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MICROHEMATURIA: AUA/SUFU GUIDELINE (2020, AMENDED 2025)

Guideline Panel

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SUMMARY

Purpose

The purpose of this guideline is to provide a clinical framework for the diagnosis, evaluation, and follow-up of microhematuria (MH).

Methodology

OVID was used to systematically search MEDLINE and EMBASE databases for articles evaluating hematuria using criteria determined by the expert panel. The initial draft evidence report included evidence published from January 2010 through February 2019. A second search conducted to update the report included studies published up to December 2019. Five systematic reviews and 91 primary literature studies met the study selection criteria and were chosen to form the evidence base. These publications were used to create the majority of the clinical framework. When sufficient evidence existed, the body of evidence for a particular modality was assigned a strength rating of A (high), B (moderate), or C (low); and evidence-based statements of Strong, Moderate, or Conditional Recommendation were developed. Additional information is provided as Clinical Principles and Expert Opinions when insufficient evidence exists. In 2024, this Guideline was reviewed via the AUA update literature review (ULR) process, which identified 82 studies for full-text review that were published between December 2019 and June 7, 2024. Of those 82 studies, 23 met inclusion criteria for qualitative synthesis. The subsequent amendment is based on data released since the initial 2020 publication of this Guideline.

GUIDELINE STATEMENTS

DIAGNOSIS AND DEFINITION OF MICROHEMATURIA

1. Clinicians should define microhematuria as ≥3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen. (*Strong Recommendation; Evidence Level: Grade C*)

2. Clinicians should not define microhematuria by positive dipstick testing alone. A positive urine dipstick test (trace blood or greater) should prompt formal microscopic evaluation of the urine. (*Strong Recommendation; Evidence Level: Grade C*)

INITIAL EVALUATION

3. In patients with microhematuria, clinicians should perform a history, physical examination including blood pressure measurement, and serum creatinine to assess risk factors for genitourinary malignancy (e.g., detailed smoking history), medical renal disease, gynecologic, and non-malignant genitourinary causes of microhematuria. (*Clinical Principle*)

4. Clinicians should perform the same evaluation of patients with microhematuria who are taking antiplatelet agents or anticoagulants (regardless of the type or level of therapy) as patients not on these agents. (*Strong Recommendation; Evidence Level: Grade C*)

5. In patients with findings suggestive of a gynecologic or non-malignant urologic etiology, clinicians should evaluate the patients with appropriate physical examination techniques and tests to identify such an etiology. (*Clinical Principle*)

6. In patients diagnosed with gynecologic or non-malignant genitourinary sources of microhematuria, clinicians should repeat urinalysis following resolution of the gynecologic or non-malignant genitourinary cause. If microhematuria persists or the etiology cannot be identified, clinicians should perform risk-based urologic evaluation. (*Clinical Principle*)

7. In patients with hematuria attributed to a urinary tract infection, clinicians should obtain a urinalysis with microscopic evaluation following treatment to ensure resolution of the hematuria. (*Strong Recommendation; Evidence Level: Grade C*)

8. Clinicians should refer patients with microhematuria for nephrological evaluation if medical renal disease is suspected. However, risk-based urologic evaluation should still be performed. (*Clinical Principle*)

RISK STRATIFICATION

9. Following initial management, clinicians should categorize patients presenting with microhematuria as low/negligible-, intermediate-, or high-risk for genitourinary malignancy based on the accompanying tables (Tables 3 and 4). (*Strong Recommendation; Evidence Level: Grade C*)

RISK-BASED EVALUATION

Low/Negligible-Risk

10. In low/negligible-risk patients with microhematuria, clinicians should obtain repeat urinalysis within six months rather than perform immediate cystoscopy or imaging. (*Moderate Recommendation; Evidence Level: Grade C)*

Initially Low/Negligible-Risk with Hematuria on Repeat Analysis

11. Low/negligible-risk patients with microhematuria on repeat urinalysis should be reclassified as intermediate- or high-risk based on repeat urinalysis. In such patients, clinicians should perform risk-based evaluation in accordance with recommendations for these respective risk strata. (*Strong Recommendation; Evidence Level: Grade C*)

Intermediate-Risk

12. Clinicians should recommend cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate risk for malignancy. (*Strong Recommendation; Evidence Level: Grade C*)

13. In appropriately counseled intermediate-risk patients who want to avoid cystoscopy and accept the risk of forgoing direct visual inspection of the bladder urothelium, clinicians may offer urine cytology or validated urine-based tumor markers (Table 5) to facilitate the decision regarding utility of cystoscopy. Renal and bladder ultrasound should still be performed in these cases. (*Conditional Recommendation; Evidence Level: Grade C*)

14. For patients with intermediate-risk microhematuria who do not undergo cystoscopy based on urinary marker results, clinicians should obtain a repeat urinalysis within 12 months. Such patients with persistent microhematuria should undergo cystoscopy. (*Strong Recommendation; Evidence Level: Grade C*)

High-Risk

15. Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy. (*Strong Recommendation; Evidence Level: Grade C*)

    Options for Upper Tract Imaging in High-Risk Patients:

    a. If there are no contraindications to its use, clinicians should perform multiphasic CT urography (including imaging of the urothelium). (*Moderate Recommendation; Evidence Level: Grade C*)
    b. If there are contraindications to multiphasic CT urography, clinicians may utilize MR urography. (*Moderate Recommendation; Evidence Level: Grade C*)
    c. If there are contraindications to multiphasic CT urography and MR urography, clinicians may utilize retrograde pyelography in conjunction with non-contrast axial imaging or renal ultrasound. (*Expert Opinion*)

16. Clinicians should perform white light cystoscopy in patients undergoing evaluation of the bladder for microhematuria. (*Moderate Recommendation; Evidence Level: Grade C*)

17. In patients with persistent or recurrent microhematuria previously evaluated with renal ultrasound, clinicians may perform additional imaging of the urinary tract. (*Conditional Recommendation; Evidence Level: Grade C*)

18. In patients with microhematuria who have a family history of renal cell carcinoma, a known genetic renal tumor syndrome, or a personal or family history of (or suspicious for) Lynch syndrome, clinicians should perform upper tract imaging regardless of risk category. (*Expert Opinion*)

URINARY MARKERS

19. Clinicians should not routinely use urine cytology or urine-based tumor markers to decide whether to perform cystoscopy in the initial evaluation of low/negligible- or high-risk patients with microhematuria. (*Strong Recommendation; Evidence Level: Grade C*)

20. Clinicians should not routinely use cytology or urine-based tumor markers as adjunctive tests in the setting of a normal cystoscopy. (*Strong Recommendation; Evidence Level: Grade C*)

21. Clinicians may obtain urine cytology for high-risk patients with equivocal findings on cystoscopic evaluation or those with persistent microhematuria and irritative voiding symptoms or risk factors for carcinoma in situ after a negative workup. (*Expert Opinion*)

FOLLOW-UP

22. In patients with a negative risk-based hematuria evaluation, clinicians should engage in shared decision-making regarding whether to repeat urinalysis in the future. (*Strong Recommendation; Evidence Level: Grade C*)

23. For patients with a prior negative hematuria evaluation and subsequent negative urinalysis, clinicians may discontinue further evaluation for microhematuria. (*Conditional Recommendation; Evidence Level: Grade C*)

24. For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding the need for additional evaluation. (*Expert Opinion*)

25. For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urologic symptoms, clinicians should initiate further evaluation. (*Moderate Recommendation; Evidence Level: Grade C*)

INTRODUCTION

BACKGROUND

Prevalence

Hematuria remains one of the most common urologic diagnoses, estimated to account for over 20% of urology evaluations.[1] Indeed, screening studies have noted a prevalence range of microhematuria (MH) among healthy volunteers of 2.4%-31.1% depending on the specific population evaluated.[2]

Etiologies

Urologic etiologies for hematuria include malignancy, infection, inflammation, calculus disease, benign prostatic hyperplasia (BPH), and congenital or acquired anatomic abnormalities.[3] Hematuria may also be confused with gynecological sources of bleeding, myoglobinuria, or pigmentation of the urine from the ingestion of certain foods and drugs. When considering the risk of malignancy in patients with hematuria, a recent prospective observational study of over 3,500 patients referred for evaluation of hematuria noted a 10.0% rate of urinary tract cancer: 13.2% for patients with gross hematuria (GH) and 3.1% among patients with MH only.[4] Similarly, aggregate data from 17 prior MH screening studies published between 1980 to 2011 identified in the 2012 AUA Guideline reported a urinary tract malignancy rate of 2.6% (range 0% to 25.8%), the vast majority of which were bladder cancers.[2] Eleven more contemporary studies enrolling MH patients in the current evidence base dating from 2010 to 2019 reported an aggregate urinary tract malignancy rate of 1% (range 0.3% to 6.25%), which varied according to the presence or absence of risk factors for malignancy.[5-15]

Diagnostic Evaluation of Microhematuria

While most experts agree that patients with GH should be evaluated with cystoscopy, upper tract imaging and urinary cytology, significant variability exists across current guidelines and consensus statements regarding MH, particularly the definition of MH, criteria for evaluation, as well as the appropriate components of the evaluation, including the optimal imaging modality.[16, 17] The 2012 AUA Guideline recommended computed tomography (CT) urography and cystoscopy in all patients over 35 years of age with MH and were largely crafted without regard to an individual patients' risk of malignancy. Indeed, the principal goal of the 2012 Guideline was to minimize the likelihood of missing a malignancy diagnosis.[2] Consistent with this intention, a theoretical simulation model determined that this

evaluation would miss detection of the fewest number of cancers relative to other existing guidelines.[16] Nevertheless, this approach has attendant patient risk (e.g., discomfort and risk of infection with cystoscopy, risk of contrast reactions, potential for radiation-induced cancers attributed to CT, detection of false-positive findings leading to further investigation),[16] and an incremental healthcare cost approximately twice that of guidelines from other organizations.[16,18] In light of the overall low rate of cancers detected among patients with MH, the implications of diagnostic studies and intensity of evaluation must be considered both at the patient and health system level.

At the same time, practice-pattern assessments have demonstrated significant inconsistencies in the evaluation of patients presenting with hematuria. For example, a 2008 study found that less than 50% of patients with hematuria diagnosed in a primary care setting were subsequently referred for urologic evaluation.[19] Of concern, contemporary studies implicate even lower evaluation rates of under 10%.[20] Moreover, in a series of patients presenting with hematuria who had known risk factors for bladder cancer, only 23% received any type of imaging, and only 13% underwent cystoscopy.[9] The underuse of cystoscopy, and the tendency to solely use imaging for evaluation, is particularly concerning when one considers that most cancers diagnosed among persons with hematuria are bladder cancers, optimally detected with cystoscopy.[7, 9, 12,13-15,21-24]

Women with hematuria have been especially prone to delays in evaluation, often due to practitioners ascribing hematuria to a urinary tract infection (UTI) or gynecologic source, resulting in inadequate evaluation and delay in cancer diagnosis.[19,25] Similarly, studies have found that African American patients are less likely than Caucasian counterparts to undergo any aspect of hematuria evaluation, including urology referral, cystoscopy, and imaging.[26] In turn, despite having a lower incidence of bladder cancer than men, women diagnosed with bladder cancer have a lower 5-year survival rate than men (73.3% versus 78.2%), which may be in part attributable to delay in diagnosis leading to higher stage disease at diagnosis.[27] Likewise, racial differences in five-year survival and stage at diagnosis for urothelial cancer have also been noted, with evidence demonstrating lower rates of referral to urology and lower use of imaging in women and African Americans with hematuria compared to men and whites, which may explain some of this variation in disease burden at diagnosis and in survival.[26, 28, 29] Delays in diagnosis of bladder cancer have been suggested to contribute to a 34% increased risk of cancer-specific mortality and a 15% increased risk of all-cause mortality.[30]

As such, the need exists to develop and disseminate clear guideline recommendations for evaluation of hematuria that limit the unnecessary risks and costs associated with the over-evaluation of patients who are at low risk for malignancy, while at the same time addressing the delays in diagnosis of important urologic conditions caused by widespread under-evaluation and variations in care. Furthermore, since the intensity of MH investigation involves tradeoffs at the individual level (risk of malignancy versus harms of evaluation), it is necessary for the clinician and patient to engage in shared decision-making, particularly in situations where the ratio of benefits to harms is uncertain, equivalent or “preference sensitive” (e.g., dependent on the value that an individual patient may place on them).[31]

The 2020 AUA Guideline for MH was developed to provide an individualized approach to microscopic hematuria evaluation based on the patient’s risk of harboring urinary tract cancer and concordant with the patient’s values. At the time, it was acknowledged that tailoring the intensity of evaluation to patient risk, as opposed to recommending intensive evaluation for every patient could introduce the potential for some missed cancers. Nonetheless, the proposed approach sought to optimize the balance of detection and risk at both the patient and health system level. In addition, the Panel put forth an actionable set of recommendations to facilitate standardization to minimize unnecessary variations and the risk of under-evaluation and delayed diagnosis of important urologic conditions. The revised recommendations herein, based on analysis of the best available evidence, represent further refinement of this patient-centered approach by maximizing the opportunities to diagnose important urologic conditions in a timely fashion, while avoiding unnecessary evaluations in low-risk patients.

METHODOLOGY

The systematic review utilized to inform this guideline was conducted by an independent methodological consultant. Determination of the guideline scope and review of the final systematic review to inform guideline statements was conducted in conjunction with the MH Panel.

Panel Formation

The Panel was created in 2018 by the American Urological Association Education and Research, Inc. (AUAER). This guideline was developed in collaboration with the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chairs who in turn appointed the additional panel members with specific expertise in this area in conjunction with SUFU. Additionally, the Panel included representation from the American College of Obstetricians and Gynecologists (ACOG) as well as a patient advocate. Funding of the Panel was provided by the AUA; panel members received no remuneration for their work. The Microhematuria Amendment Panel was created in 2024 by the AUA to review new literature and provide updates herein.

Searches and Article Selection

A systematic review was conducted to inform on appropriate diagnosis, evaluation, and follow-up in patients with suspected and confirmed MH. The methodologist, in consultation with the expert panel, developed criteria for inclusion and exclusion of studies based on the Key Questions and the populations, interventions, comparators, and outcomes (PICO) of interest. OVID was used to systematically search MEDLINE and EMBASE databases for articles evaluating hematuria using the criteria determined by the expert panel. For the 2020 guideline, 5 systematic reviews and 91 primary literature studies from January 2010 through December 2019 met the study selection criteria and were chosen to form the evidence base. Based on a low volume of studies identified enrolling solely MH patients, studies that enrolled a combination MH and GH population were included in the evidence base. Studies enrolling the two populations were described separately in text and tables.

Control articles, which were deemed important and relevant by the Panel, were compared with the draft literature search strategy output, and the final strategy was updated as necessary to capture all control articles. In addition to the MEDLINE and EMBASE databases searches, reference lists of systematic reviews and primary literature were scanned for potentially useful studies.

