Guidelines

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Guideline of guidelines: asymptomatic microscopic haematuria

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The aim of the present study was to review major organizational guidelines on the evaluation and management of asymptomatic microscopic haematuria (AMH). We reviewed the haematuria guidelines from: the American Urological Association; the consensus statement by the Canadian Urological Association, Canadian Urologic Oncology Group and Bladder Cancer Canada; the American College of Physicians; the Joint Consensus Statement of the Renal Association and British Association of Urological Surgeons; and the National Institute for Health and Care Excellence. All guidelines reviewed recommend evaluation for AMH in the absence of potential benign aetiologies, with the evaluation including cystoscopy and upper urinary tract imaging. Existing guidelines vary in their definition of AMH (role of urine dipstick vs urine microscopy), the age threshold for recommending evaluation, and the optimal imaging method (computed tomography vs ultrasonography). Of the reviewed guidelines, none recommended the use of urine cytology or urine markers during the initial AMH evaluation. Patients should have ongoing follow-up after a negative initial AMH evaluation. Significant variation exists among current guidelines for AMH with respect to who should be evaluated and in what manner. Given the patient and health system implications of balancing appropriately focused and effective diagnostic evaluation, AMH represents a valuable future research opportunity.

Keywords

haematuria, guidelines, microscopic haematuria, review, international

Introduction

Haematuria is among the most commonly encountered diagnoses in urology [1]. The importance of the finding of haematuria is secondary to the potential underlying risk of clinically significant pathology, including malignancy, urolithiasis and medical renal disease [2,3]. A number of national organizations and specialty societies have released guidelines for the diagnosis and evaluation of haematuria [4–16]. Notably, while visible haematuria is recognized as a symptom that should prompt urological referral for evaluation [4–16], the recommended investigation of microscopic haematuria, and in particular asymptomatic microscopic haematuria (AMH) is inconsistent among the available guidelines. Indeed, in Sweden, testing for microscopic haematuria was abandoned in 1999 [13].

The differences between guidelines are attributable in large part to limited availability of high-quality evidence on the subject, and the difficulty of balancing the risks and benefits of a diagnostic evaluation. Clearly, in addition to managing healthcare costs, there exists a balance for patients and providers in the setting of AMH between proceeding with a set of relatively low-risk, but uncomfortable and inconvenient tests vs the (albeit relatively small) chance that a clinically relevant underlying pathology would be missed if the tests were not pursued. These consequences entail risks of disease progression for the patient, as well as issues of potential litigation, and guilt for the provider.

As such, the available guidelines vary regarding salient details such as the definition of AMH, the optimum method for radiological evaluation, and the role of urine cytology. We review similarities and differences amongst existing guidelines to provide a clinically useful reference framework for practitioners.

Methods

We performed a MEDLINE/Pubmed search, from 2006 to the present, and manually searched the websites of urological societies and journals to identify available guidelines for AMH evaluation. Guidelines have been published by the AUA [4], the American College of Physicians (ACP) [5], the Canadian Urological Association (CUA) [6], a consensus statement from the CUA, Canadian Urologic Oncology

 | doi:10.1111/bju.14016
Published by John Wiley & Sons Ltd. www.bjui.org

Group, and Bladder Cancer Canada [7], the BAUS [8], the National Institute for Health and Care Excellence (NICE) [9], the Japanese [10] and Dutch Associations of Urology [11], the Scottish Intercollegiate Guidelines Network [12], and a study in Sweden [13]. Many of the differences between the available AMH guidelines probably arise because of a lack of high-level evidence on the subject. In an effort to account for this, guidelines typically provide an assessment of the strength of the underlying evidence, a rationale and strength for the recommendations made, and a discussion of other possible conclusions from the available evidence [17].

