Screening for bladder cancer

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INTRODUCTION

Urothelial carcinoma of the bladder is the most frequently diagnosed cancer of the urinary tract other than prostate cancer, and its incidence has been slowly rising over several decades.

Risk factors for bladder cancer, tests to detect it, and a discussion of screening will be reviewed here.

Overviews of management of bladder cancer are presented separately:

- (See "Overview of the initial approach and management of urothelial bladder cancer".)
- (See "Clinical presentation, diagnosis, and staging of bladder cancer".)
- (See "Overview of the management of bladder cancer in older adults".)

EPIDEMIOLOGY AND PATHOLOGY

Worldwide, there are over 500,000 cases of bladder cancer and almost 200,000 deaths related to bladder cancer each year [1]. There is a 10-fold variation in bladder cancer incidence among different countries, with the highest rates in Europe, North America, Western Asia, and Northern Africa [2]. In the United States, there are approximately 80,000 new cases per year and 17,000 deaths [3].

The natural history of bladder cancer is highly variable and depends on the stage of disease (table 1). The majority of bladder cancers (65 percent) are diagnosed at an early stage and are low-grade non-muscle-invasive tumors with a very low risk of progression [4]. However,

high-grade non-muscle-invasive disease has a 50 to 70 percent risk of recurrence and a 10 to 30 percent risk of progressing to muscle-invasive disease [5]. Diagnosis at a later stage can be associated with high-grade muscle-invasive disease that can progress quickly, metastasize, and become fatal [4,5]. (See "Clinical presentation, diagnosis, and staging of bladder cancer".)

Bladder cancer classification, cell types, and specifics about pathology are described in detail separately. (See "Pathology of bladder neoplasms".)

RISK FACTORS

The biggest risk factors for urothelial carcinoma are exposures to toxins (tobacco and certain industrial chemicals) that are thought to cause more than two-thirds of bladder cancers. Other contributors to risk include male sex, older age, White race [6], medical treatments (eg, pelvic irradiation, cyclophosphamide, chronic indwelling urinary catheter), and heredity/family history of bladder cancer. A personal history of bladder cancer is also a risk factor due to the high recurrence rate [7]. (See "Epidemiology and risk factors of urothelial (transitional cell) carcinoma of the bladder", section on 'Risk factors'.)

Risk estimation for bladder cancer is not a precise science; it involves rough approximations. Estimates may be made by assessing the degree of exposure to factors known to increase risk for bladder cancer. Generally, bladder cancer risk is heightened among people with greater duration and extent of direct exposure to cigarette smoke or to industrial chemicals. For example, people in high-risk occupations include aluminum workers, those who work directly with vats of chemical carcinogens such as aromatic amines, or those who are exposed to diesel exhaust [8]. Specific chemicals that pose increased risk, as well as additional risk factors for bladder cancer, are discussed in detail elsewhere. (See "Epidemiology and risk factors of urothelial (transitional cell) carcinoma of the bladder", section on 'Risk factors'.)

Several attempts have been made to develop models to define a "high-risk population" [9]. There are models that use known sociodemographic and clinical risk factors; however, these models have generally been used for research and are seldom used in clinical practice. Such models have typically included age, sex, and other factors (eg, family history, smoking history, race, occupational exposure). In two studies, such models were able to identify a group of study participants who were more likely to develop bladder cancer [10,11]. In another study, cigarette smoking served as the strongest risk factor [12]. One study's findings suggested that screening high-risk patients would be significantly more cost-effective and feasible than screening the general population; however, the study used comparisons with historical controls, and thus the conclusions cannot be considered definitive [10].

RATIONALE NOT TO SCREEN

Although screening for bladder cancer might appear to have the potential to be beneficial based upon an understanding of known risk factors and the availability of urine tests that are easy to administer, studies do not show sufficient benefit of screening for bladder cancer. Urine analysis testing lacks specificity, there are no randomized trials evaluating screening, and available observational studies do not present convincing evidence even for screening high-risk populations.