All hits from the OVID literature search were input into reference management software (EndNote 21), where duplicate citations were removed. Abstracts were reviewed by the methodologist to determine if the study addressed the Key Questions and if the study met study design inclusion criteria. For all research questions, randomized controlled trials (RCTs), observational studies, and case-control studies were considered for inclusion in the evidence base. Studies had to enroll at least 30 patients per study arm for all Key Questions. Additionally, studies evaluating urinary cytology and urine-based tumor markers (UBTM) were required to enroll at least 100 MH patients and in studies of mixed MH and GH populations, at least 25% were required to be MH. Case series, letters, editorials, *in vitro* studies, studies conducted in animal models, and studies not published in English were excluded from the evidence base.

Full-text review was conducted on studies that passed the abstract screening phase. Studies were compared to the predetermined PICO as outlined below. Nine panel members were paired with the methodologist and completed duplicate full-text study selection of 10% of studies undergoing full-text review. The dual-review trained the methodologist, who then completed full-time review of the remaining studies.

Population

- All adult (≥18 years) patients with suspected or confirmed MH
- Studies enrolling populations of both MH and GH patients were considered for inclusion and were used to support recommendations when a paucity of data in exclusively MH patients was available, with additional restrictions detailed above for cytology and UBTM studies.
    - Studies enrolling solely GH populations were excluded

Interventions

- Hematuria detection by urinalysis (UA) or dipstick
- Complete hematuria work-up components
- Risk factors for malignancy and/or mortality
- Imaging modalities
- Cystoscopy

- Urinary cytology and urine-based tumor markers (UBTMs)
- Patient engagement tools and decision aids
- Follow-up schedules in patients with initial negative hematuria evaluation

Comparators

- Any of the included interventions of interest when defined as the control group and compared to another intervention
    - It was anticipated that most of the identified studies would be single arm

Outcomes

- Critical outcomes
    - Hematuria detection concordance (UA versus dipstick)
    - Diagnostic yield, incorporating prevalence of malignant and/or benign diagnoses
    - Diagnostic test characteristics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and false positive rate
    - Risk stratification for urologic malignancy
    - Risk stratification system performance characteristics, including predictive ability, prognostic ability, number needed to screen
    - Rate of adverse events and number needed to harm
- Important outcomes
    - Disease specific survival rates
    - Diagnostic grade/stage of malignancy
    - Prevalence of risk factors in hematuria patients
    - Patient satisfaction
    - Quality of life

The initial draft evidence report included evidence published from January 2010 through February 2019. A second search was conducted to update the report to include studies published up to December 2019.

In 2024, the Microhematuria Guideline was updated through the AUA amendment process in which newly published literature was reviewed and integrated into previously published guidelines. An updated literature search of Ovid MEDLINE and Embase identified 82 studies for full-text review that were published between December 2019 and June 7, 2024. An additional search was conducted in August 2025 that identified 5 additional relevant studies.

Data Abstraction

Data were extracted from all studies that passed full-text review by the methodologist. All extracted data were audited by an independent auditor.

Risk of Bias Assessment

Quality assessment for all retained studies was conducted. Using this method, studies deemed to be of low quality would not be excluded from the systematic review, but would be retained, and their methodological strengths and weaknesses discussed where relevant. To define an overall study quality rating for each included study, risk of bias as determined by validated study-type specific tools, was paired with additional important quality features. To evaluate the risk of bias within the identified studies, the Assessment of Multiple Systematic Reviews (AMSTAR)[32] tool was used for systematic reviews, the Cochrane Risk of Bias Tool[33] was used for randomized studies, and a Risk of Bias in Non-Randomized Studies – of Intervention (ROBINS-I)[34] was used for observational studies. Additional important quality features, such as study design, comparison type, power of statistical analysis, and sources of funding were extracted for each study.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[35] system was used to determine the aggregate evidence quality for each guideline statement. GRADE defines a body of evidence in relation to how confident guideline developers can be that the estimate of effects as reported by that body of evidence is correct. Evidence is categorized as high, moderate, low, and very low; and assessment is based on the aggregate risk of bias for the evidence base plus limitations introduced because of inconsistency, indirectness, imprecision, and publication bias across the studies.[36] Additionally, certainty of evidence can be

downgraded if confounding across the studies has resulted in the potential for the evidence base to overestimate the effect. Upgrading of evidence is possible if the body of evidence indicates a large effect or if confounding would suggest either spurious effects or would reduce the demonstrated effect.

Data Synthesis

One of the main objectives for the guideline is to establish a risk model to stratify patients based on their risk for underlying urologic malignancy. To this end, pooling of data was conducted in three areas using RevMan.[37] For studies that reported adjusted odds ratios (without raw data) for risk factors associated with malignancy, the odds ratios were pooled using a random-effects inverse-variance method. For studies that reported raw data on patient factors and their association with malignant diagnosis, unadjusted odds ratios were calculated and pooled using a random-effects Mantel-Haenszel method. Finally, prevalence of both malignant and benign diagnoses in relation to the type of hematuria work-up received by patients were calculated and pooled using a random-effects inverse-variance method. For all other areas, pooling was determined to be inappropriate based on heterogeneity of population, reference standard, or reported outcomes.

Determination of Evidence Strength

The AUA employs a three-tiered strength of evidence system to underpin evidence-based guideline statements. In short, high certainty by GRADE translates to AUA A-category strength of evidence, moderate to B, and both low and very low to C. (**Table 1**)

The AUA categorizes body of evidence strength as Grade A (well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent findings), Grade B (RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.[38]

As with the 2020 AUA guideline, there remains low and very low strength of evidence to support the guideline statements, highlighting the need to strengthen the evidence through focused research questions in the future.

Table 1: Strength of Evidence Definitions

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	• Very confident that the true effect lies close to that of the estimate of the effect
B	Moderate	• Moderately confident in the effect estimate • The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	• Confidence in the effect estimate is limited • The true effect may be substantially different from the estimate of the effect
	Very Low	• Very little confidence in the effect estimate • The true effect is likely to be substantially different from the estimate of effect

AUA Nomenclature: Linking Statement Type to Evidence Strength

The AUA nomenclature system explicitly links statement type to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (**Table 2**). ***Strong Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. ***Moderate Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. ***Conditional Recommendations*** are non-directive statements used when the evidence indicates that there is no apparent net benefit or harm or when the balance between benefits and risks/burden is unclear. All three statement types may be supported by any body of evidence strength grade. A body of evidence strength Grade A in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances and that future research is *unlikely to change confidence*. A body of evidence strength Grade B in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but that better evidence *could change confidence*. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but that better evidence *is likely to change confidence*. Conditional Recommendations also can be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates that benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is *unlikely to change confidence*. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances and better evidence *could change confidence*. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens, alternative strategies may be equally reasonable, and better evidence *is likely to change confidence*.

Where gaps in the evidence existed, the Panel provides guidance in the form of ***Clinical Principles*** or ***Expert Opinions*** with consensus achieved using a modified Delphi technique if differences of opinion emerged.[39] A *Clinical Principle* is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. *Expert Opinion* refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment.

Peer Review and Document Approval

An integral part of the guideline development process at the AUA is external peer review. The AUA conducted a thorough peer review process to ensure that the document was reviewed by experts in the diagnosis, evaluation, and follow-up of MH. In addition to reviewers from the AUA PGC, Science and Quality Council (SQC), and Board of Directors (BOD), the document was reviewed by representatives from SUFU and ACOG as well as external content experts. Additionally, a call for reviewers was placed on the AUA website from December 2-16, 2019, to allow any additional interested parties to request a copy of the document for review. The guideline was also sent to the Urology Care Foundation and representatives of the Bladder Cancer Advocacy Network (BCAN) to open the document further to the patient perspective. The draft guideline document was distributed to 115 peer reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 66 reviewers provided comments, including 51 external reviewers. At the end of the peer review process, a total of 443 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the guideline was submitted for approval to the AUA PGC, SQC, and BOD as well as the governing body of SUFU for final approval.

For the 2025 Amendment, a call for reviewers was placed on the AUA website from September 4-15, 2024, to allow any additional interested parties to request a copy of the document for review. The draft guideline document was distributed to 90 peer reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 27 reviewers provided comments, including 16 external reviewers. At the end of the peer review process, a total of 133 comments were received. Following comment discussion, the Panel revised the draft as

needed. Once finalized, the guideline was submitted for approval to the original panel and the AUA PGC, SQC, and BOD as well as the governing body of SUFU for final approval.

Table 2: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength

Evidence Grade	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) is substantial • Applies to most patients in most circumstances and future research is unlikely to change confidence	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) is substantial • Applies to most patients in most circumstances but better evidence could change confidence	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) appears substantial • Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) is moderate • Applies to most patients in most circumstances and future research is unlikely to change confidence	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) is moderate • Applies to most patients in most circumstances but better evidence could change confidence	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) appears moderate • Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (Net benefit or harm comparable to other options)	• Benefits=Risks/Burdens • Best action depends on individual patient circumstances • Future research is unlikely to change confidence	• Benefits=Risks/ Burdens • Best action appears to depend on individual patient circumstances • Better evidence could change confidence	• Balance between Benefits & Risks/Burdens unclear • Net benefit (or net harm) comparable to other options • Alternative strategies may be equally reasonable • Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement achieved by consensus of the Panel that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

GUIDELINE STATEMENTS

DIAGNOSIS AND DEFINITION OF MICROHEMATURIA (MH)

1. **Clinicians should define microhematuria as ≥3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen. (*Strong Recommendation; Evidence Level: Grade C*)**

To inform clinicians of the degree of hematuria with sufficient detail to determine whether further evaluation is warranted, the Panel emphasizes the importance of laboratories reporting red blood cells per high-power field (RBC/HPF) quantitatively. Although various thresholds may be utilized, the Panel encourages the use of ≥3 RBC/HPF as a minimum reporting threshold, consistent with prior AUA guidelines as well as newer data subsequently highlighted.[2] While several automated methods for assessing hematuria, including the use of flow cytometry, have diffused into clinical practice, at present, there is insufficient evidence regarding the accuracy of these devices in comparison to microscopic evaluation. As such, microscopic quantification remains the referent standard for defining hematuria.[40]

In a recent study evaluating the correlation between degree of MH and malignancy among a group of over 46,000 patients, Matulewicz et al. noted that the highest sensitivity for detecting bladder cancer (0.73) and lowest negative likelihood ratio (0.40) existed at the threshold of ≥3 to 10 RBC/HPF.[5] By defining a low threshold for defining MH, the potential for inadvertently excluding patients at risk for harboring urologic malignancy was considered low. With the risk stratified evaluation approach outlined below, the Panel felt it was necessary to be inclusive at this definition stage whilst subsequent evaluation would be modulated by individual patient risk.

Meanwhile, the Panel noted limited new data since the previous iteration of the AUA Guideline regarding the role of single versus multiple UAs as part of the diagnostic evaluation. One retrospective MH cohort study reporting on the diagnostic yield of a single UA compared with multiple noted that the initial UA detected MH in 95% of the patients, while addition of the second and third UA detected the remaining 5%.[41, 42] Given the intermittent nature of hematuria and the absence of robust new evidence to alternatively inform practice, the Panel maintained that only a single UA with ≥3 RBC/HPF is necessary to establish the presence of MH. The Panel does recognize that although a positive dipstick does not warrant MH evaluation, data exist correlating the extent of dipstick positivity with the likelihood of identifying a greater number of RBC/HPF on UA.[5,43] Therefore, in patients with a greater degree of blood on urine dipstick but a negative UA, clinicians may consider follow-up with repeat UA, including patient risk and preference in the decision process.

Proper Sample Collection

For most initial evaluations, a random midstream clean-catch collection is sufficient. Patients should be instructed to discard the initial 10 mL of voided urine into the toilet in order to collect the midstream void. If a significant number of squamous cells are present in the sample, then contamination is possible, and a repeat specimen collection or catheterization should be considered. Providing basic instructions to patients on proper sample collection, verbally, in writing, or on posted signs, could minimize contaminated or faulty samples.

Male patients: Midstream voided specimens are adequate unless the patient is unable to void. The specimen can be collected into the sterile specimen cup after gently cleaning the urethral meatus with a sterilization towelette. In uncircumcised men, it is important to retract the foreskin to avoid contamination.

Female patients: A voided midstream specimen should be the primary method unless there are circumstances such as known problems with repeated specimen contamination or a history of difficulty voiding. The patient should be instructed to spread the labia adequately to allow for cleansing of the urethral meatus with a sterilization towelette and to avoid introital contamination.

In some patients, catheterization may be necessary in order to obtain an appropriate specimen. This subgroup includes obese female patients and patients with a non-intact urinary tract, an indwelling urethral or suprapubic catheter, or who use intermittent catheterization. Women with concurrent menstruation should be reevaluated after its cessation or should undergo catheterization to determine if the blood is in fact present in the urine or is only noted as a result of vaginal contamination.

Specimen: The specimen container should be labeled per institutional protocol and analyzed within standard laboratory regulations. Method of collection, date, and time should be included in the labeling.

Analytic Technique

Analytic techniques vary, with some now using flow cytometry rather than microscopy. For more details, one can consult with the local laboratory director.

Urine specimens collected immediately after prolonged recumbency (first void in morning) or the first voiding after vigorous physical or sexual activity should not be examined to assess for microhematuria.[44, 45] It should also be remembered that in dilute urine, usually below an osmolality of 308 mOsm, most RBCs lyse; therefore, the number of RBCs per 400x magnification may be artificially reduced.[46]

The Panel emphasizes that a positive dipstick merits microscopic examination of the urinary sediment as described but does not warrant full evaluation unless microscopic evaluation confirms ≥3 RBC/HPF. If this is not the case but the clinician is suspicious that the findings could reflect true MH, then repeat microscopic testing may be reasonable after assessing patient risk and preference.

2. **Clinicians should not define microhematuria by positive dipstick testing alone. A positive urine dipstick test (trace blood or greater) should prompt formal microscopic evaluation of the urine. (*Strong Recommendation; Evidence Level: Grade C*)**

Urine dipstick testing detects the peroxidase activity of hemoglobin using benzidine but does not correlate perfectly with microscopic evaluation. For example, myoglobinuria, dehydration, exercise, menstrual blood, or povidone-iodine (betadine) can produce false-positive dipstick results.[47] Two retrospective cohort studies reported the concordance of dipstick diagnosis with MH defined as ≥3 RBC/HPF on UA with microscopy. In a series of 237 female patients with a positive dipstick, Bradley et al. observed that 20.3% of such patients had a normal UA.[8] Meanwhile, Rao and colleagues noted that amongst 54 patients referred for MH evaluations based solely on a positive dipstick, only 14 (26%) had a positive UA result.[48]

At the same time, the degree of hematuria on dipstick has been associated with the degree of hematuria on a UA, as well as the subsequent likelihood of identifying bladder cancer. Specifically, in a series of over 46,000 patients, a Spearman's rank order correlation analysis determined a positive correlation between degree of MH on dipstick and UA (rho 0.66).[5] In the same study, 143 patients with bladder cancer were identified, and index readings of dipstick showed a sensitivity of 29% through 69%, with 69% representing at least trace blood on dipstick. Meanwhile, the highest specificity for dipstick was observed with index readings of large (95%) and the lowest at an index reading of trace.

In reviewing these data, the Panel concluded that a positive urine dipstick test (trace blood or greater) should prompt UA with microscopic evaluation but should not be used alone to diagnose MH.