AUA Guidelines

The 2012 AUA guidelines [4] were created after a systematic evaluation of the MEDLINE database for peer-reviewed publications from 1980 to 2011 relevant to the definition, diagnosis and evaluation and follow-up of AMH. Notably, these guidelines are focused on AMH, without direct reference to the evaluation or management of visible haematuria. Evidence strength was graded as: A (high), B (moderate) or C (low). Evidence-based statements, classified as 'Standard', 'Recommendation' or 'Optional', were developed, and when insufficient evidence existed, information was provided as Clinical Principles and Expert Opinion. The AUA guidelines are available at: https://www.auanet.org/common/pdf/education/clinical-guidance/Asymptomatic-Microhematuria.pdf

Canadian Urological Association Guidelines

The CUA guidelines [6,7] include an English-language literature review for publication years 1998 to 2008 using MEDLINE. Using this, the previous 1998 CUA guidelines were revised. Because of lack of evidence, a consensus opinion was developed from an informal survey of Canadian urologists and a final algorithm designed. Recommendations are classified according to their level of evidence (I–IV) and are given a grade of recommendation (A–D) according to the modified Oxford Centre for Evidence-Based Medicine Levels of Medicine [18]. These guidelines are available at: https://www.cua.org/themes/web/assets/files/guidelines/en/amh_2008_e.pdf

In 2016, an additional consensus document for the improvement of bladder cancer quality of care in Canada was jointly released by the CUA, the Canadian Urologic Oncology Group, and Bladder Cancer Canada [7]. Given that there was overlap with the CUA microscopic haematuria guideline [6], with both documents providing recommendations, we used the statements from the updated consensus document [7]. When content was non-overlapping, we used recommendations from the CUA guideline on haematuria [6]. The consensus document is available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4771569/.

High-Value Care Advice from the American College of Physicians

The ACP published a non-formal literature review of published clinical guidelines on the topic of haematuria [5]. The evidence was synthesized and the article generated was reviewed and approved by the ACP's High Value Care Task Force, whose members are physicians trained in internal medicine and its subspecialties, and which includes experts in evidence synthesis. These recommendations are available at: http://annals.org/aim/article/2484287/hematuria-marker-occult-urinary-tract-cancer-advice-high-value-care

European Association of Urology Guidelines

The European Association of Urology (EAU) has not published specific guidelines regarding the evaluation of haematuria. Instead, guidance is provided on a malignancy-by-malignancy basis, with haematuria as a presenting symptom being comprehensively covered in each section as appropriate [14,15]. The recommendations for each malignancy were provided by appointed expert groups and composed after systematic reviews of the literature, using databases such as MEDLINE to identify level 1 scientific papers. The evidence underlining practice recommendations is extensively explored and reviewed. Following this, each recommendation is graded from A to C. 'A' is ascribed to recommendations based on high-quality clinical studies including at least one randomized clinical trial, 'B' to those where good-quality non-randomized trials exist, and 'C' to those where quality studies are lacking. Before publication, the reviews and recommendations were subject to double-blind peer review. The full guidelines are freely available at: http://uroweb.org/wp-content/uploads/EAU-Extended-Guidelines-2015-Edn.pdf.

National Institute of Health and Care Excellence Guidelines

While NICE has not published specific guidance for AMH, it does refer to haematuria in its 'Suspected cancer: recognition and referral', published in 2015 [9]. As part of an ongoing process, this guidance was reviewed and revised by the National Collaborating Centre for Cancer (NCC-C) on request by NICE. This involved identifying a set of clinical questions as part of a PICO (Population; Intervention; Comparison; Outcome) framework, namely the population under study, the index test, sign or symptom, the comparison or reference standard and the outcomes. An initial search of published guidelines, systematic reviews, health economics evaluations and ongoing research was conducted using the following databases or websites: NHS Evidence; Cochrane Databases of Systematic Reviews; Health Technology Assessment Database; NHS Economic Evaluations Database;

Health Economic Evaluations Database; MEDLINE; and Embase. After this initial search, a more comprehensive and question-specific systematic review of existing literature was conducted using the Cochrane Library, MEDLINE, Embase and Web of Science. A positive predictive value (PPV) of 3% was chosen as the risk threshold for cancer by which any recommendation was underpinned. The NICE guidance document is available at: https://www.nice.org.uk/guidance/ng12/chapter/1-Recommendations-organised-by-site-of-cancer.

BAUS Guidelines

The BAUS guidelines for the investigation of haematuria were published in 2008. Since NICE published their 2015 guidance [9], these have been withdrawn; however, the NICE guidance was reviewed for findings relevant to urological practice by two expert urologists on behalf of the BAUS Section of Oncology [16]. This summary can be found at: https://www.baus.org.uk/_userfiles/pages/files/Publications/BAUS%20Cancer%20Guidelines%20Summary.pdf.