Limited evidence

Average-risk population — Evidence of the efficacy of screening for bladder cancer is lacking. There are no randomized trials or case-control studies that assess outcomes in screened versus unscreened populations. Most evidence on bladder cancer is from observational studies, which show mixed results. However, observational studies are of limited usefulness because they are subject to multiple confounders as well as to lead-time bias and length-time bias. (See "Evidence-based approach to prevention".)

In one observational study, screening for bladder cancer was associated with a low bladder cancer mortality rate [13]. In this study, microscopic hematuria was detected in 16 percent of 1575 men aged ≥50 years who were tested repeatedly during one year, and bladder cancer was identified on cystoscopy in 8 percent of those men (21 men, 1.3 percent of the tested cohort). Of those bladder cancers, 11 were low-grade, 9 were high-grade, and 1 was invasive. Two men with hematuria who had initial negative cystoscopy later developed bladder cancer [13,14]. After 14 years of follow-up, bladder cancer mortality among the 21 men with screening–detected bladder cancer was lower than the mortality rate among men identified via a bladder cancer registry (0 versus 20 percent). However, although mortality due to bladder cancer was lower, overall mortality was not significantly lower in the screening-detected group than in the registry-identified group (relative risk 0.80, 95% CI 0.48-1.32).

By contrast, other observational studies have not suggested that early detection of bladder cancer has such a benefit on mortality due to bladder cancer. Progression of disease despite detection at the non-muscle invasive stage was illustrated in a study involving 2356 asymptomatic men aged ≥60 years screened weekly for 10 weeks using dipstick testing [15]. Of the 20 percent (474 men) who had hematuria, 317 underwent further evaluation that identified asymptomatic bladder cancer in 0.7 percent of the screened population (17 men). Of these 17 men with bladder cancer, 10 had positive urine cytology and none had muscle-invasive disease at diagnosis. After at least 7 years of follow-up, eight men with well-differentiated superficial

tumors at diagnosis had no progression to muscle-invasive disease; however, among the nine men with prognostically less favorable cancers at diagnosis, six had died (three due to bladder cancer, three due to unrelated causes) and two had developed muscle-invasive disease (including one of those who died of unrelated causes) [16].

High-risk screening — Studies do not show that screening of even a high-risk population confers a strong survival benefit or alters the natural history of the disease in those who do develop bladder cancer. Various non-randomized observational, retrospective, and cohort studies have shown that, among high-risk workers occupationally exposed to known carcinogens, urine screening tests can find bladder cancer at a relatively early stage [17-19]. Other studies have shown the yield of screening urine tests to be lower than expected among high-risk groups [19,20]. Interpretation of studies about screening these high-risk populations is difficult because of problems in assessing the extent of toxin exposure, changes in screening methods over time, and the absence of randomized trials.

In one observational study, screening a very high-risk population did suggest a trend toward improved five-year survival; however, the data did not reach statistical significance and the study had limitations [17]. In this study beginning in 1970, very high-risk aluminum production workers exposed to coal tar derivatives were followed for 16 years, during which 79 cases and 19 deaths from bladder cancer were found. Beginning in 1980, the workers were screened annually with urine cytology. Those diagnosed via urine cytology screening had a non-significantly higher percentage of noninvasive disease compared with those diagnosed prior to the initiation of screening (77 versus 67 percent). Although there was a trend toward increased five-year survival after screening (relative risk [RR] 0.54, 95% CI 0.20-1.48), there was no adjustment for confounders and the use of historical controls raised the possibility that factors other than screening could account for any observed differences.

Another cohort study showed that certain urinary biomarkers could be used to stratify workers into risk groups, but the study could not address whether early identification of bladder cancer had a survival benefit. In the study, workers occupationally exposed to benzidine and non-exposed workers were tested for six years with urinary biomarkers (DNA ploidy, bladder tumor-associated antigen p300, and G-actin) to identify risk groups for bladder cancer [18]. Initial urine screening was performed with biomarkers and cytology for 1788 exposed and 373 non-exposed workers, and the results were used to stratify workers to determine screening schedules; those at high risk (two positive markers or extremely high titers of one marker, hematuria, or positive cytology) were screened every six months with cystoscopy, urine cytology, and biomarkers; moderate-risk workers (one positive biomarker) were screened annually with biomarkers only; and those at low risk (all initial tests negative) were not rescreened for over three years.