INITIAL EVALUATION

3. **In patients with microhematuria, clinicians should perform a history, physical examination including blood pressure measurement, and serum creatinine to assess risk factors for genitourinary malignancy (e.g., detailed smoking history), medical renal disease, gynecologic, and non-malignant genitourinary causes of MH. (*Clinical Principle*)**

A detailed history and physical examination should be performed in patients who are confirmed to have MH as defined in Statement 1. Important aspects of the history should include age, sex, history of GH, irritative urinary symptoms, and overall health status. Careful consideration should be given to risk factors for malignancy (**Table 3**), with specific emphasis on assessing for family history of urologic malignancies, and genetic or other risk factors for bladder or urothelial cancer, such as environmental/occupational exposures. Due to the causal association between tobacco use and both bladder and kidney cancer, a detailed tobacco exposure history should be performed at the initial consultation and should include smoking intensity (pack-year quantification) and other tobacco product usage to aid with risk stratification. For patients who currently smoke or use other tobacco products, clinicians should assist with cessation by providing a recommendation to quit and facilitating evidence-based smoking cessation treatment through institutional or other publicly available

resources.[49] Of note, the association between bladder cancer and non-combustible tobacco products such as heat-not-burn devices or electronic cigarettes is not well established at this time. However, patients who use non-combustible tobacco products have significant levels of urinary carcinogens and metabolites of exposure that are associated with bladder cancer development.[50-54] Physical examination should include measurement of blood pressure and a genitourinary examination as dictated by clinical history. For example, in women, examination of the external genitalia, introitus, and periurethral tissue may identify urethral pathology or other gynecologic pathology to explain the noted MH.

Clinicians should also understand that the differential diagnosis for MH is broad, including a number of benign conditions (e.g., benign prostatic enlargement, nephrolithiasis, urethral strictures and diverticula, exposure to trauma, or recent urological procedures/catheterization), some of which in turn will merit treatment. Thus, the MH patient should be questioned regarding these potential causes. For example, rates of calculus disease in MH patients range from 1.0% to 20.0%,[55] with most studies reporting calculus disease rates above 5.0%;[8, 10, 12, 21-23,56, 57] rates of benign prostatic hyperplasia range from 3.9%[57] to 52.7%;[55] and urethral stricture rates of 1% or less were reported in two studies of MH patients.[9, 15]

A retrospective study[14] of 1,049 patients undergoing evaluation for MH is further illustrative of the diverse etiologies. Only 12 (1.1%) patients were diagnosed with urologic malignancy, including 1 upper tract urothelial tumor, 5 renal masses (3 small), and 6 bladder tumors, of which 2 were high grade and 4 were low grade. Conversely, 620 patients had a negative work-up, while 417 patients had benign diagnoses, including 119 with stones and 298 with other benign diagnoses including urethral strictures, BPH, and renal cysts.

Given this broad differential diagnosis that includes non-malignant urologic etiologies that may nevertheless require intervention, clinicians should perform a probative history and physical examination. As gynecological bleeding may be confused with MH, a menstrual and gynecological history should be obtained, and a catheterized UA may be helpful to confirm MH. A more extensive gynecologic history and pelvic examination should be performed by a clinician capable of assessing gynecologic conditions when indicated by gynecologic history. Symptoms and signs of UTI, such as fever and dysuria, should be elicited. Patients should be asked about the presence of flank pain, which may herald a urinary tract stone, and obstructive urinary symptoms, which may signal the presence of prostatic hyperplasia or urethral stricture. Hypertension, history of kidney disease, dysmorphic RBCs, and proteinuria may indicate glomerular disease. Thus, the initial evaluation should also include measurement of serum creatinine and an estimate of glomerular filtration rate, both to identify kidney disease and to guide the choice of imaging modality, should that be deemed necessary based on patient risk (see below). Patients should also be asked about recent perineal trauma or genitourinary instrumentation.

Table 3: Urothelial Cancer Risk Factors

Risk Factors Included in AUA Microhematuria Risk Stratification System	Additional Urothelial Cancer Risk Factors[6, 14,58-62]
Age	Irritative lower urinary tract symptoms
Male sex	Prior pelvic radiation therapy
Smoking use	Prior cyclophosphamide/ifosfamide chemotherapy
Degree of microhematuria	Family history of urothelial cancer or Lynch Syndrome
Persistence of microhematuria	Occupational exposures to benzene chemicals or aromatic amines (e.g., rubber, petrochemicals, dyes)
History of gross hematuria	Chronic indwelling foreign body in the urinary tract
* The Panel recognizes that this list is not exhaustive.	

4. **Clinicians should perform the same evaluation of patients with microhematuria who are taking antiplatelet agents or anticoagulants (regardless of the type or level of therapy) as patients not on these agents. (*Strong Recommendation; Evidence Level: Grade C*)**

Patients on antiplatelet agents and/or anticoagulants should be assessed in the same manner as patients who are not anticoagulated regardless of type or level of therapy (i.e., aspirin, warfarin, or other antiplatelet or antithrombotic agents) because these patients have a risk of malignancy that is similar to other populations.[63-65] Although few studies have specifically stratified cancer detection rates according to anticoagulation status, several prior studies of MH patients included a substantive representation of patients who were receiving antiplatelet or anticoagulant therapy. For example, Koo et al. demonstrated a 5.8% detection of bladder cancer in 411 consecutive patients with MH, of whom 15.3% were anticoagulated.[23] Further, a series of patients with GH on either anticoagulant or aspirin therapy found tumors in a quarter of patients, and other treatable findings in approximately half the cohort.[66] Meanwhile, a population-based cohort study from Ontario reported that patients exposed to antithrombotic medications were significantly more likely to be diagnosed with bladder cancer within six months than patients not exposed to these medications,[67] suggesting the potential that such anticoagulation may unmask bleeding from an underlying malignancy. Therefore, clinicians should not dismiss MH in patients on anticoagulants or antiplatelet agents; rather, these patients should undergo standard risk-based evaluation.

5. **In patients with findings suggestive of a gynecologic or non-malignant urologic etiology, clinicians should evaluate the patients with appropriate physical examination techniques and tests to identify such an etiology. (*Clinical Principle*)**

6. **In patients diagnosed with gynecologic or non-malignant genitourinary sources of microhematuria, clinicians should repeat urinalysis following resolution of the gynecologic or non-malignant genitourinary cause. If microhematuria persists or the etiology cannot be identified, clinicians should perform risk-based urologic evaluation. (*Clinical Principle*)**

7. **In patients with hematuria attributed to a urinary tract infection, clinicians should obtain a urinalysis with microscopic evaluation following treatment to ensure resolution of the hematuria. (*Strong Recommendation; Evidence Level: Grade C*)**

If the history and physical examination suggest the presence of a gynecologic or non-malignant source of MH, the clinician should perform a directed evaluation to assess for such an etiology. For example, women with a suspected gynecologic source of MH should be evaluated by a clinician capable of assessing for and treating gynecologic disorders, whether that is a urologist with such expertise, a gynecologist, an experienced primary care provider, or other experienced clinician. A catheterized UA may be helpful to confirm MH in patients when findings suggest a potential gynecologic source of MH. Patients suspected of having UTI should undergo urine culture and, if necessary, antibiotic treatment. Similarly, patients suspected of having urolithiasis, urethral stricture disease, urethral diverticulum, or other non-malignant sources of MH should be evaluated appropriately to rule in or rule out these causes.

Following a directed evaluation, if no etiology is identified, further risk-based urologic evaluation should be undertaken. In patients who are found to have a non-malignant source of hematuria, the non-malignant diagnosis should be treated appropriately and then the urine should be re-tested for presence of MH. Persistent MH after resolution of the non-malignant cause should prompt risk-based urologic evaluation. Those patients suspected to have a UTI as the etiology of MH should be treated for the UTI and then should undergo repeat UA to confirm resolution of the MH. If the MH does not resolve following treatment of the UTI, a risk-based urologic evaluation should be performed. The Panel acknowledges that there are some non-malignant urologic and gynecologic conditions, such as BPH, non-obstructing nephrolithiasis, vaginal atrophy, interstitial cystitis, or pelvic organ prolapse, which will not merit treatment or in which the MH may not resolve completely even with appropriate management. In these cases, clinicians must use careful judgment and shared decision-making to decide whether to pursue MH evaluation. Attention to the patient's risk factors for urologic malignancy should inform these decisions.

The risks of under-evaluating women with MH, and specifically the frequent misattribution of MH to UTI without sufficient evidence to support the diagnosis, or sufficient follow-up to confirm resolution of MH after treatment of UTI, merit mention. Cohn et al. evaluated gender disparities in the diagnosis of bladder cancer following presentation with hematuria and found that women with bladder cancer had a higher mortality relative to incidence compared to men.[25] Women who present with irritative symptoms are frequently treated empirically with antibiotics for a presumed UTI, as supported by practice-pattern data demonstrating that women have more urinalyses and cultures submitted compared to men and are more often treated with multiple rounds of antibiotics.[25] Indeed, Cohn et al. found the mean number of urinalyses sent for men versus women were 1.19 (95%CI: 1.16 to 1.45) and 1.39 (95%CI: 1.16 to 1.23), respectively ($p<0.001$).[25] Similarly, a mean of 0.53 (95%CI: 0.51 to 0.55) and 0.83 (95%CI: 0.78 to 0.88) urine cultures were sent in men and women with hematuria, respectively ($p<0.001$).[25] When reviewing antibiotic treatment, 8.7% of women were treated with >3 courses of antibiotics compared to 5.2% of men ($p<0.001$).[25] Moreover, a separate investigation found that in the year prior to bladder cancer diagnosis, symptomatic treatment without evaluation was given to 47% of women, with nearly 16% receiving ≥3 treatments for presumptive UTI.[68] In addition, studies have demonstrated sex-based disparities in evaluation of hematuria as well. In one such series, women with hematuria were significantly less likely than men to undergo cystoscopy (OR 0.48; 95%CI 0.37 to 0.62; $p<0.001$), upper tract imaging (OR 0.47; 95%CI 0.36 to 0.61; $p<0.001$), and complete evaluation with both cystoscopy with upper tract imaging (OR 0.31; 95%CI 0.24 to 0.45; $p<0.001$). The sequelae of such a delay and of under-evaluation may explain (in part) the longer reported time from presentation with hematuria to diagnosis of bladder cancer noted in women.[69]

Considering these noted practice patterns, the Panel believes it important to emphasize the need for follow-up UA following resolution of a presumed gynecologic or non-malignant urologic cause of MH to confirm resolution of the MH. While there is no evidence-based interval for repeating the UA, MH may not resolve for several weeks to a few months following treatment of a gynecologic or non-malignant cause of MH, or treatment of a UTI. As such, the panel concludes that waiting at least three weeks after resolution of the non-malignant etiology and no more than three months would be appropriate. If the MH persists at that time, a risk-based urologic evaluation should be performed.

8. **Clinicians should refer patients with microhematuria for nephrological evaluation if medical renal disease is suspected. However, risk-based urologic evaluation should still be performed. (*Clinical Principle*)**

Patients with proteinuria, dysmorphic RBCs, cellular casts, or renal insufficiency may have medical renal disease, which can cause hematuria. Therefore, patients with these features should be referred for nephrological evaluation. While evaluation for medical renal disease should be performed, this does not preclude the need to proceed with risk-based urologic evaluation. In fact, several studies have suggested an increased risk of renal cancer in patients with impaired renal function. For example, in a retrospective cohort study of 1,190,538 adult patients in a single healthcare system, Lowrance et al.[70] demonstrated an increased risk in the development of renal and urothelial cancers associated with lower eGFR. For renal cancers, the risk increased with decrease in eGFR (adjusted HR 1.39; 95%CI 1.22 to 1.58 for eGFR=45-59; HR 1.81; 95%CI 1.51 to 2.17 for eGFR=30-44; HR 2.28; 95%CI 1.78 to 2.92 for eGFR<30). The increased risk of urothelial cancer was noted in patients with an eGFR <30.

RISK STRATIFICATION

9. **Following initial management, clinicians should categorize patients presenting with microhematuria as low/negligible-, intermediate-, or high-risk for genitourinary malignancy based on the accompanying tables (Tables 3 and 4). (*Strong Recommendation; Evidence Level: Grade C*)**

Table 4: AUA/SUFU Microhematuria Risk Stratification System 2025

Risk of malignancy*	Low/Negligible 0-0.4%[21, 22, 24]	Intermediate 0.2-3.1%[21, 22, 24]	High 1.3-6.3%[21, 22, 24]
Number of criteria patient must meet	All	One or more	One or more
Degree of hematuria on a single urinalysis	3-10 RBC/HPF+	11-25 RBC/HPF+	>25 RBC/HPF+
Alternative criteria for degree of hematuria		Previously low/negligible-risk patient with no prior evaluation and 3-25 RBC/HPF* on repeat urinalysis	History of gross hematuria
Age for women	<60 years	≥60 years	*Women should not be categorized as high-risk solely based on age*
Age for men	<40 years	40-59 years	≥60 years
Smoking history	Never smoker or <10 pack years	10-30 pack years	>30 pack years
Presence of additional risk factors for urothelial cancer (see Table 3)	None	Any	One or more plus any high-risk feature

*Risk of malignancy is based on the definition from the 2020 AUA/SUFU Guideline in which women being age < 50 year was a criterion for low-risk, women being age 50-59 years was a criterion for intermediate-risk, and women being age > 60 was a criterion for high-risk. Based on interval studies showing significantly lower risk of urothelial malignancy in women, women being age < 60 years is a criterion for low-risk, women being age > 60 years is a criterion for intermediate-risk, and women cannot be categorized as high-risk based on age alone in the 2025 guideline iteration.

+HPF: High-Power Field

The 2020 AUA/SUFU Guideline proposed a risk stratification system and risk-based approach to MH evaluation based on age, sex, degree of hematuria, smoking history and other risk factors for urothelial malignancy. The approach was intended to be patient-centered by tailoring the intensity of the evaluation to match the risk of malignancy. Simultaneously, it was intended to maintain the sensitivity of evaluation for identification of malignancy.

The risk stratification system in the 2020 AUA/SUFU Guideline was based on a systematic review of the literature on risk factors for urothelial cancer and several publications on risk stratification systems. However, the initial risk stratification approach was largely empirical. Since 2020, several groups have sought to validate the AUA/SUFU risk stratification system, determine the actual risk of malignancy in each risk stratum, and assess if the risk stratification approach reliably discerns unique risk to patients. This Guideline revision aims to refine the risk stratification system and risk-based evaluation recommendations to align with the findings of these validation studies.

Sanci et al. conducted a retrospective study of 1,018 men and women who presented with MH, defined as 3 or more

RBC/HPF on UA with microscopy in the absence of an obvious benign cause.[71] All patients were evaluated according to the older 2012 AUA Guideline and underwent cystoscopy and urinary tract imaging (96.2% had CT urography). Overall, urinary tract malignancy was detected in 34 patients (3.3%), of which 32 (94%) had low-grade Ta and 2 (6%) had high-grade T1 urothelial carcinoma. Retrospectively, patients were risk-stratified according to the 2020 AUA/SUFU system, and 21.4% were low-risk, 43.9% were intermediate-risk and 34.6% were high-risk. No cancers (0%) were detected in the low-risk group (n=218). Among 447 intermediate-risk patients, 14 (3.1%) were diagnosed with urothelial cancer, and among 353 high-risk patients, 20 (5.7%) were diagnosed with urothelial cancer. Thus, the risk of malignancy in this cohort did vary according to AUA/SUFU risk stratum. Notably, however, no malignancies were identified in the low-risk group, suggesting that their risk is negligible.