Joint Consensus Statement of the Renal Association and the BAUS

The joint consensus statement of the Renal Association (RA) and BAUS was released in 2008 [8] after the publication of a major review in 2006 by the National Institute for Health Research Health Technology Assessment Programme. This highlighted a lack of high-quality studies contributing to an evidence base for this topic, and identified a number of unanswered clinical questions. The RA and BAUS therefore produced guidelines to inform clinicians and commissioners in regard to the investigation of haematuria. The group was formed of a panel of urologists and nephrologists with guidance constructed from their informed opinions. The document is available at: http://www.renal.org/docs/default-source/what-we-do/RA-BAUS_Haematuria_Consensus_Guidelines.pdf?sfvrsn=0

Results

In the following section, we review the guidelines that have been most recently updated [4–9,14–16]. A more complete comparison, including all guidelines identified, is provided in Table 1 [4,5,7,8,10–13,16]. We evaluate recommendations with regard to the diagnosis of AMH including a review of specific scenarios that may warrant inclusion or exclusion from AMH evaluation, the recommended evaluation for those with AMH, and the follow-up of patients after a negative evaluation.

Defining Who Needs Evaluation

Method of diagnosis

The method of diagnosis for AMH varies among existing guidelines, particularly with regard to the role of dipstick urine analysis. There is consensus among the North American guidelines that urine dipstick alone is inadequate to establish a diagnosis of microscopic haematuria [4–7]. Indeed, the guidelines assert that, if a dipstick is positive for haematuria, results should be confirmed by performing a urine analysis with microscopic evaluation of the urinary sediment of a freshly voided, clean-catch, midstream urine sample [4–7]. This is secondary to the rate of false-positives on urine dipstick given the attendant cost, patient anxiety and potential morbidity of an ensuing evaluation [19–21]. In the event of a positive urine dipstick and negative urine analysis with microscopy, the AUA recommends that urine analysis with microscopy be repeated three times, with full evaluation if any are positive [4].

Guidelines from Europe comment little on urine dipstick testing and urine microscopy [8,9,14–16]. The EAU guidelines simply state that, for bladder, renal and upper tract urothelial carcinoma, haematuria (visible or otherwise) is the most common symptom at presentation [14,15]. The NICE guidelines do not state whether microscopic haematuria should be diagnosed by urine dipstick or urine microscopy and go on to state that many of the studies investigating the PPV of haematuria do not differentiate between visible and non-visible presentations [9]. BAUS recommendations simply summarize those developed by NICE [16], recommending urgent referral as a suspected cancer specifically in patients aged >60 years with non-visible haematuria and either dysuria or a raised white cell count, but do not make any recommendations specifically regarding AMH, as this did not meet the 3% PPV threshold to warrant urgent referral as a suspected cancer. The joint RA/BAUS statement, however, does recommend urological referral of patients with AMH (present in two out of three dipsticks) if the patient is aged ≥40 years [8].

Degree of haematuria on urine microscopy

Both the AUA and ACP define AMH as the presence of ≥3 red blood cells (RBCs) per high-power field in a single properly collected specimen [4,5]. The reliance on a single positive sample is secondary to the potential intermittency of haematuria, even when an underlying pathology is present [22,23]. Interestingly, by comparison, the Canadian Consensus Statement defined AMH as ≥3 RBCs per high-power field in two separate urine samples [7]. None of the European guidelines comment on the degree of haematuria on urine microscopy.

Age threshold for diagnostic evaluation

While all the reviewed guidelines acknowledge that age is a risk factor for underlying cancer diagnosis, the age threshold for recommending evaluation among patients diagnosed with AMH varies. That is, the BAUS/RA statement recommends

Table 1 Summary of available haematuria guideline statements.