Compared with workers negative for both markers, the risk of developing bladder cancer was 81 times higher (95% CI 33.3-199.3) among workers positive for the two markers found to be useful for risk stratification (DNA ploidy and p300) and 20 times higher (95% CI 8.0-47.9) for workers positive for only one of those two markers [18].

Two observational studies showed a low detection of bladder cancer even when screening a very high-risk population. In a 15-year study of 408 workers with probable past industrial exposure to a beta-naphthylamine, a carcinogen associated with 20- to 30-fold excess mortality due to bladder cancer, 350 people were screened with dipstick urinalysis, cytology, and newer biomarkers (as those became available) [20,21]. Bladder cancer was diagnosed in 1 percent of the screened cohort (a total of three subjects: one carcinoma in situ, two transitional cell papillomas) and eventually another 2 of the 14 workers initially diagnosed with dysplasia developed urothelial cancer. In another study, 1322 men previously exposed to aromatic amines were screened annually for seven years with urine dipstick and microscopy, cytology, NMP22, and UroVysion fluorescence in situ hybridization (FISH) assay [22]. Bladder cancer was detected in 14 patients, 9 of whom had high-grade tumors.

Limitations of potential screening tests — An ideal screening test for a general population should be relatively inexpensive and easy to administer, with high sensitivity and reasonable specificity. Specificity is particularly important when the disease prevalence is low, as in bladder cancer.

Potential tests to screen for bladder cancer include urine testing for microscopic hematuria, cytology, and biomarkers (tumor-specific molecular markers) that are shed into the urine. Urine testing is noninvasive and easy to administer; however, there are few data to compare the accuracy of urine tests for screening for bladder cancer in a general population. Some testing modalities known to be effective for diagnosing bladder cancer in the presence of signs or symptoms (eg, radiologic and cystoscopic testing) are not warranted for screening due to the associated potential for harm, the expense, and the low prevalence of disease in the asymptomatic population.

Microhematuria testing — Microscopic hematuria has a low predictive value for bladder cancer.

Although microhematuria is present in most patients with bladder cancer, even in the early stages of disease, microscopic hematuria is also associated with a number of causes that are far more prevalent than bladder cancer, and urologic cancers account for only approximately 2 to 3 percent of cases of microscopic hematuria (figure 1) [15,23]. The prevalence of asymptomatic microscopic hematuria identified by dipstick testing or urinalysis in the general population is

variable (eg, ranging from 2 to 31 percent of the United States population [23,24]), and microscopic hematuria may be intermittent even in patients with bladder cancer [15]. (See "Etiology and evaluation of hematuria in adults", section on 'Microscopic hematuria'.)

Prospective observational studies reaffirm that hematuria lacks specificity for bladder cancer even when using dipstick testing for a population at somewhat higher risk for bladder cancer (healthy older men) [13,15]. For example, even among men at high risk due to exposure to aromatic amines, the positive predictive value of microscopic hematuria was only 1.2 percent [22].

Although the presence of microscopic hematuria in the general population has a low predictive value for urothelial carcinoma, prompt urologic evaluation is recommended by American Urologic Association (AUA) guidelines for all patients 35 years or older in whom benign causes of microhematuria have been ruled out, and in patients of any age at the discretion of the treating clinician, particularly when there is a high suspicion for malignancy [25]. (See "Clinical presentation, diagnosis, and staging of bladder cancer", section on 'Clinical presentation'.)

AUA defines microscopic hematuria as three or more red blood cells per high-powered field on a single test [24]. Even though dipstick testing is inexpensive, widely available, and can be self-administered, if a dipstick test is done and is positive, it must be confirmed with microscopy because of the higher false-positive rate of dipstick testing for blood compared with microscopic testing [24]. (See "Etiology and evaluation of hematuria in adults", section on 'Microscopic hematuria'.)

Urine cytology — Urine cytology has relatively low sensitivity for bladder cancer, requires interpretation by a pathologist, and has a high cost [26]. (See "Clinical presentation, diagnosis, and staging of bladder cancer", section on 'Urine cytology'.)