Woldu et al. compiled a dataset of 15,779 patients with MH from 5 clinical trials of urinary biomarkers and 2 prospective registries and compared bladder cancer detection across 2020 AUA/SUFU risk categories.[72] Of note, all the included studies contained a subset of patients presenting with GH who were included in the high-risk group, which may have inflated the cancer detection rate in that risk stratum. Furthermore, there was a lack of granularity regarding degree of MH, number of pack-years of smoking, and use of imaging. Among the 15,779 patients, all of whom underwent cystoscopy, there were 857 bladder cancers diagnosed (5.4%, ranging among source cohorts from 2.3% to 11.5%). Of the 727 (4.6%) patients categorized as low-risk, 3 patients (0.4%) were diagnosed with bladder cancer. In the 1,863 (11.8%) intermediate-risk patients, 18 cancers (1.0%) were detected. Finally, of the 13,189 (83.6%) high-risk patients, 836 (6.3%) were diagnosed with bladder cancer. Among the high-risk group, 2.6% of those with solely with MH (i.e., without GH) had bladder cancer, while 10.9% of those with GH had bladder cancer. Although the percentage of patients with cancer in the intermediate- and high-risk strata was lower than in the Sanci study, the risk of malignancy varied by risk stratum and, similar to the Sanci study, cancer incidence among patients in the low-risk category was negligible.

Lastly, Saxon et al. conducted a retrospective study of 1,730 women evaluated in a university-based urology practice for MH.[73] Of note, 431 or 31.3% of women included in the study were considered inappropriate referrals because they were diagnosed on dipstick alone or had <3 RBC/HPF on UA with microscopy. Of the 1,730 patients, 864 “appropriate” evaluations were performed. A total of 13 genitourinary malignancies were identified, 9 renal cell carcinomas (RCC), and 4 bladder cancers. Assuming that these were all among the patients who were considered appropriate for evaluation, this is a detection rate of 1.5%. Malignancy detection rate was 0% among 322 (18.6%) low-risk patients; 0.2% (n=1) among 463 (26.8%) intermediate-risk patients; and 1.3% (n=12) among 945 (54.6%) high-risk patients. While the detection rate may be somewhat diluted by the high proportion of patients who were referred and/or evaluated inappropriately, this study also shows some variation in cancer detection rate by risk stratum, with risk being negligible in the low-risk category. Furthermore, the investigators found that 11 of the 13 malignancies were diagnosed in women over the age of 60, indicating that the risk of malignancy in younger women is quite low. Interestingly, 12 of the 13 malignancies were identified in women with 3-10 RBC/HPF on UA, while 1 was found in a woman with 11-25 RBC/HPF and none in women with >25 RBC/HPF. This indicates that evaluation is justified in women with lower degrees of MH, provided that other risk factors, particularly age, are present. Additionally, almost 70% of malignancies were observed in the kidney underscoring the importance of imaging the upper tract.

Collectively, these studies validate the 2020 AUA/SUFU risk stratification system to define distinct groups that have varying degrees of risk of genitourinary malignancy. However, they also justify several important changes to the risk stratification system. First, women under the age of 60 have a very low risk of malignancy in the absence of other risk factors. Thus, the Panel changed the age range for women in the low-risk group from <50 years to <60 years and similarly changed the age range for women in the intermediate-risk group from 50-59 years to ≥60 years. Second, to account for the lower risk of malignancy in women, the risk groups have been updated such that women should not be characterized as high-risk based on age alone. As such, they should be categorized as high-risk only if one or more of the other high-risk criteria are present. Notably, the risk of malignancy listed in the table is based on the aforementioned studies that used the 2020 AUA/SUFU risk stratification system.

The Panel notes that the proposed risk stratification system is imperfect. For example, it groups together the risk of urothelial malignancy with other urologic cancers

while the risk factors are primarily those for bladder cancer. A risk categorization system for renal cortical neoplasms among people with microhematuria may look quite different. Furthermore, the risk- stratification system weighs different risk factors such as smoking and degree of hematuria equally, though they may contribute differently to risk of malignancy. To account for the differential weighting of various risk factors, some have proposed and developed nomograms or calculators to estimate an individual's risk for malignancy.[74, 75] Each of these has its strengths and limitations; while none of these has been sufficiently validated to recommend for regular use, there may be instances in which such estimates could influence decision-making.

RISK-BASED EVALUATION

Low/Negligible-Risk

10. **In low/ negligible-risk patients with microhematuria, clinicians should obtain repeat urinalysis within six months rather than perform immediate cystoscopy or imaging. (*Moderate Recommendation; Evidence Level: Grade C*)**

The Sanci, Woldu, and Saxon studies, intending to validate the 2020 AUA/SUFU risk stratification system, found extremely low rates of malignancy among patients in the low-risk category (0%, 0.4% and 0%, respectively).[71-73, 76] Additionally, the Sanci study followed low-risk patients for a median of 26 months, and no additional cancers were identified. Thus, given the low risk of malignancy and the potential harms of over-evaluation, the Panel recommends against routine cystoscopy and imaging for the initial evaluation of patients in the low-risk category and has renamed the category as low/negligible-risk to emphasize this point. The Panel acknowledges, however, that there may be scenarios in which cystoscopy in low/negligible-risk patients may be warranted based on symptoms, clinical suspicion or patient preference. Notably, given the intermittent nature of hematuria (both with regards to presence and degree), the Panel does recommend a repeat UA with subsequent risk-based evaluation predicated on those results.

Initially Low/Negligible-Risk with Hematuria on Repeat Urinalysis

11. **Low/negligible-risk patients with microhematuria on repeat urinalysis should be reclassified as intermediate- or high-risk based on repeat urinalysis. In such patients, clinicians should perform risk-based evaluation in accordance with recommendations for these respective risk strata. (*Strong Recommendation; Evidence Level: Grade C*)**

Low/negligible-risk patients should undergo a repeat UA to evaluate for the resolution versus persistence of MH. A study of over 11,000 patients from a large public health system determined that patients with persistent MH on repeat urine testing had a significantly higher rate of malignancy on subsequent evaluation as compared with those who had negative repeat urine testing (0.35% versus 0.07%).[20] If the repeat UA shows no evidence of MH, then no further evaluation of the bladder or upper tract is needed at this time. In that case, further evaluation would only be merited if new symptoms, more severe MH on subsequent opportunistic testing, or GH develop. If the patient experiences recurrence of similar level of MH (3-10 RBCs/HPF) on subsequent opportunistic testing, further evaluation may be considered in a shared decision-making process.

Patients with *persistent* MH, however, are classified as either intermediate- or high-risk for malignancy, depending upon the degree of MH at the repeat UA and other risk factors. (**Table 4**)

Intermediate-Risk

12. **Clinicians should recommend cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate risk for malignancy. (*Strong Recommendation; Evidence Level: Grade C*)**

Studies of MH patients have consistently demonstrated that bladder cancer is the most frequently detected urologic malignancy during evaluation.[7, 9, 12-15, 21-24] As such, cystoscopy should be recommended for bladder evaluation in intermediate-risk MH patients. Notably, Tan et al. explored the ability of renal-bladder ultrasound in conjunction with a risk index (Hematuria Cancer Risk Score [HCRS]) to inform use of cystoscopy in hematuria patients.[4, 77, 78] In their validation cohort (27% with MH), the sensitivity for identification of bladder cancer was 97%

with 117 patients (25%), theoretically avoiding cystoscopy at the cost of missing a single patient of G1 Ta bladder cancer. While these observations are compelling, the cohort included a relative minority of MH patients. As such, cystoscopy is still currently the preferred recommendation for MH evaluation in intermediate- and high-risk patients.[4, 55, 79]

The goal of upper tract imaging in MH patients is to identify malignancies of the renal parenchyma and upper tract urothelium as well as to identify actionable non-malignant diagnoses of the kidney, collecting system, and ureters. Admittedly, the overall risk of renal parenchymal cancer and UTUC is low. Kang et al. determined that among 911 patients with MH,[10] only 3 (0.3%) had upper tract malignancy— all 3 RCC. Meanwhile, a Samson et al. study of 1,049 patients with MH found 1 patient (0.1%) with upper tract urothelial carcinoma (UTUC) and 2 patients (0.2%) with RCC,[14] while the Matulewicz et al. series of 15,161 patients with MH noted only 96 patients (0.6%) with an upper tract malignancy.[13] Additionally, the DETECT I study reported only a 1.7% incidence in a mixed cohort of microscopic and gross hematuria, and Fankhouser et al. noted an even lower 0.7% incidence in a pure MH cohort.[77, 80] Thus, the choice of imaging is guided by the patient's risk category, which seeks to balance diagnostic accuracy versus risk.

CT urography provides excellent delineation of the excretory urinary tract, is very sensitive for urinary stones, readily identifies renal cortical lesions, and provides extra-urinary information.[81] However, CT urography is generally more expensive than renal ultrasound and involves ionizing radiation and iodine-based intravenous contrast. Renal ultrasonography is relatively less expensive, does not involve ionizing radiation, and has reasonable discrimination for cortical lesions, though image quality is dependent on operator experience and the patient's body habitus. Importantly, optimal bladder distension is important for radiographic bladder cancer assessment. With a lack of bladder distention, smaller tumors may not be visible secondary to detrusor folds or detrusor muscle thickening.[82]

A modeling study by Georgieva et al. determined that for a cohort of 100,000 patients with hematuria, there would be a total of 93 patients with UTUC (0.09%) versus 443 (0.44%) patients with RCC.[16] A more contemporary study by Fankhouser et al. reported on a retrospective cohort of 847 hematuria patients (432 with MH) and noted that 0.7% of the MH population had RCC or UTUC.[2,80] In this analysis, performance characteristics for ultrasonography included sensitivity of 33%, specificity of 96%, positive predictive value (PPV) of 6%, and negative predictive value (NPV) of 100%. Prior studies note that for UTUC, the sensitivity of CT urography has been reported to be 94%, compared with 14% for renal ultrasound.[4] Additional studies evaluating CT urography reported adequate sensitivity for detection of both cortical tumors (100% sensitivity) and UTUC (80 – 99% sensitivity).[83-85] While CT urography offers the most sensitive detection of upper tract malignancy,[16] the use of this modality must be balanced with the overall low rate of upper tract malignancy in MH patients[5] as well as the potential harms associated with CT, including ionizing radiation, intravenous contrast reactions, and false-positive results.[17,86,87,88]

Notably, given the overall population-level prevalence of MH, healthcare resource allocation is impacted by the choice of imaging to evaluate these patients. Halpern et al. evaluated the cost of CT urography plus cystoscopy versus renal ultrasound plus cystoscopy in a theoretical population of 10,000 patients with MH and found the overall cost was over three times greater for the CT group despite only detecting one additional UTUC tumor.[18]

Additionally, the risk of diagnosing a malignancy must be balanced against the potential harms of false-positive detection. A prior modeling analysis estimated up to a 22% false-positive rate of cystoscopy and/or imaging in the evaluation of MH, leading to additional evaluation, cost, and patient concern.[27] A separate study of 202 patients undergoing CT urography for MH noted incidental urinary tract findings in 61% and incidental extra-urinary findings in 74%, resulting in additional imaging, referrals to specialists, and additional associated hospital costs.[8] The authors defined an incidental finding as one for which the patient had no prior history and was not related to the reason for the examination. Nevertheless, it should be recognized that some extra-urinary findings may be clinically relevant.

Collectively, the Panel believes the risk of RCC and UTUC is low enough in the intermediate-risk group that the balance of benefits and harms of imaging favors renal ultrasound over cross-sectional imaging. While less intense evaluation (e.g., renal ultrasound) risks missing a very small number of upper tract malignancies compared to a more intense evaluation (e.g., CT), routine use of

renal ultrasound instead of CT urography for low- and intermediate-risk patients would decrease costs, complications of iodinated contrast, and patient radiation exposure.[17]

13. **In appropriately counseled intermediate-risk patients who want to avoid cystoscopy and accept the risk of forgoing direct visual inspection of the bladder urothelium, clinicians may offer urine cytology or validated urine-based tumor markers (Table 5) to facilitate the decision regarding utility of cystoscopy. Renal and bladder ultrasound should still be performed in these cases. (*Conditional Recommendation; Evidence Level: Grade C*)**

The gold standard to evaluate for bladder cancer is cystoscopy, but this procedure is associated with patient discomfort, complications (including infection in 1-3%),[89-96] and anxiety that can impact patient adherence with recommendations. Urine-based tumor markers (UBTMs) and urine cytology were developed to provide a non-invasive method to detect urothelial carcinoma. A systematic review of the literature evaluated the performance of cytology and commercially available UBTMs and included 11 studies, with study populations of 8,302 patients for cytology evaluation and a range of 354 to 6,474 patients for the commercially available UBTMs.[76] Likelihood ratios (LR), which represent the relative likelihood of cancer presence, were calculated. A LR of ~1 indicates a test is not capable of changing the post-test probability of disease. A positive LR >1 increases probability of disease in the presence of a positive test, while a negative LR <1 decreases the probability of disease in the presence of a negative test. In this analysis, the positive LR for cytology was 7.67 while the negative LR was 0.35. For other UBTMs, positive LR ranged from 2.14-6.6, while the negative LR ranged from 0.07-0.48.

The value of urine cytology or UBTMs is to assist in cases where the test results may inform the added value of performing cystoscopy. For low/negligible-risk cases where the risk of bladder cancer is approximately 0.4%, the use of cytology and UBTMs would be exceptionally unlikely to identify any cancers and would be more likely to increase the risk of unnecessary evaluations attributable to false-positive results. For example, a marker with a theoretical 100% sensitivity would need to be utilized 1,000 times to identify 4 cancers. Additionally, if such a marker had 90% specificity, it would still result in 100 negative/unnecessary cystoscopy evaluations. Conversely, in high-risk patients, the incidence of cancer exceeds 2.5%, and there is insufficient evidence that use of cytology or UBTM would safely obviate the need for cystoscopy evaluation of the bladder. While this could be an area for future research, the risk of missing cancer currently outweighs the benefit of avoiding cystoscopy in high-risk patients. Therefore, the Panel recommends against routine use of urine cytology or UBTMs in the initial evaluation of low/negligible- or high-risk patients with MH.

In patients with intermediate-risk disease, where the baseline prevalence of disease is approximately 1% (0.2-3.1%), the high NPV of most markers would result in a low likelihood of cancer in patients with negative marker evaluations.[71-73, 76] For example, based on the above-mentioned LR of cytology, a patient with a 1% pre-test probability of bladder cancer would have a post-test probability of 0.4% in the setting of a negative cytology. Similarly, a negative test on other UBTM can reliably re-stratify a patient who might be otherwise classified as intermediate-risk into a low/negligible-risk category, with the (post-test) probability of cancer detection decreasing to 0.1%-0.4%.