	Definition of non-visible haematuria	Age threshold, years	Time to evaluation	Nephrology referral	Cystoscopy	Imaging	Cytology	Follow-up
AUA, Davis et al. [4]	≥3 RBCs/ hpf on one sample	≥35	Not stated	Abnormal eGFR, creatinine, BUN, dysmorphic RBCs, cellular casts, proteinuria	All those aged ≥35 years; those aged <35 years at provider discretion. Recommended for all with risk factors (e.g. irritative LUTS, tobacco use, chemical exposures)	CT urogram recommended for both VH and AMH	Not recommended for initial evaluation	Annual urine analysis for at least 2 years
Canadian Consensus Document, Kassouf et al. [7]	≥3 RBCs/hpf on two samples	≥35	AMH:12 weeks VH: 4 weeks	Abnormal eGFR, proteinuria, isolated haematuria with hypertension in those aged <40 years, VH with intercurrent infection	All those aged ≥35 years	AMH: recommended, method at provider discretion. VH: CT urogram preferred	AMH: not recommendedVH: recommended	AMH: annual urine analysis for at least 2 years VH: annual urine analysis for 3 yearsCytology: yearly for 3 years in patients with risk factors for urothelial ca
ACP, Nielsen et al. [5]	≥3 RBCs/hpf	Not stated	Not stated	Not stated	Not stated	Not stated	Not recommended for initial evaluation	Not stated
NICE, Jeffries et al. [16]	Not stated	AMH: 60 (must also have dysuria or elevated WBC count) VH: >45	2 wks	Not stated	Not stated	Not stated	Not stated	Not stated
RA/BAUS, Anderson et al. [8]	≥ 1 + dipstick on two/three samples	≥40	Not stated	Declining eGFR, proteinuria, isolated haematuria with hypertension in those aged <40 years, VH with intercurrent infection	All those aged ≥40 years	All those aged ≥40 years (method not specific)	Not stated	Monitoring for LUTS, VH, proteinuria, declining eGFR, hypertension
Japanese Urological Association, Horie et al. [10]	≥5 RBCs/hpf	≥40	Not stated	Proteinuria	All those aged ≥40 years	Ultrasonography	Patients without risk factors	Retesting if VH, LUTS, or persistent haematuria. Urine analysis is part of annual health examinations

Table 1 (continued)

	Definition of non-visible haematuria	Age threshold, years	Time to evaluation	Nephrology referral	Cystoscopy	Imaging	Cytology	Follow-up
Dutch Association of Urology, van der Molen et al. [11]	>3 RBCs/hpf from 2 of 3 specimens	>50	Not stated	Hypertension, MDRD-GFR, proteinuria, albuminuria, dysmorphic RBCs	AMH: those aged >50 years; those aged <50 years at provider discretionVH: All	AMH: ultrasonograpy; those aged >50 years with postitive ultrasonography or cystoscopy findings undergo CT urogram; those aged <50 years at provider's discretionVH: aged >50 years, CT urogram; aged <50 years, ultrasonography	Those aged >50 years with negative evaluation on imaging and cystoscopy; or aged <50 years with VH and negative imaging in setting of risk factors	Those aged >40 years, with tobacco use, chemical exposure. Urine analysis, cytology, blood pressure at 6, 12, 24, 36 months
Scottish guideline on Chronic Kidney Disease, Scottish Intercollegiate Guidelines Network (SIGN) [12]	'A single positive dipstick is not sufficient to indicate pathology' no further definition provided	More urgent in those aged >50 years	Not stated	Proteinuria, elevated creatinine	Not stated	Not stated	Not stated	Not stated
Sweden, Malmstrom et al. [13]	Not stated	Not stated	Not stated	Not stated	Not stated. Does not recommend for assessment of AMH	Not stated. Does not recommend for assessment of AMH	Not stated. Does not recommend for assessment of AMH	Not stated

ACP, American College of Physicians; AMH, asymptomatic microscopic haematuria, BUN, blood urea nitrogen; eGFR, estimated GFR; hpf, high power field; MDRD, Modification of Diet in Renal Disease; NICE, National Institute for Health and Care Excellence; RA, Renal Association; RBC, red blood cell; VH, visible haematuria; WBC, white blood cell.

that patients aged >40 years undergo evaluation for AMH [8], while the AUA Guidelines and the updated Canadian Consensus Statement recommend cystoscopic evaluation for all patients aged ≥35 years [4,7]. Moreover, for those aged <35 years, while imaging is still recommended, the AUA states that cystoscopy should be at the treating physician's discretion [4], but should be performed in patients with risk factors for urological malignancies regardless of age [4,7].

The latest NICE guidelines increased the recommended age limit for a urgent evaluation of AMH to 60 years from 50 years, and specified that either dysuria or increased white blood cell count also be present [9]. Furthermore, because of the low PPV of haematuria for either bladder or renal cancer for men aged <45 years (PPV 0.99%, 13 cancers in 1311 patients with haematuria) and women aged <45 years (PPV 0.22%, three cancers in 1362 patients with haematuria) [24], NICE only recommend urgent (2-week) referral for visible haematuria in people aged >45 years.