Cytology is an important technique for surveillance in those with a prior history of urothelial carcinoma and for diagnostic evaluation for those with suspicious symptoms [26,27]. (See "Etiology and evaluation of hematuria in adults", section on 'Urine cytology' and "Management of recurrent or persistent non-muscle invasive bladder cancer" and "Overview of the management of bladder cancer in older adults".)

Urine biomarkers — Urine biomarkers have relatively low specificity and high costs and are not well suited for screening for bladder cancer.

Biomarkers are produced by cellular alterations (eg, upregulated oncogenes, downregulated tumor suppressor genes, changes in protein expression and receptors, methylation) in malignant cells that produce specific chromosomal changes and proteins unique to bladder

cancer. The presence of urine biomarkers has the potential to indicate disease before phenotypic changes can be seen by cystoscopy or cytology.

However, a low specificity of urine biomarkers for bladder cancer was shown among men with positive microscopic hematuria screening and positive biomarker testing. Among 1984 men age 50 to 75 years, hematuria was detected in 409, of whom 75 (18 percent) had positive biomarker tests (NMP22, microsatellite analysis, fibroblast growth factor receptor-3, and DNA methylation analysis). Only four men (0.2 percent) with positive urine biomarkers were found to have cancer, a rate too low to justify the use of urine biomarkers for routine screening [28].

Urine biomarkers have been studied primarily for surveillance after a diagnosis of bladder cancer (ie, detection in individuals who have had prior non-muscle-invasive urothelial cancers and are at risk for recurrent disease). (See "Urine biomarkers for the detection of urothelial (transitional cell) carcinoma of the bladder" and "Clinical presentation, diagnosis, and staging of bladder cancer", section on 'Urine-based markers'.)

Multiple urinary biomarkers and related technologies are under development to detect early evidence of bladder malignancy, but they have not yet demonstrated strong enough performance characteristics to justify their use in screening [29-33]. Studies suggest that serum biomarkers such as circulating micro RNA panels may also be useful for early detection of bladder cancer or perhaps for screening, but the data are still best characterized as investigational [34].

Cystoscopy — Cystoscopy is the gold standard for bladder cancer detection. Despite the high sensitivity and positive predictive value for bladder cancer of office-based flexible cystoscopy, it is not practical for screening due to its procedural nature, associated (though small) risks, and costs.

Although not used for screening, cystoscopy is an important technique used in diagnostic evaluation (eg, hematuria), where direct visualization of the urothelium is important to guide the choice of sites for biopsy and transurethral resection, and for evaluation of hematuria. (See "Clinical presentation, diagnosis, and staging of bladder cancer", section on 'Cystoscopy'.)

Cystoscopy using imaging ("virtual cystoscopy," eg, computed tomography [CT] or magnetic resonance imaging [MRI]) has been explored to try to reproduce the benefits of cystoscopy in assessing bladder urothelium without invasive instrumentation. Neither virtual cystoscopy method is typically used in clinical practice.

In a 2011 meta-analysis, CT virtual cystoscopy was superior to ultrasound for diagnosing bladder cancer [35]. Although CT virtual cystoscopy can identify some papillary bladder lesions,

it appears less effective than direct cystoscopy for identifying carcinoma in situ or flat minimally invasive tumors [36]. Furthermore, CT exposes the patient to potential harms of ionizing radiation.

The meta-analysis also found that MRI was superior to ultrasound for diagnosing bladder cancer [35]. A theoretical benefit of virtual MRI cystoscopy over gold-standard cystoscopy is its minimally invasive nature, as well as its ability to evaluate the ureteral orifices and urethra from all angles, its evaluation of diverticula, and its lack of radiation exposure [37]. However, it is cost-prohibitive as a routine screening tool used broadly.

Potential harms of screening — There are no direct data regarding the actual harms of bladder cancer screening [19]. However, potential harms include false-positive test results that can lead to anxiety and to subsequent diagnostic procedures that carry risks. Typically, follow-up tests would include upper tract imaging with radiation risk and cystoscopy with or without biopsy, with associated risks of perforation, bleeding, and infection. Given the low positive predictive value of positive urine screening tests for hematuria or biomarkers (<10 percent), the burden of additional diagnostic testing to evaluate what would frequently turn out to be false-positive findings would affect a significant number of screened individuals. In contrast to screening for certain other cancers, overdiagnosis of bladder cancer is unlikely to occur, because bladder cancer is rarely an incidental finding at autopsy.