Currently, the strength of evidence regarding different urine markers and cytology is highly variable. Most of the studies evaluating urine markers were performed in mixed populations (MH and GH). Since patients with a history of GH are classified as high-risk, the Panel focused on studies with sufficient numbers of patients with MH. As such, there was a requirement that studies were comprised of a hematuria population whereby at least 25% were MH with an absolute number of at least 100 MH patients (**Table 5**). The principal outcome of interest was NPV given the theoretical intent of identifying patients who can safely avoid cystoscopy with a lower risk of missing cancer.[97] The highest level of evidence was an evaluation of CxBladder Triage based on an RCT comparing a marker-based approach versus standard of care routine cystoscopy to evaluate MH. In this study, the marker had a NPV of 99%. Several other urine-based tumors markers (AssureMDx, CxBladder Resolve, EarlyTectBCD, NMP22 BladderChek, UroVysion FISH assay, Xpert® Bladder Cancer Detection) and urine cytology also had reported NPV of 95-100% in the target population.

Table 5: Reported Negative Predictive Values for the Detection of Bladder Cancer Using the Available Urine Cytology and Urine-Based Biomarkers

Assay[A]	Hematuria Population	Total Patients (n)	Reported Negative Predictive Value	AUA Strength of Evidence[B]
AssureMDx	MH and GH	Total n=838; MH n=457	99.4% - 100%[C98, 99]	C
CxBladder Resolve	MH and GH	Total n=548; MH n=289	99.8%[100]	B
CxBladder Triage	MH[D]	n=390	99%;[97] 95%CI: 95 to 100%[E]	A
	MH and GH	Total n=571; MH n=185	100%;[101] 95%CI: 94 to 100%[F]	C
EarlyTectBCD	MH and GH	Total n=1465; MH n=643	97.6% - 98.7%[C,F102, 103]	C
NMP22 BladderChek (qualitative)	MH	n=876	95% - 100%[104-106]	C
Urine cytology	MH	n=513	95.0% - 98.7%[104, 107, 108]	C
	MH and GH	Total n=4,497; MH n=1,743	89.5%[F] - 96.0%[77, 109-111]	C
UroVysion	MH and GH	Total n=828; MH n=384	97%[109]	C
Xpert	MH and GH	Total n=1,152; MH n=597	98.0% - 99.6%[109, 110]	C

A. To be included in the table, NPV for the assay was reported in a purely MH population or MH patients comprised ≥25% of total hematuria population. All studies included ≥100 microhematuria patients.
B. Strength of evidence in relation to reported NPV. Refer to Table 1 for strength of evidence definition and methodology.
C. NPV reported for MH subgroup.
D. The RCT[97] is the only identified study designed to evaluate use of a urine-based biomarker to guide evaluation.
E. NPV for detection of high-grade disease[97], 100%; 95%CI: 97 to 100%. NPV for lower risk patients, 100%; 95%CI: 94 to 100%.
F. NPV for detection of high-grade disease[102, 103], 100%; 95% CI: 99 to 100%.
G. NPV of 89.5%[111] reported for detection of bladder cancer and UTUC.

There were other markers evaluated in patients with hematuria, but these either lacked sufficient data regarding the absolute number or percent of patients with MH to evaluate in this population. Future research could evaluate the role for these markers in evaluating patients with MH.

Patients with intermediate-risk microhematuria who choose to forego cystoscopy based on the results of UBTM or cytology should still be evaluated with a renal and bladder ultrasound to evaluate the upper tract and renal parenchyma (See Statements 11 and 12). While UBTM and cytology have a role in determining which patients can safely avoid cystoscopy, the potential upper-tract pathologies including (but not limited to) larger or

obstructing UTUC, renal cortical tumors, hydronephrosis, and nephrolithiasis merits investigation with imaging.

These patients should already have been evaluated with renal and bladder ultrasound at initial presentation and further evaluation of the upper tracts with cross-sectional imaging (e.g., CT urography) could be considered (see Statement 13.) For patients with a negative follow-up UA, clinicians should engage in shared decision-making regarding whether to repeat UA in the future. (See statements 22-24)

14. **For patients with intermediate-risk microhematuria who do not undergo cystoscopy based on urinary marker results, clinicians should obtain a repeat urinalysis within 12 months. Such patients with persistent microhematuria should then undergo cystoscopy. (*Strong Recommendation; Evidence Level: Grade C*)**

The STRATA study aimed to evaluate whether a UBTM (CxBladder Triage) could help identify patients with MH at high risk of having bladder cancer while also safely avoiding evaluation in those with a negative marker result. Specific to this statement, for those deemed “lower risk” (defined as a 3-29 RBC/HPF and up to a 10 pack-year smoking history) who had a negative marker and did not undergo cystoscopy [n=57], follow up renal/bladder ultrasound, urine cytology, and repeat UBTM were offered. This resulted in the detection of 1 subsequent pTa high-grade bladder cancer diagnosis 13 months after initial presentation,[97] though subsequent follow up evaluation and data availability among all patients was not uniform. Given that the data supporting the use of UBTM remains nascent, the Panel believes that a repeat UA within 12 months should be considered, primarily for safety, with persistent MH on subsequent UAs prompting a recommendation for cystoscopy. The recommendation specifically for repeat UA among those who choose not to initially undergo a cystoscopy is based on a 2021 Pak et al. study in which 637 patients with initial negative evaluations underwent repeat evaluation due to persistent or recurrent MH.[112] In this study, 1.2% of patients were found to have a bladder tumor. It can be assumed that the potential risk of a bladder tumor in patients who chose not to undergo cystoscopy based on UBTM results is similar to or potentially higher than the rate reported in the Pak et al. study, but no data exist to precisely estimate or quantify this risk.[112]

These patients should already have been evaluated with renal and bladder ultrasound at initial presentation and further evaluation of the upper tracts with cross-sectional imaging (e.g., CT urography) could be considered (see Statement 13.) For patients with a negative follow-up UA, clinicians should engage in shared decision-making regarding whether to repeat UA in the future. (See statements 22-24)

High-Risk

15. **Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy. (*Strong Recommendation; Evidence Level: Grade C*)**

    Options for Upper Tract Imagine in High-Risk Patients

    a. If there are no contraindications to its use, clinicians should perform multiphasic CT urography (including imaging of the urothelium). (*Moderate Recommendation; Evidence Level: Grade C*)

    b. If there are contraindications to multiphasic CT urography, clinicians may utilize MR urography. (*Moderate Recommendation; Evidence Level: Grade C*)

    c. If there are contraindications to multiphasic CT urography and MR urography, clinicians may utilize retrograde pyelography in conjunction with non-contrast axial imaging or renal ultrasound. (*Expert Opinion*)

As previously stated, cystoscopy represents a critical component of the MH evaluation because imaging with CT urography or ultrasound has limited sensitivity for identifying bladder cancer.[4, 79] As such, the Panel views cystoscopy as an important part of the work-up of patients with MH identified as high-risk for malignancy.

The Panel concluded that patients who meet the high-risk criteria are at a sufficient risk for harboring a diagnosis of urinary tract cancer to also warrant multiphasic cross-sectional imaging to evaluate both the renal parenchyma and the urothelium, using CT urography if there are no contraindications to its use. Of note, while multiple protocols fall under the moniker of CT urography, the overall intent of these studies is to provide unenhanced and enhanced views of the kidneys to accurately

characterize renal cortical tumors; and to provide delayed views of the renal collecting systems and ureters to identify upper tract urothelial tumors. A host of additional urinary tract and extra-urinary findings may also be identified, including urinary lithiasis and anatomic abnormalities. Given the range of options available for evaluation of the renal parenchyma and upper tract urothelium with CT and the absence of strong evidence to support one technique over another, the Panel recommends using a protocol that optimizes imaging performance characteristics while minimizing radiation exposure. While there is not presently a single practiced standardized dose reduction strategy, options include split bolus protocols and radiation dosage adjustment for body mass index (BMI).[113]

Contraindications to contrast-enhanced CT include chronic kidney disease and allergy to iodine-based contrast. In such patients, the Panel recommends magnetic resonance (MR) urography as an alternative imaging modality. Pregnant patients constitute a unique population for which there is little data for guidance. Since few pregnant patients will fall into the high-risk group, the Panel recommends initially obtaining renal ultrasonography for MH during pregnancy, with consideration of multiphasic CT or MR urography after delivery.

MR urography has adequate sensitivity for renal cortical tumors and upper tract urothelial tumors, but lower sensitivity for nephrolithiasis.[114] The harms and limitations of MR urography include risk of false positive results, inconvenience of the lengthy exam, cost, limited accessibility, and risk of nephrogenic systemic fibrosis (NSF). In addition, absolute and relative contraindications to MR urography include mobile metal implants and claustrophobia. Of note, NSF was initially described in patients with poor renal function receiving gadolinium for MRI studies; however, contemporary rates of NSF have decreased, likely due to awareness of the risk and the development of newer gadolinium-based contrast agents.[115, 116] Indeed, the American College of Radiology issued recommendations in 2018 that relax the concern for NSF, particularly with the use of newer gadolinium agents (e.g., gadobutrol, gadoxetate), even in patients with low renal function.[117] Ultimately, if MR urography is being considered for a patient with poor renal function and MH, the Panel recommends discussion with institutional radiologists regarding the agent being used on site and the relative risk-yield ratio of the study. Moreover, it should be acknowledged that MRI has a lower detection rate than CT for the detection of stone disease. Therefore, if nephrolithiasis is suspected based on the patient's history, then non-contrast CT should be undertaken.

For patients with contraindications to CT and MR urography, imaging of the renal cortex may be achieved with either non-contrast CT or renal ultrasound to assess the renal cortex and retrograde pyelography (RPG) to assess the urothelium.

16. Clinicians should perform white light cystoscopy in patients undergoing evaluation of the bladder for microhematuria. (*Moderate Recommendation; Evidence Level: Grade C*)

White light cystoscopy (WLC) remains the standard for evaluation of MH.[118] The Panel recognizes that the reliability of WLC for the detection of flat lesions (i.e., carcinoma in situ [CIS]) is lower relative to papillary tumors, with a false-negative rate as high as 20%.[119-121] Further, the Panel acknowledges the development of enhanced cystoscopy techniques such as blue light cystoscopy (BLC) to improve bladder cancer detection and resection among patients previously diagnosed with bladder cancer.[122, 123] Indeed, BLC has been associated with several benefits, including improved detection of CIS and papillary tumors as well as reduction in disease recurrence compared with WLC in patients with bladder cancer.[119, 124]

Nevertheless, BLC studies to date have been reported among patients with bladder cancer rather than MH cohorts being screened for bladder cancer. As such, the generalizability of this approach to MH patients remains uncertain. In addition, the available studies have noted a somewhat reduced specificity for BLC compared with WLC, which in turn could lead to an increased rate of unnecessary biopsy. Moreover, BLC involves additional cost and time expenditure, and has not been widely validated for flexible cystoscopy.

Thus, given the lack of evidence supporting a role for enhanced cystoscopy to evaluate MH patients in the absence of an established bladder cancer diagnosis, the Panel concludes that WLC should be utilized in the evaluation of MH.

17. In patients with persistent or recurrent microhematuria previously evaluated with renal ultrasound, clinicians may perform additional

imaging of the urinary tract. (*Conditional Recommendation; Evidence Level: Grade C*)

While renal ultrasound provides an evaluation of the renal cortex, the sensitivity of this modality for detecting ureteral pathology, particularly UTUC, is diminished.[4, 86,125] The patient with persistent or recurrent MH who has undergone prior renal ultrasound represents a clinical scenario in which the diagnosis of UTUC is possible, although admittedly still uncommon. Nevertheless, in these cases, clinicians may choose to obtain further imaging to include delineation of the urothelium such as CT urography, MR urography, or RPG.

18. **In patients with microhematuria who have a family history of renal cell carcinoma, a known genetic renal tumor syndrome, or a personal or family history of (or suspicious for) Lynch syndrome, clinicians should perform upper tract imaging regardless of risk category. (*Expert Opinion*)**

RCC is associated with several genetic syndromes (**Table 6**)[126-129] and with a family history of RCC.[58] Furthermore, patients with a personal or family history of Lynch syndrome (also known as hereditary nonpolyposis colon cancer or HNPCC) are at increased risk for upper tract urothelial carcinoma, among other malignancies. Thus, the Panel believes that patients with MH who have such a history warrant upper tract imaging regardless of risk classification. As insufficient evidence exists regarding the preferred modality in this scenario, the choice of imaging remains at provider discretion, although CT or MR urography or RPG would be preferred in Lynch syndrome.[130]

Table 6: Inherited Risk Factors for Renal Cortical Tumors

Known genetic renal tumor syndrome
1. von Hippel-Lindau
2. Birt-Hogg-Dube
3. Hereditary papillary RCC
4. Hereditary leiomyomatosis RCC
5. Tuberous sclerosis

URINARY MARKERS

19. **Clinicians should not routinely use urine cytology or urine-based tumor markers to decide whether to perform cystoscopy in the initial evaluation of low/negligible- or high-risk patients with microhematuria. (*Strong Recommendation; Evidence Level: Grade C*)**

20. **Clinicians should not routinely use cytology or urine-based tumor markers as adjunctive tests in the setting of a normal cystoscopy. (*Strong Recommendation; Evidence Level: Grade C*)**

As noted in discussion for statement 13, low/negligible-risk patients have a very low probability of harboring cancer; as such, the use of cytology or UBTMs in the initial evaluation of low/negligible-risk patients would lead to identification of very few cancers even if those tests had very high sensitivity and would lead to a large number of avoidable cystoscopy evaluations even if those tests had very high specificity. Thus, the use of UBTM and cytology in low/negligible-risk patients would be very inefficient and the harms would outweigh the benefits. Conversely, for high-risk patients, the overall incidence of cancer is relatively high. At present, there is insufficient evidence to demonstrate the safety and efficacy of using results of cytology or UBTMs to exclude the need for cystoscopy in the initial evaluation of high-risk patients.

While the current Guideline finds potential value in using cytology and UBTMs in patients with intermediate-risk MH as part of a shared decision-making, this does not extend as an adjunctive diagnostic test in addition to cystoscopy for the evaluation of patients with MH. The additional value of these tests in the setting of a negative cystoscopy during an initial evaluation of MH is unsupported by the current literature since the NPV of cystoscopy alone is very high. As such, an additional test is unlikely to significantly improve detection and may lead to unnecessary testing or anxiety if the marker is positive. For example, a prospective study of 2,778 patients evaluated the added benefit of obtaining cytology during the initial evaluation of MH.[111] Of the 2,778 patients, only 2 with a negative evaluation (cystoscopy, ultrasound and intravenous pyelogram) and a positive cytology were eventually diagnosed as having urothelial carcinoma. In addition, there are risks and financial toxicity associated with the 10.5% false-positive rate from cytology in this

study, as these patients will often undergo additional evaluations.

