval in July 2025. The MMAI test was validated in multiple post-hoc analyses of completed randomized trials.[159-161]

The MMAI test also has developed a potential predictive model to guide the use of short-term ADT. The predictive model was validated in RTOG 9408, a randomized trial of low-dose radiotherapy with or without 4 months of ADT, and was shown to identify patients more likely to benefit from ADT.[162] A similar, but unique model also was developed that may predict

the benefit of short-term versus long-term ADT and validated in RTOG 9202.[163] Given the considerable changes in staging, grading, and treatment since the start of RTOG 9202 and 9408 (>30 years ago), it is unclear if the predictive models still work in contemporarily treated patients, and further validation is recommended by the Panel.

The relevant disease settings and more details for this tool are available in the *Principles of Risk Stratification* in the algorithm above.