OUR APPROACH

Asymptomatic patients — Overall, we do **not** screen for bladder cancer in the general population due to the absence of data showing efficacy, the lack of tests with adequate specificity, and the potential harms of follow-up testing done to evaluate abnormalities detected on initial urine testing. (See 'Rationale not to screen' above.)

If there is any benefit to screening, it would most likely be among high-risk patients who have a higher incidence of bladder cancer (eg, those with known risk factors such as a prolonged smoking history or high-risk occupational exposure) (see 'Risk factors' above). However, the available data do not show that screening confers a survival benefit even for these patients. Because of this lack of supportive evidence, some UpToDate contributors do not screen for bladder cancer, even in high-risk patients. However, other UpToDate contributors do offer bladder cancer screening with annual urinalysis to high-risk patients (and, in some patients at very high risk, urine cytology as well) because of the simple collection process, the low risk of the actual test, and the overall limited body of evidence. Given the inadequate data, an individualized approach to the decision to screen high-risk patients is appropriate, with the

choice based on the patient's values and preferences. For instance, for a patient with long-term exposure in a high-risk industry who is also a substantial tobacco user, it would be reasonable to consider screening based on a shared decision-making process. If a screening test is done and the findings are abnormal, further workup is warranted to determine whether the patient has bladder cancer or another disease that needs treatment. (See "Clinical presentation, diagnosis, and staging of bladder cancer", section on 'Initial evaluation'.)

Recommendations from expert groups are somewhat mixed with regard to screening high-risk patients; all acknowledge the lack of evidence to support a survival benefit of screening. All also agree that screening is not warranted for those without high-risk exposure. (See 'Recommendations of expert groups' below.)

Although the impact of education and screening on survival has not been well-established, education might facilitate early intervention for high-risk patients. Patients at high risk should be educated about risk factors and early symptoms of bladder cancer, especially gross hematuria. Education should also emphasize risk reduction including smoking cessation and minimizing occupational exposure. All individuals, and especially those with occupational exposures known to increase risk, should be strongly counseled not to smoke, and smokers should be offered smoking cessation treatment. (See "Overview of smoking cessation management in adults" and 'Recommendations of expert groups' below.)

Those with known high-risk occupational exposure also should use appropriate work safety precautions. These include personal protective equipment that minimizes carcinogen exposure, strict hygiene measures, and increased stringency of workplace safety regulations.

The effects of healthy diet, good fluid intake, and the potential for chemoprevention (not suggested outside of a clinical trial) are discussed separately. (See "Chemoprevention of urothelial carcinoma of the bladder".)

Patients with hematuria — Individuals with urinary symptoms such as gross hematuria, or with microhematuria on a urine test, warrant evaluation to determine if the patient has bladder cancer or another condition that needs treatment. Such evaluation is considered diagnostic evaluation rather than screening. Diagnostic evaluation of hematuria is discussed separately. (See "Etiology and evaluation of hematuria in adults".)

Follow-up of bladder cancer — Ongoing testing in patients previously treated for cancer (surveillance) is critical for early identification of recurrence. Over one-half of patients diagnosed with noninvasive bladder cancer and managed with organ-sparing therapy will develop recurrent disease, and many will progress to have invasive disease. The role of and approach to surveillance in patients with a history of noninvasive urothelial cell carcinoma are discussed

separately. (See "Overview of the initial approach and management of urothelial bladder cancer", section on 'Surveillance' and "Overview of the initial approach and management of urothelial bladder cancer", section on 'Posttreatment surveillance'.)

RECOMMENDATIONS OF EXPERT GROUPS

There is **no** major organization that recommends screening for bladder cancer in asymptomatic non-high-risk adults, noting insufficient evidence about screening.