Likewise, a study of urine cytology obtained from 660 patients noted that a positive cytology detected urothelial carcinoma in only 4 patients with normal cystoscopy, of whom 2 had CIS and 2 had upper tract disease. Meanwhile, the DETECT I study recruited 3,556 patients presenting with hematuria (30.3% MH, 69.7% GH), of whom urine cytology was performed in 567 (15.9%).[77] A positive/atypical urinary cytology was reported to have a sensitivity of 57.7%, specificity 94.9%, PPV 35.7%, and NPV 97.9%, with an ROC of 0.688. Moreover, no bladder cancer or UTUC was diagnosed based on a suspicious urinary cytology test alone. Twenty-two patients had a positive urinary cytology result despite a normal cystoscopy and upper tract imaging. Twelve patients (54.5%) had a further diagnostic procedure in the form of ureteroscopy with/without biopsy (n = 5) or interval cystoscopy (n = 7). No bladder cancer, ureteral, or renal pelvis UTUC was identified. Five patients (22.7%) underwent repeat urinary cytology, which was normal.

Similarly, while UBTMs have been evaluated in conjunction with cystoscopy in the hematuria setting, studies have not evaluated the likelihood of cancer in the setting of a normal cystoscopy.[131] Collectively, therefore, data currently indicate that cytology rarely identifies cancer in the setting of normal cystoscopy and imaging and data are lacking for UBTMs in this space.

21. **Clinicians may obtain urine cytology for high-risk patients with equivocal findings on cystoscopic evaluation or those with persistent microhematuria and irritative voiding symptoms or risk factors for carcinoma in situ after a negative work up. (*Expert Opinion*)**

One area for which cytology may have a role is in improving detection of CIS. CIS is often associated with irritative voiding symptoms, and it has been recognized that white light cystoscopy may fail to identify some bladder cancers, especially CIS.[132] For example, in a prospective cohort study enrolling MH and GH patients, the diagnostic sensitivity of cytology was 57.7% (95%CI: 38.7 to 75.3) for high-risk bladder cancers.[77] As such, there may be a role for cytology in high-risk patients with persistent MH after negative evaluation or in other scenarios in which clinical suspicion for CIS is high due to risk factors such as irritative voiding symptoms. Additionally, there may be a role for cytology in adjudicating cases of high-risk patients with equivocal cystoscopic evaluation to decide whether to perform biopsy.[131]

Thus, while there is a lack of convincing evidence for its routine use, there are instances in which clinical suspicion for CIS is sufficiently high that urinary cytology may be warranted as an adjunctive test.

FOLLOW-UP

22. **In patients with a negative risk-based hematuria evaluation, clinicians should engage in shared decision-making regarding whether to repeat urinalysis in the future. (*Strong Recommendation; Evidence Level: Grade C*)**

23. **For patients with a prior negative hematuria evaluation and subsequent negative urinalysis, clinicians may discontinue further evaluation for microhematuria. (*Conditional Recommendation; Evidence Level: Grade C*)**

24. **For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding the need for additional evaluation. (*Expert Opinion*)**

25. **For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urologic symptoms, clinicians should initiate further evaluation. (*Moderate Recommendation; Evidence Level: Grade C*)**

Most patients who have an appropriate risk-stratified negative hematuria evaluation do not require ongoing urologic monitoring and may be safely discharged from the urology clinic after shared decision-making and discussion of the best available evidence. After a negative MH evaluation and in the absence of a change in clinical condition, (i.e., GH, new symptoms) repeated evaluation has minimal diagnostic yield. However, the Panel recognizes that select patients (for example those with multiple risk factors shown in Table 3 or a heavy smoking history) may benefit from and/or request follow-up after a negative hematuria evaluation. For these patients, a future UA may be considered.

Patients with a past negative MH evaluation do not appear to be at increased risk of developing malignancy

compared to a patient without a history of MH. A retrospective case-control study compared 8,465 patients with MH and initial negative work-up to 8,465 hematuria naïve controls and found no significant difference in rates of urinary tract malignancy between the groups over a period of at least 3 years.[133] Similarly, in a study of 258 men age ≥50 years with a negative MH evaluation and a mean of 14 years of follow-up, just 2 bladder cancers were subsequently diagnosed at 6.7 years and 11.4 years of follow-up.[134]

In situations where ongoing follow up after a negative hematuria evaluation is desired following shared decision-making, the Panel recommends obtaining a repeat UA with microscopy. This simple, non-invasive test provides quantitative information about the degree of MH. Patients who have a negative repeat UA after a negative MH evaluation do not need further MH follow up. However, even among patients with persistent or recurrent MH, the incidence of malignancy is low, and these cancers are diagnosed years after the initial evaluation. Pak et al. reported that amongst a retrospective cohort study of 1,332 patients with complete MH evaluation, 637 patients (47.80%) with a negative initial evaluation had persistent or recurrent MH.[112] Repeat cystoscopy in 161 of the 637 patients revealed two new bladder cancers (1.2%), while repeat imaging detected a new suspicious renal mass in 4 of 317 patients (1.3%). Notably, both the bladder and renal cancers were detected more than 36 months following the initial evaluation.[112]

Further supporting these findings, in a retrospective evaluation of 250 patients with a negative MH evaluation, 87 low-risk patients (32.2%) had persistent MH and underwent repeat cystoscopy and imaging three years following initial evaluation, per institutional protocol.[135] The only malignancy identified was a single case of prostate cancer.[135] Based on these data, the Panel recommends shared decision-making regarding the utility of a repeat UA among patients with a negative MH and the optimal timing of obtaining it, if desired.

If a complete MH evaluation reveals a benign etiology not requiring intervention (e.g., enlarged prostate with surface vessels, Randall's plaques and non-obstructing stones, pelvic organ prolapse, asymptomatic vaginal atrophy, interstitial cystitis) and a subsequent UA shows a persistent, stable degree of MH, the Panel recommends shared decision-making regarding whether to proceed with further repeat evaluation. Factors that may be considered are time since the initial (or prior) negative evaluation, presence of other risk factors, and overall risk stratification.

Changes in a patient's clinical status require careful consideration. Specifically, given the associations noted between the presence of GH,[4, 21, 22, 55-57, 79, 136-147] higher degrees of MH,[13, 79, 148] and new or worsening urologic symptoms[21, 138] with the diagnosis of malignancy or clinically significant benign conditions, presentation with any of these should merit further evaluation. Further supporting this, in the aforementioned case-control series of 8,465 patients, subsequent GH in both males (OR: 2.35; 95%CI: 1.42 to 3.91; p=0.001) and females (OR: 4.25; 95% CI: 1.94 to 9.34; p<0.001) was significantly associated with an increased risk of malignancy.[133] Nevertheless, the low overall risk of malignancy in this population must again be acknowledged; therefore, a uniform approach to investigation in this setting cannot be mandated.

Ultimately, clinicians' judgement and patients' preferences are critical in the shared decision-making process regarding whether to repeat the urinalysis in the future or to release the patient from care.

FUTURE DIRECTIONS

While this Guideline update aims to further refine the evaluation and management of patients with MH, the diagnostic approach to MH is challenging due to its high prevalence and concomitant low incidence of clinically significant disease in the adult population. Despite previous long-standing guidelines recommending urologic evaluation for all patients over 35 years old with MH, referral patterns demonstrated that proportionally very few patients undergo a full evaluation. This highlighted the need for a risk-stratified approach to evaluate MH, as provided by the 2020 AUA/SUFU Microhematuria Guideline. This Guideline introduced risk stratification into low-, intermediate-, and high-risk disease, which the Panel has further refined in this amendment. Nevertheless, the Panel recognizes the lack of high-level supporting evidence for many of the Guideline Statements and acknowledges several existing knowledge gaps that represent opportunities for future investigation to meaningfully enhance care.

Recent validation studies demonstrated the 2020 risk stratification system separated MH patients into clinically meaningful categories justifying the graduated intensity of evaluation. However, both retrospective and prospective studies utilizing the 2020 stratification system still result in most patients being classified as high-risk (>75%). The current guideline removes otherwise lower-risk women over age 60 from the high-risk group and eliminates the immediate evaluation of low-risk patients, which will mitigate evaluation intensity for these groups. However, further refinement of the risk stratification system, particularly the high-risk cohort, is needed for more accurate identification of those at greatest risk of harboring malignancy and those in whom evaluation can be de-escalated or avoided entirely. While this revised Guideline modifies the existing risk stratification, future work could include incorporation of nomograms or machine learning algorithms for more personalized risk assessment and urinary biomarkers.

The optimal management of MH may be, at its core, a health system and care delivery issue. Urinalysis is often ordered inappropriately for general screening purposes. Order sets and diagnostic protocols in a variety of settings including annual well visits, emergency department, and preoperative clinic often contain urinalysis orders despite a lack of evidence supporting the practice. For example, 62% of general medicine inpatients have a urinalysis ordered despite 84% being asymptomatic.[149] Despite the high prevalence of MH, most patients never undergo evaluation for MH, and most patients evaluated in urologic clinics appear to be high-risk. Whether this is due to existing referral bias (in that low-risk patients are not referred) or a true limitation of the stratification system is unknown. Future work to understand provider referral practices and how these vary by provider type at a system, regional, and national level is needed. Similarly, an improved understanding of actual risk in patients at low/negligible- and intermediate-risk who are frequently under-evaluated would be of value.

There is a significant need to apply implementation science methodology and principles to better understand the dissemination and uptake of MH guidelines within healthcare systems. In addition, MH evaluation presents an opportune time for discussion regarding modifiable risk factors – namely smoking. Future work may focus on developing a systems-based approach to incorporating smoking/tobacco use cessation support utilizing institutional or other publicly available resources.

In addition to evaluating practice patterns regarding asymptomatic MH diagnosis and referral, better understanding of how clinicians diagnose and define MH is needed. New methods for performing urine microscopy are needed. For example, new automated instruments based either on flow cytometry or digitized microscopy are increasingly utilized to perform urinalysis. These machines may not correlate directly with traditional urine microscopy; thus, it will be important to determine if the threshold of 3 RBC/HPF used in the Guideline will be an equivalent predictor of risk when these new technologies are used in evaluation.

The current risk stratification focuses primarily on risk factors for urothelial cancer. Smoking, obesity, hypertension, and chronic kidney disease all represent established risk factors for RCC, of which only smoking is represented in the current risk stratification.[24] Depending on the goals of evaluation, a different risk stratification may be necessary to improve recommendations regarding upper tract imaging. The potential benefits of reducing exposure to radiation and contrast agents (with attendant risk of renal issues and allergies) and decreasing healthcare cost are substantial;[16, 18, 86] however, there exists the risk with this approach of missing small renal masses, UTUC, and small stones. Furthermore, opportunities to reduce radiation exposure with lower or reduced dose protocols deserve additional investigation.[84,85] The need remains to determine whether using lower doses of radiation provides similar sensitivity to detect benign and malignant urologic findings, and which, if any, patient populations or risk groups would be particularly suited for such modified protocols.

The utility of UBTMs in the evaluation of patients with MH is evolving. Urothelial cancers are in contact with the urine, and this fact has been utilized to evaluate the differential expression of proteins, RNA, DNA, and changes in methylation and cells among patients with malignant and benign conditions. Previous guidelines recommended against using UBTMs including cytology for evaluating MH. While data now exist to support consideration in intermediate-risk populations, use of UBTMs and cytology in low- and high-risk groups is not supported at this time as the results should not change recommended evaluation.

The appropriate incorporation of UBTM/cytology in the evaluation of MH is reliant on accurate risk stratification. Effort and education will need to be undertaken to ensure

UBTM/cytology is limited to use in appropriate populations per current Guideline recommendations as a tool to reduce the use of cystoscopy during MH evaluation. Similarly, optimizing follow-up in patients with negative marker testing will be valuable. The necessity of such repeated evaluation should be evaluated as well as the optimal timing and should be a key endpoint for designing prospective marker-based trials.

This revised Guideline includes recent data demonstrating the low risk of diagnosis of a subsequent malignancy among patients with MH who have a negative evaluation, even among those with persistent (stable) MH. While these patients may be discharged from urologic follow-up, dissemination and implementation beyond urologists may be needed to prevent repeated referrals. Many patients with MH will have persistent findings of microscopic blood – likely due to benign causes that may or may not be recognized – and depending on local practice patterns, may be a risk for persistent re-referral for evaluation. Strategies to mitigate this may be needed in the future. Thus, additional prospective research is needed to determine when and how patients with persistent or recurrent MH should be re-evaluated and when it is potentially safe to stop repeat evaluations. Further studies are also needed to guide management and follow up of patients who have a presumed false-positive UBTM test, particularly if done inappropriately in low/negligible- or high-risk groups, and additional non-invasive means of evaluating for the presence of bladder cancer.

Overall, the revised Guideline represents an effort to improve the detection of clinically significant disease while reducing the indiscriminate allocation of healthcare resources and subjecting patients to tests with risk and attendant discomfort/anxiety. MH is a highly prevalent condition, impacting a large population whose evaluation is managed by a wide variety of practitioners. The impact of this Guideline on frequency, intensity, yield of evaluation will need to be studied to determine the impact of the updated recommendations on public health and to inform the next Guideline update.

ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
AUA	American Urological Association
BCAN	Bladder Cancer Advocacy Network
BLC	Blue light cystoscopy
BMI	Body mass index
BOD	Board of Directors
BPH	Benign prostatic hyperplasia
CIS	Carcinoma in situ
CT	Computed tomography
GH	Gross hematuria
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HCRS	Haematuria Cancer Risk Score
HPF	High-power field
HRI	Hematuria Risk Index
MH	Microhematuria
MR	Magnetic resonance
NBI	Narrow Band Imaging
NMIBC	Non-muscle invasive bladder cancer
NPV	Negative predictive value
NSF	Nephrogenic systemic fibrosis
PGC	Practice Guidelines Committee
PICO	Populations, interventions, comparators, and outcomes
PPV	Positive predictive value
RBC	Red blood cell
RCC	Renal cell carcinoma
RCT	Randomized controlled trial
ROC	Receiver Operating Characteristics
RPG	Retrograde pyelography
SQC	Science & Quality Council
SUFU	Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
UA	Urinalysis
UTI	Urinary tract infection
UTUC	Upper tract urothelial carcinoma
WLC	White light cystoscopystenosis

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DISCLAIMER

This document was written by the Microhematuria Panel of the American Urological Association Education and Research, Inc., which was created in 2020 and updated in 2025. The PGC of the AUA selected the Panel Chair. Panel members were selected by the Panel and PGC Chair.

Membership of the Panel included specialists in urology, gynecology, and primary care with specific expertise on this disorder. The mission of the panel was to develop recommendations that are analysis based or consensus-based, depending on panel processes and available data, for optimal clinical practices in the evaluation of microhematuria.

Funding of the panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the panel provides an ongoing conflict of interest disclosure to the AUA, and the Panel Chair, with the support of AUA Guidelines staff and the PGC, reviews all disclosures and addresses any potential conflicts per AUA's Principles, Policies and Procedures for Managing Conflicts of Interest.

While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses (“off label”) that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not intended to provide legal advice about use and misuse of these substances.

Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.

For this reason, the AUA does not regard technologies or management which are too new to be addressed by this guideline as necessarily experimental or investigational.