- The US Preventive Services Task Force (USPSTF) 2011 revised recommendation concluded that the current evidence was insufficient to assess the benefits or harms of screening [19]. If screening is offered, patients should understand that there is uncertainty about benefits and harms. Previously, USPSTF had concluded that there was no high-quality evidence that screening adults for bladder cancer improves outcomes compared with no screening [4].
- The American Academy of Family Physicians supports the recommendation of the USPSTF [38].
- The National Cancer Institute (United States) notes inadequate evidence to determine whether screening for bladder cancer would impact mortality and fair evidence that screening would result in unnecessary procedures with associated morbidity [39].
- The International Consultation on Urologic Diseases (ICUD) - European Association of Urology (EAU) 2012 notes that there is insufficient evidence of impact of screening on bladder cancer survival [40]. For this reason, they suggest that bladder cancer screening be confined to high-risk patients [41]. They recommend prevention of bladder cancer by eliminating active and passive smoking [40].
- The American Cancer Society does not include screening for bladder cancer on its list of recommended cancer screening [42].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Screening for bladder cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- (See "Patient education: Blood in the urine (hematuria) in adults (The Basics)".)
- (See "Patient education: Bladder cancer (The Basics)".)
- (See "Patient education: Blood in the urine (hematuria) in adults (Beyond the Basics)".)

SUMMARY AND RECOMMENDATIONS

- Urothelial carcinoma of the bladder is the second-most frequently diagnosed cancer of the urinary tract. Once urothelial carcinoma is muscle-invasive, it can quickly progress and metastasize, leading to death. Non-muscle-invasive, low-grade tumors constitute approximately 65 percent of all new cases of urothelial cell carcinoma of the bladder and have low risk of progression. High-grade non-muscle-invasive disease has a 50 to 70 percent risk of recurrence and 10 to 30 percent risk of progression to muscle-invasive disease. (See 'Epidemiology and pathology' above.)

- There are no randomized trials to evaluate the effectiveness of screening for bladder cancer in preventing cancer mortality or limiting morbidity from treatment of early disease. Prospective studies confirm a low positive predictive value for screening in older men at average risk. Studies of screening in populations of industrial workers at high risk for bladder cancer confirm that screening can identify noninvasive bladder cancer, but it is not known whether screening has an impact on disease outcome. (See 'Rationale not to screen' above.)

- Tests considered to screen for bladder cancer include urine dipstick for red blood cells, microscopic analysis for red blood cells, urine cytology, and urine biomarkers. The relatively low prevalence of bladder cancer in an average-risk screening population requires greater specificity for bladder cancer than these tests provide. (See 'Limitations of potential screening tests' above.)

- Microscopic hematuria identified on urinalysis is present in most patients with bladder cancer, even in the early stages of disease. However, microscopic hematuria is associated with a number of causes that are far more prevalent than bladder cancer in the general population. Overall urologic cancers account for only approximately 2 to 3 percent of cases of microscopic hematuria. (See 'Microhematuria testing' above.)

- Factors associated with increased risk for developing bladder cancer include exposure to chemical carcinogens (eg, tobacco, occupational and environmental exposures), older age, and male sex. (See 'Risk factors' above.)

- For patients at average risk, we suggest **not** screening for bladder cancer (**Grade 2C**). Screening tests lack specificity, follow-up testing for abnormalities on screening tests is burdensome and potentially harmful, and evidence that screening confers a survival benefit is lacking. (See 'Rationale not to screen' above and 'Asymptomatic patients' above.)

- Available data do not show that screening confers a survival benefit, even for a high-risk population. Because of this lack of supportive evidence, some UpToDate contributors do not screen for bladder cancer, even in high-risk patients. However, other UpToDate contributors do offer bladder cancer screening with annual urinalysis to high-risk patients (and in some patients at very high risk, urine cytology as well). An individualized approach to the decision to screen high-risk patients is appropriate, with the choice based on the patient's values and preferences, given the inadequate data. (See 'Our approach' above.)

- Smoking cessation should be emphasized, and patients should be educated regarding risk factors and early symptoms of bladder cancer, such as gross hematuria. High-risk individuals with occupational exposures should use personal protective equipment and minimize chemical exposures when possible. (See 'Rationale not to screen' above and 'Asymptomatic patients' above.)