REFERENCE

1. Mariani, A. J., Mariani, M. C., Macchioni, C. et al: The significance of adult hematuria: 1,000 hematuria evaluations including a risk-benefit and cost-effectiveness analysis. J Urol 1989; **141:** 350
2. Davis, R., Jones, J. S., Barocas, D. A. et al: Diagnosis, evaluation and follow-up of asymptomatic microhematuria (amh) in adults: Aua guideline. J Urol 2012; **188:** 2473
3. Campbell Walsh Wein Urology. 12th Edition. Editors: Partin AW, P. C., Kavoussi LR, Dmochowski RR, Wein AJ: 2020;
4. Tan, W. S., Sarpong, R., Khetrapal, P. et al: Can renal and bladder ultrasound replace computerized tomography urogram in patients investigated for microscopic hematuria? Journal of Urology 2018; **200:** 973
5. Matulewicz, R. S., DeLancey, J. O., Pavey, E. et al: Dipstick urinalysis as a test for microhematuria and occult bladder cancer. Bladder Cancer 2017; **3:** 45
6. Gonzalez, A. N., Lipsky, M. J., Li, G. et al: The prevalence of bladder cancer during cystoscopy for asymptomatic microscopic hematuria. Urology 2019; **21:** 21
7. Aguilar-Davidov, B., Ramirez-Mucino, A., Culebro-Garcia, C. et al: Performance of computed tomographic urography for the detection of bladder tumors in patients with microscopic hematuria. Actas Urologicas Espanolas 2013; **37:** 408
8. Bradley, M. S., Willis-Gray, M. G., Amundsen, C. L. and Siddiqui, N. Y.: Microhematuria in postmenopausal women: Adherence to guidelines in a tertiary care setting. Journal of Urology 2016; **195:** 937
9. Elias, K., Svatek, R. S., Gupta, S. et al: High-risk patients with hematuria are not evaluated according to guideline recommendations. Cancer 2010; **116:** 2954
10. Kang, M., Lee, S., Jeong, S. J. et al: Characteristics and significant predictors of detecting underlying diseases in adults with asymptomatic microscopic hematuria: A large case series of a korean population. International Journal of Urology 2015; **22:** 389
11. Lai, W. S., Ellenburg, J., Lockhart, M. E. and Kolettis, P. N.: Assessing the costs of extraurinary findings of computed tomography urogram in the evaluation of asymptomatic microscopic hematuria. Urology 2016; **95:** 34
12. Loo, R. K., Lieberman, S. F., Slezak, J. M. et al: Stratifying risk of urinary tract malignant tumors in patients with asymptomatic microscopic hematuria. Mayo Clinic Proceedings 2013; **88:** 129
13. Matulewicz, R. S., Demzik, A. L., DeLancey, J. O. et al: Disparities in the diagnostic evaluation of microhematuriaand implications for the detection of urologic malignancy. Urologic Oncology 2019; **17:** 17
14. Samson, P., Waingankar, N., Shah, P. et al: Predictors of genitourinary malignancy in patients with asymptomatic microscopic hematuria. Urologic Oncology 2018; **36:** 10.e1
15. Sundelin, M., Jensen JB: Asymptomatic microscopic hematuria as a predictor of neoplasia in the urinary tract. Scandinavian Journal of Urology and Nephrology 2017; **51:** 373
16. Georgieva, M. V., Wheeler, S. B., Erim, D. et al: Comparison of the harms, advantages, and costs associated with alternative guidelines for the evaluation of hematuria. JAMA Internal Medicine 2019; **29:** 29
17. Linder, B. J., Bass, E. J., Mostafid, H. and Boorjian, S. A.: Guideline of guidelines: Asymptomatic microscopic haematuria. BJU Int 2018; **121:** 176
18. Halpern, J. A., Chughtai, B. and Ghomrawi, H.: Cost-effectiveness of common diagnostic approaches for evaluation of asymptomatic microscopic hematuria. JAMA Intern Med 2017; **177:** 800
19. Johnson, E. K., Daignault, S., Zhang, Y. and Lee, C. T.: Patterns of hematuria referral to urologists: Does a gender disparity exist? Urology 2008; **72:** 498
20. Ghandour, R., Freifeld, Y., Singla, N. and Lotan, Y.: Evaluation of hematuria in a large public health care system. Bladder Cancer 2019; **5:** 119
21. Bromage, S. J., Liew, M., Moore, K. et al: The evaluation of ct urography in the haematuria clinic. Journal of Clinical Urology 2013; **6:** 153
22. Eisenhardt, A., Heinemann, D., Rubben, H. and Hes, J.: Haematuria work-up in general care-a german observational study. International Journal of Clinical Practice 2017; **71**
23. Koo, K. C., Lee, K. S., Choi, A. R. et al: Diagnostic impact of dysmorphic red blood cells on evaluating microscopic hematuria: The urologist's perspective. Int Urol Nephrol 2016; **48:** 1021
24. Todenhofer, T., Hennenlotter, J., Tews, V. et al: Impact of different grades of microscopic hematuria on the performance of urine-based markers for the detection of urothelial carcinoma. Urologic Oncology 2013; **31:** 1148
25. Cohn, J. A., Vekhter, B., Lyttle, C. et al: Sex disparities in diagnosis of bladder cancer after initial presentation with hematuria: A nationwide claims-based investigation. Cancer 2014; **120:** 555

26. Ark, J. T., Alvarez, J. R., Koyama, T. et al: Variation in the diagnostic evaluation among persons with hematuria: Influence of gender, race and risk factors for bladder cancer. J Urol 2017; **198:** 1033
27. Howlader N, N. A., Krapcho M et al: Seer cancer statistics review, 1975-2016, national cancer institute. Bethesda, md, https://seer.Cancer.Gov/csr/1975_2016/, based on november 2018 seer data submission, posted to the seer web site. 2019;
28. Bassett, J. C., Alvarez, J., Koyama, T. et al: Gender, race, and variation in the evaluation of microscopic hematuria among medicare beneficiaries. J Gen Intern Med 2015; **30:** 440
29. Klaassen, Z., DiBianco, J. M., Jen, R. P. et al: Female, black, and unmarried patients are more likely to present with metastatic bladder urothelial carcinoma. Clin Genitourin Cancer 2016; **14:** e489
30. Hollenbeck, B. K., Dunn, R. L., Ye, Z. et al: Delays in diagnosis and bladder cancer mortality. Cancer 2010; **116:** 5235
31. Wennberg, J. E.: Unwarranted variations in healthcare delivery: Implications for academic medical centres. BMJ 2002; **325:** 961
32. Shea, B. J., Grimshaw, J. M., Wells, G. A. et al: Development of amstar: A measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 2007; **7:** 10
33. Higgins, J. P., Altman, D. G., Gotzsche, P. C. et al: The cochrane collaboration's tool for assessing risk of bias in randomised trials. Bmj 2011; **343:** d5928
34. Sterne, J. A., Hernan, M. A., Reeves, B. C. et al: Robins-i: A tool for assessing risk of bias in non-randomised studies of interventions. Bmj 2016; **355:** i4919
35. Guyatt, G., Oxman, A. D., Akl, E. A. et al: Grade guidelines: 1. Introduction-grade evidence profiles and summary of findings tables. J Clin Epidemiol 2011; **64:** 383
36. Balshem, H., Helfand, M., Schunemann, H. J. et al: Grade guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011; **64:** 401
37. The Nordic Cochrane Centre: Review manager (revman), Version 5.3 ed. Copenhagen: The Chochrane Collaboration 2014
38. Faraday, M., Hubbard, H., Kosiak, B. and Dmochowski, R.: Staying at the cutting edge: A review and analysis of evidence reporting and grading; the recommendations of the american urological association. BJU Int 2009; **104:** 294
39. BA, H. C. a. S.: The delphi technique: Making sense of concensus. Practical Assessment, Research & Evaluation 2007; **12**
40. Hertz, A. M., Perez, D. S., Anderson, M. I. and Brand, T. C.: Automated urinalysis for evaluation of microscopic hematuria: Current options and revising the gold standard. Urol Pract 2020; **7:** 199
41. Rosser, C. J., Nakamura, K., Pendleton, J. et al: Utility of serial urinalyses and urinary cytology in the evaluation of patients with microscopic haematuria. West Afr J Med 2010; **29:** 384
42. Matulewicz, R. S. and Raman, J. D.: Microhematuria: Aua/sufu guideline. Letter.J urol 2020; 204: 778. J Urol 2021; **205:** 1533
43. Dune, T. J., Kliethermes, S., Mueller, E. R. et al: Screening for microscopic hematuria in a urogynecologic population. Female Pelvic Med Reconstr Surg 2020; **26:** 382
44. Addis, T.: The number of formed elements in the urinary sediment of normal individuals. J Clin Invest 1926; **2:** 409
45. Kincaid-Smith, P.: Haematuria and exercise-related haematuria. Br Med J (Clin Res Ed) 1982; **285:** 1595
46. Vaughan, E. D., Jr. and Wyker, A. W., Jr.: Effect of osmolality on the evaluation of microscopic hematuria. J Urol 1971; **105:** 709
47. Litwin, M. S. and Graham, S. D., Jr.: False-positive hematuria. JAMA 1985; **254:** 1724
48. Rao, P. K., Gao, T., Pohl, M. and Jones, J. S.: Dipstick pseudohematuria: Unnecessary consultation and evaluation. J Urol 2010; **183:** 560
49. Bassett, J. C., Matulewicz, R. S., Kwan, L. et al: Prevalence and correlates of successful smoking cessation in bladder cancer survivors. Urology 2021; **153:** 236
50. Lee, P. N. and Hamling, J.: The relation between smokeless tobacco and cancer in northern europe and north america. A commentary on differences between the conclusions reached by two recent reviews. BMC Cancer 2009; **9:** 256
51. Inoue-Choi, M., Shiels, M. S., McNeel, T. S. et al: Contemporary associations of exclusive cigarette, cigar, pipe, and smokeless tobacco use with overall and cause-specific mortality in the united states. JNCI Cancer Spectr 2019; **3:** pkz036
52. Herriges MJ, P. R., Shapiro O, et al: E-cigarette use and the risk of bladder and lung cancer. Journal of Clinical Oncology 2022; **40**

53. Hsiao, Y. C., Matulewicz, R. S., Sherman, S. E. et al: Untargeted metabolomics to characterize the urinary chemical landscape of e-cigarette users. Chem Res Toxicol 2023; **36:** 630
54. Bjurlin, M. A., Matulewicz, R. S., Roberts, T. R. et al: Carcinogen biomarkers in the urine of electronic cigarette users and implications for the development of bladder cancer: A systematic review. Eur Urol Oncol 2021; **4:** 766
55. Ahmed, F. O., Hamdan, H. Z., Abdelgalil, H. B. and Sharfi, A. A.: A comparison between transabdominal ultrasonographic and cystourethroscopy findings in adult sudanese patients presenting with haematuria. International Urology & Nephrology 2015; **47:** 223
56. Bretlau, T., Hansen, R. H. and Thomsen, H. S.: Ct urography and hematuria: A retrospective analysis of 771 patients undergoing ct urography over a 1-year period. Acta Radiologica 2015; **56:** 890
57. Richards, K. A., Ruiz, V. L., Murphy, D. R. et al: Diagnostic evaluation of patients presenting with hematuria: An electronic health record-based study. Urologic Oncology 2018; **36:** 88.e19
58. Clague, J., Lin, J., Cassidy, A. et al: Family history and risk of renal cell carcinoma: Results from a case-control study and systematic meta-analysis. Cancer Epidemiol Biomarkers Prev 2009; **18:** 801
59. Cumberbatch, M. G. K., Jubber, I., Black, P. C. et al: Epidemiology of bladder cancer: A systematic review and contemporary update of risk factors in 2018. Eur Urol 2018; **74:** 784
60. Dobbs, R. W., Hugar, L. A., Revenig, L. M. et al: Incidence and clinical characteristics of lower urinary tract symptoms as a presenting symptom for patients with newly diagnosed bladder cancer. Int Braz J Urol 2014; **40:** 198
61. Koutros, S., Silverman, D. T., Baris, D. et al: Hair dye use and risk of bladder cancer in the new england bladder cancer study. Int J Cancer 2011; **129:** 2894
62. Maltseva, A., Serra, C. and Kogevinas, M.: Cancer risk among workers of a secondary aluminium smelter. Occup Med (Lond) 2016; **66:** 412
63. Culclasure, T. F., Bray, V. J. and Hasbargen, J. A.: The significance of hematuria in the anticoagulated patient. Arch Intern Med 1994; **154:** 649
64. Jeong, C. W., Lee, S., Byun, S. S. et al: No increase in risk of microscopic hematuria with aspirin use by asymptomatic healthy people. JAMA Intern Med 2013; **173:** 1145
65. Khadra, M. H., Pickard, R. S., Charlton, M. et al: A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. J Urol 2000; **163:** 524
66. Avidor, Y., Nadu, A. and Matzkin, H.: Clinical significance of gross hematuria and its evaluation in patients receiving anticoagulant and aspirin treatment. Urology 2000; **55:** 22
67. Wallis, C. J. D., Juvet, T., Lee, Y. et al: Association between use of antithrombotic medication and hematuria-related complications. JAMA 2017; **318:** 1260
68. Henning, A., Wehrberger, M., Madersbacher, S. et al: Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? BJU Int 2013; **112:** 68
69. Friedlander, D. F., Resnick, M. J., You, C. et al: Variation in the intensity of hematuria evaluation: A target for primary care quality improvement. Am J Med 2014; **127:** 633
70. Lowrance, W. T., Ordonez, J., Udaltsova, N. et al: Ckd and the risk of incident cancer. J Am Soc Nephrol 2014; **25:** 2327
71. Sanci, A., Oktar, A., Gokce, M. I. et al: Comparison of microscopic hematuria guidelines as applied in 1018 patients with microscopic hematuria. Urology 2021; **154:** 28
72. Woldu, S. L., Ng, C. K., Loo, R. K. et al: Evaluation of the new american urological association guidelines risk classification for hematuria. Journal of Urology 2021; **205:** 1387
73. Saxon, G. M., Patil, D. and Hammett, J.: Microhematuria in women: Prevalence of malignancy and risk score evaluation. Urology 2022; **160:** 34
74. Matulewicz, R. S., Rademaker, A. and Meeks, J. J.: A simplified nomogram to assess risk of bladder cancer in patients with a new diagnosis of microscopic hematuria. Urologic Oncology 2020; **38:** 240
75. Khadhouri, S., Gallagher, K. M., MacKenzie, K. R. et al: Developing a diagnostic multivariable prediction model for urinary tract cancer in patients referred with haematuria: Results from the identify collaborative study. European Urology Focus 2022; **8:** 1673
76. Woldu, S. L., Souter, L., Boorjian, S. A. et al: Urinary-based tumor markers enhance microhematuria risk stratification according to baseline bladder cancer prevalence. Urologic Oncology 2021; **39:** 787.e1
77. Tan, W. S., Sarpong, R., Khetrapal, P. et al: Does urinary cytology have a role in haematuria investigations? BJU International 2019; **123:** 74
78. Tan, W. S., Ahmad, A., Zhou, Y. et al: Hematuria cancer risk score with ultrasound informs cystoscopy use in patients with hematuria. European Urology Oncology 2024; **28:** 28