- Patients with a history of treated urothelial carcinoma do require surveillance testing to detect disease recurrence due to the high likelihood of developing recurrent disease or a second primary. The role of and approaches to surveillance in this setting are discussed separately. (See "Management of recurrent or persistent non-muscle invasive bladder cancer" and "Overview of the management of bladder cancer in older adults".)

- Urinary signs or symptoms (eg, microhematuria) do warrant evaluation, which is considered diagnostic evaluation rather than screening. Diagnostic evaluation of hematuria is discussed separately. (See "Etiology and evaluation of hematuria in adults".)

- All individuals, and especially those with occupational exposures known to increase risk, should be strongly counseled not to smoke, and smokers should be offered smoking cessation treatment. (See "Overview of smoking cessation management in adults" and 'Asymptomatic patients' above.)

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GRAPHICS

Bladder cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Urothelial carcinoma *in situ*: "Flat tumor"
T1	Tumor invades lamina propria (subepithelial connective tissue)
T2	Tumor invades muscularis propria
pT2a	Tumor invades superficial muscularis propria (inner half)
pT2b	Tumor invades deep muscularis propria (outer half)
T3	Tumor invades perivesical soft tissue
pT3a	Microscopically
pT3b	Macroscopically (extravesical mass)
T4	Extravesical tumor directly invades any of the following: Prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a	Extravesical tumor invades directly into prostatic stroma, seminal vesicles, uterus, vagina
T4b	Extravesical tumor invades pelvic wall, abdominal wall
Regional lymph nodes (N)	
N category	**N criteria**
NX	Lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)
N2	Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)
N3	Lymph node metastasis to the common iliac lymph nodes
Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis

M1	Distant metastasis
M1a	Distant metastasis limited to lymph nodes beyond the common iliacs
M1b	Non-lymph-node distant metastases

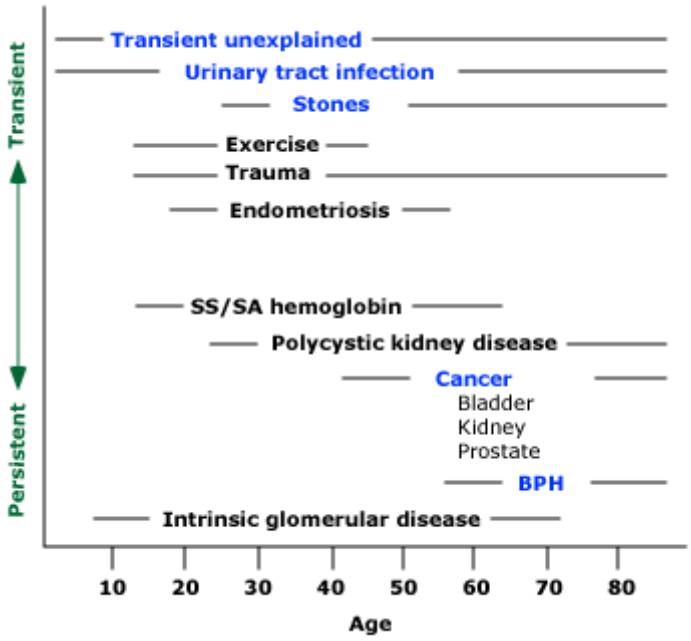
Prognostic stage groups

When T is...	And N is...	And M is...	Then the stage group is...
Ta	N0	M0	0a
Tis	N0	M0	0is
T1	N0	M0	I
T2a	N0	M0	II
T2b	N0	M0	II
T3a, T3b, T4a	N0	M0	IIIA
T1-T4a	N1	M0	IIIA
T1-T4a	N2, N3	M0	IIIB
T4b	Any N	M0	IVA
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Graphic 110763 Version 9.0

Major causes of hematuria by age and duration



Schematic representation of the major causes of hematuria in relation to the age at which they usually occur (horizontal axis), transience or persistence (vertical axis), and frequency (blue implies more frequent).

BPH: benign prostatic hyperplasia.

Graphic 61296 Version 1.0

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