79. Trinh, T. W., Glazer, D. I., Sadow, C. A. et al: Bladder cancer diagnosis with ct urography: Test characteristics and reasons for false-positive and false-negative results. Abdominal Radiology 2018; **43:** 663
80. Fankhauser, C. D., Waisbrod, S., Fierz, C. et al: Diagnostic accuracy of ultrasonography, computed tomography, cystoscopy and cytology to detect urinary tract malignancies in patients with asymptomatic hematuria. World Journal of Urology 2021; **39:** 97
81. Bagheri, M. H., Ahlman, M. A., Lindenberg, L. et al: Advances in medical imaging for the diagnosis and management of common genitourinary cancers. Urol Oncol 2017; **35:** 473
82. Lin, W. C. and Chen, J. H.: Pitfalls and limitations of diffusion-weighted magnetic resonance imaging in the diagnosis of urinary bladder cancer. Transl Oncol 2015; **8:** 217
83. Ascenti, G., Mileto, A., Gaeta, M. et al: Single-phase dual-energy ct urography in the evaluation of haematuria. Clin Radiol 2013; **68:** e87
84. Chen, C. Y., Tsai, T. H., Jaw, T. S. et al: Diagnostic performance of split-bolus portal venous phase dual-energy ct urography in patients with hematuria. AJR Am J Roentgenol 2016; **206:** 1013
85. Janssen, K. M., Nieves-Robbins, N. M., Echelmeier, T. B. et al: Could nonenhanced computer tomography suffice as the imaging study of choice for the screening of asymptomatic microscopic hematuria? Urology 2018; **120:** 36
86. Yecies, T., Bandari, J., Fam, M. et al: Risk of radiation from computerized tomography urography in the evaluation of asymptomatic microscopic hematuria. Journal of Urology 2018; **200:** 967
87. Bromage, S. J., Liew, M. P., Moore, K. C. et al: The economic implications of unsuspected findings from ct urography performed for haematuria. Br J Radiol 2012; **85:** 1303
88. Song, J. H., Beland, M. D. and Mayo-Smith, W. W.: Incidental clinically important extraurinary findings at mdct urography for hematuria evaluation: Prevalence in 1209 consecutive examinations. AJR Am J Roentgenol 2012; **199:** 616
89. Clark, K. R. and Higgs, M. J.: Urinary infection following out-patient flexible cystoscopy. Br J Urol 1990; **66:** 503
90. Cusumano, J. A., Hermenau, M., Gaitanis, M. et al: Evaluation of post-flexible cystoscopy urinary tract infection rates. Am J Health Syst Pharm 2020; **77:** 1852
91. Gregg, J. R., Bhalla, R. G., Cook, J. P. et al: An evidence-based protocol for antibiotic use prior to cystoscopy decreases antibiotic use without impacting post-procedural symptomatic urinary tract infection rates. J Urol 2018; **199:** 1004
92. Herr, H. W.: The risk of urinary tract infection after flexible cystoscopy in patients with bladder tumor who did not receive prophylactic antibiotics. J Urol 2015; **193:** 548
93. Roth, V., Espino-Grosso, P., Henriksen, C. H. and Canales, B. K.: Office cystoscopy urinary tract infection rate and cost before and after implementing new handling and storage practices. Urol Pract 2021; **8:** 23
94. van der Aa, M. N., Steyerberg, E. W., Sen, E. F. et al: Patients' perceived burden of cystoscopic and urinary surveillance of bladder cancer: A randomized comparison. BJU Int 2008; **101:** 1106
95. Wilson, L., Ryan, J., Thelning, C. et al: Is antibiotic prophylaxis required for flexible cystoscopy? A truncated randomized double-blind controlled trial. J Endourol 2005; **19:** 1006
96. Jimenez Cruz, J. F., Sanz Chinesta, S., Otero, G. et al: [antimicrobial prophylaxis in urethrocystoscopy. Comparative study]. Actas Urol Esp 1993; **17:** 172
97. Lotan, Y., Daneshmand, S., Shore, N. et al: A multicenter prospective randomized controlled trial comparing cxbladder triage to cystoscopy in patients with microhematuria. The safe testing of risk for asymptomatic microhematuria trial. Journal of Urology 2024**:** 101097JU0000000000003991
98. de Jong, J. J., Pijpers, O. M., van Kessel, K. E. M. et al: A urine-based genomic assay improves risk stratification for patients with high-risk hematuria stratified according to the american urological association guidelines. European Urology Oncology 2023; **6:** 183
99. van Kessel, K. E. M., de Jong, J. J., Ziel-van der Made, A. C. J. et al: A urine based genomic assay to triage patients with hematuria for cystoscopy. Journal of Urology 2020; **204:** 50
100. Raman, J. D., Kavalieris, L., Konety, B. et al: The diagnostic performance of cxbladder resolve, alone and in combination with other cxbladder tests, in the identification and priority evaluation of patients at risk for urothelial carcinoma. Journal of Urology 2021; **206:** 1380
101. Davidson, P. J., McGeoch, G. and Shand, B.: Inclusion of a molecular marker of bladder cancer in a clinical pathway for investigation of haematuria may reduce the need for cystoscopy. New Zealand Medical Journal 2019; **132:** 55
102. Jeong, I. G., Yun, S. C., Ha, H. K. et al: Urinary DNA methylation test for bladder cancer diagnosis. JAMA Oncology 2025; **11:** 293
103. Oh, T. J., Lee, J. Y., Seo, Y. et al: Evaluation of sensitive urine DNA-based penk methylation test for detecting bladder cancer in patients with hematuria. Journal of Molecular Diagnostics 2023; **25:** 646

104. Sagnak, L., Ersoy, H., Gucuk, O. et al: Diagnostic value of a urine-based tumor marker for screening lower urinary tract in low-risk patients with asymptomatic microscopic hematuria. Urologia Internationalis 2011; **87:** 35
105. Bangma, C. H., Loeb, S., Busstra, M. et al: Outcomes of a bladder cancer screening program using home hematuria testing and molecular markers. European Urology 2013; **64:** 41
106. Turkeri, L., Mangir, N., Gunlusoy, B. et al: Identification of patients with microscopic hematuria who are at greater risk for the presence of bladder tumors using a dedicated questionnaire and point of care urine test--a study by the members of association of urooncology, turkey. Asian Pacific Journal of Cancer Prevention: Apjcp 2014; **15:** 6283
107. Pan, T., Lehman, E. and Raman, J. D.: Performance characteristics of urinary cytology in patients presenting with gross and microscopic hematuria. American Journal of Clinical & Experimental Urology 2021; **9:** 384
108. Feifer, A. H., Steinberg, J., Tanguay, S. et al: Utility of urine cytology in the workup of asymptomatic microscopic hematuria in low-risk patients. Urology 2010; **75:** 1278
109. van Valenberg, F. J. P., Hiar, A. M., Wallace, E. et al: Validation of an mrna-based urine test for the detection of bladder cancer in patients with haematuria. European Urology Oncology 2021; **4:** 93
110. Schmitz-Drager, C., Goebell, P. J., Paxinos, E. et al: Potential of an mrna-based urine assay (xpert bladder cancer detection¹) in hematuria patients - results from a cohort study. Bladder Cancer 2024; **10:** 25
111. Mishriki, S. F., Aboumarzouk, O., Vint, R. et al: Routine urine cytology has no role in hematuria investigations. Journal of Urology 2013; **189:** 1255
112. Pak, J. S., Wang, E. Y., Lee, K. et al: Diagnostic yield of repeat evaluation for asymptomatic microscopic hematuria after negative initial workup. Urologic Oncology 2021; **39:** 300.e1
113. Dallmer, J. R., Robles, J., Wile, G. E. et al: The harms of hematuria evaluation: Modeling the risk-benefit of using split bolus computerized tomography urography to reduce radiation exposure in a theoretical cohort. J Urol 2019; **202:** 899
114. Martingano, P., Cavallaro, M. F., Bertolotto, M. et al: Magnetic resonance urography vs computed tomography urography in the evaluation of patients with haematuria. Radiol Med 2013; **118:** 1184
115. Disorders, N. O. f. R.: Nephrogenic systemic fibrosis. Https://rarediseases.Org/rare-diseases/nephrogenic-systemic-fibrosis/.
116. Communication, F. D. S.: New warnings for using gadolinium-based contrast agents in patients with kidney dysfunction: Https://www.Fda.Gov/drugs/drug-safety-and-availability/fda-drug-safety- communication-new-warnings-using-gadolinium-based-contrast-agents-patients-kidney.
117. ACR Manual on Contrast Media, v., published June 2018: Available at https://www.Acr.Org/-/media/acr/files/clinical-resources/contrast_media.Pdf.
118. Babjuk, M., Bohle, A., Burger, M. et al: Eau guidelines on non-muscle-invasive urothelial carcinoma of the bladder: Update 2016. Eur Urol 2017; **71:** 447
119. Fradet, Y., Grossman, H. B., Gomella, L. et al: A comparison of hexaminolevulinate fluorescence cystoscopy and white light cystoscopy for the detection of carcinoma in situ in patients with bladder cancer: A phase iii, multicenter study. J Urol 2007; **178:** 68
120. Rink, M., Babjuk, M., Catto, J. W. et al: Hexyl aminolevulinate-guided fluorescence cystoscopy in the diagnosis and follow-up of patients with non-muscle-invasive bladder cancer: A critical review of the current literature. Eur Urol 2013; **64:** 624
121. Schneeweiss, S., Kriegmair, M. and Stepp, H.: Is everything all right if nothing seems wrong? A simple method of assessing the diagnostic value of endoscopic procedures when a gold standard is absent. J Urol 1999; **161:** 1116
122. Lotan, Y., Bivalacqua, T. J., Downs, T. et al: Blue light flexible cystoscopy with hexaminolevulinate in non-muscle-invasive bladder cancer: Review of the clinical evidence and consensus statement on optimal use in the USA - update 2018. Nat Rev Urol 2019; **16:** 377
123. Schubert, T., Rausch, S., Fahmy, O. et al: Optical improvements in the diagnosis of bladder cancer: Implications for clinical practice. Ther Adv Urol 2017; **9:** 251
124. Stenzl, A., Burger, M., Fradet, Y. et al: Hexaminolevulinate guided fluorescence cystoscopy reduces recurrence in patients with nonmuscle invasive bladder cancer. J Urol 2010; **184:** 1907
125. Cauberg, E. C., Nio, C. Y., de la Rosette, J. M. et al: Computed tomography-urography for upper urinary tract imaging: Is it required for all patients who present with hematuria? Journal of Endourology 2011; **25:** 1733
126. Haas, N. B. and Nathanson, K. L.: Hereditary kidney cancer syndromes. Adv Chronic Kidney Dis 2014; **21:** 81
127. Pavlovich, C. P., Walther, M. M., Eyler, R. A. et al: Renal tumors in the birt-hogg-dube syndrome. Am J Surg Pathol 2002; **26:** 1542

128. Varshney, N., Kebede, A. A., Owusu-Dapaah, H. et al: A review of von hippel-lindau syndrome. J Kidney Cancer VHL 2017; **4:** 20
129. Yang, P., Cornejo, K. M., Sadow, P. M. et al: Renal cell carcinoma in tuberous sclerosis complex. Am J Surg Pathol 2014; **38:** 895
130. Coleman, J. A., Clark, P. E., Bixler, B. R. et al: Diagnosis and management of non-metastatic upper tract urothelial carcinoma: Aua/suo guideline. J Urol 2023; **209:** 1071
131. Sathianathen, N. J., Butaney, M., Weight, C. J. et al: Urinary biomarkers in the evaluation of primary hematuria: A systematic review and meta-analysis. Bladder Cancer 2018; **4:** 353
132. Daneshmand, S., Patel, S., Lotan, Y. et al: Efficacy and safety of blue light flexible cystoscopy with hexaminolevulinate in the surveillance of bladder cancer: A phase iii, comparative, multicenter study. J Urol 2018; **199:** 1158
133. Lisanti, C. J., Graeber, A., Syed, H. et al: What is the relative risk of urologic malignancy in microscopic hematuria patients after negative evaluation? A long-term population-based retrospective analysis of 8465 patients. Abdominal Radiology 2023; **48:** 1011
134. Madeb, R., Golijanin, D., Knopf, J. et al: Long-term outcome of patients with a negative work-up for asymptomatic microhematuria. Urology 2010; **75:** 20
135. Pichler, R., Heidegger, I., Leonhartsberger, N. et al: The need for repeated urological evaluation in low-risk patients with microscopic hematuria after negative diagnostic work-up. Anticancer Research 2013; **33:** 5525
136. Cha, E. K., Tirsar, L. A., Schwentner, C. et al: Accurate risk assessment of patients with asymptomatic hematuria for the presence of bladder cancer. World J Urol 2012; **30:** 847
137. Commander, C. W., Johnson, D. C., Raynor, M. C. et al: Detection of upper tract urothelial malignancies by computed tomography urography in patients referred for hematuria at a large tertiary referral center. Urology 2017; **102:** 31
138. Elmussareh, M., Young, M., Ordell Sundelin, M. et al: Outcomes of haematuria referrals: Two-year data from a single large university hospital in denmark. Scandinavian Journal of Urology 2017; **51:** 282
139. Lokken, R. P., Sadow, C. A. and Silverman, S. G.: Diagnostic yield of ct urography in the evaluation of young adults with hematuria. AJR American Journal of Roentgenology 2012; **198:** 609
140. Norgaard, M., Veres, K., Ording, A. G. et al: Evaluation of hospital-based hematuria diagnosis and subsequent cancer risk among adults in denmark. JAMA Network Open 2018; **1:** e184909
141. Pesch, B., Nasterlack, M., Eberle, F. et al: The role of haematuria in bladder cancer screening among men with former occupational exposure to aromatic amines. BJU International 2011; **108:** 546
142. Ramirez, D., Gupta, A., Canter, D. et al: Microscopic haematuria at time of diagnosis is associated with lower disease stage in patients with newly diagnosed bladder cancer. BJU International 2016; **117:** 783
143. Sapre, N., Hayes, E., Bugeja, P. et al: Streamlining the assessment of haematuria: 3-year outcomes of a dedicated haematuria clinic. ANZ Journal of Surgery 2015; **85:** 334
144. Song, J. H., Beland, M. D. and Mayo-Smith, W. W.: Hematuria evaluation with mdct urography: Is a contrast-enhanced phase needed when calculi are detected in the unenhanced phase? AJR American Journal of Roentgenology 2011; **197:** W84
145. Buteau, A., Seideman, C. A., Svatek, R. S. et al: What is evaluation of hematuria by primary care physicians? Use of electronic medical records to assess practice patterns with intermediate follow-up. Urologic Oncology 2014; **32:** 128
146. Price, S. J., Shephard, E. A., Stapley, S. A. et al: Non-visible versus visible haematuria and bladder cancer risk: A study of electronic records in primary care. British Journal of General Practice 2014; **64:** e584
147. Vasdev, N. and Thorpe, A. C.: Should the presence of a culture positive urinary tract infection exclude patients from rapid evaluation hematuria protocols? Urologic Oncology 2013; **31:** 909
148. Jung, H., Gleason, J. M., Loo, R. K. et al: Association of hematuria on microscopic urinalysis and risk of urinary tract cancer. Journal of Urology 2011; **185:** 1698
149. Yin, P., Kiss, A. and Leis, J. A.: Urinalysis orders among patients admitted to the general medicine service. JAMA Intern Med 2015; **175:** 1711