Exclusion criteria

There is consensus among the North American guidelines that benign aetiologies for AMH should be screened for and excluded prior to proceeding with, or referring for, a complete haematuria evaluation [4–7]. While the specific list of benign conditions varies between guidelines, the intent is similar. Several of the guideline statements highlight the need to repeat a urine analysis after the specific benign cause is excluded before ceasing further evaluation [4–6]. Also critical for clinicians to be aware of are statements from the AUA, ACP guidelines, and the Canadian Consensus Statement on bladder cancer care, noting that the use of anticoagulation in a patient diagnosed with AMH does not preclude the need for an AMH evaluation [4,5,7], as the rate of pertinent findings in these patients is still significant [25,26].

Time to completion of haematuria evaluation

The recent Canadian consensus document on bladder cancer quality of care advises that for patients with AMH, urological evaluation, including cystoscopy, be completed within 12 weeks [7]. Those with visible haematuria should undergo evaluation within 4 weeks [7]. The NICE recommendations state that if a referral meets their criteria, a urologist should see the patient within 14 days as a suspected cancer and if cancer is found treatment should be within 62 days [9].

Evaluation of Asymptomatic Microscopic Haematuria

History and physical examination

A careful history and physical examination, including measurement of blood pressure, is recommended by all of the reviewed guidelines as part of the evaluation for AMH [4–9,14–16]. This is necessary to identify potential benign aetiologies of AMH which, if confirmed, may obviate the need for progressing with further evaluation if AMH resolves on repeat urine analysis [4–6].

Laboratory evaluation

Laboratory evaluation of AMH, including serum creatinine (with eGFR) in addition to urine analysis, is recommended by the AUA guidelines, the Canadian Consensus Statement, and the joint statement of BAUS/RA [4,7,8], while the AUA and Canadian Consensus Statement also recommend testing blood urea nitrogen [4,7] and the BAUS/RA statement recommends measuring of proteinuria on a random urine sample with protein:creatinine ratio or albumin:creatinine ratio [8]. Obtaining baseline renal function testing allows decision-making regarding the most appropriate imaging technique (e.g. use of contrast) and may be used to identify patients for nephrology evaluation. For example, proteinuria, cellular casts and renal insufficiency warrant nephrological evaluation [4,7,27]. Additionally, the Canadian Consensus Statement recommends that those aged <40 years with isolated haematuria (no proteinuria) and hypertension, as well as those with visible haematuria and concurrent infection, be referred to nephrology [7]. The need for nephrological evaluation, however, does not preclude the need for completion of urological evaluation [4,7].

Diagnostic cystoscopy

There is consensus among the guidelines that cystoscopy should be performed in the evaluation of AMH, although age thresholds vary [4–9,14–16]; however, the role of fluorescence/blue-light cystoscopy is less well defined. The AUA guidelines specifically assert that blue-light cystoscopy should not be used in the initial evaluation of patients with AMH [4]. Meanwhile, the CUA guidelines advocate cystoscopy without discussion of white vs blue light, and the Canadian Consensus Statement notes that the evidence is inconclusive as to which method is preferred [6,7]. The EAU guidelines make no comment on the use of these diagnostic adjuncts, leaving discussion of utility to the time of bladder tumour resection, where usage has demonstrated improved sensitivity over white light alone [15].

Upper tract imaging

The need for radiological evaluation of the upper urinary tract in patients with AMH is supported by the EAU, AUA and Canadian Consensus Statement guidelines [4,6,7,14,15]. Nevertheless, the preferred imaging method varies. The AUA guidelines, and American College of Radiology Appropriateness Criteria, choose multiphase CT urogram as

the preferred study for the initial AMH evaluation because it has the highest sensitivity and specificity for identifying upper tract pathology [4,28]. Notably, the AUA is the only national urological organization recommending CT urography as the first-line imaging method for patients with AMH [4]. Likewise, the EAU guidelines recommend CT urogram in non-muscle-invasive bladder cancer for evaluation of papillary tumours in the urinary tract [15].

By comparison, in the CUA microscopic haematuria guidelines, renal ultrasonography is the recommended first-line imaging method for patients with AMH, with CT urography used in cases where additional tests are needed for abnormal or inconclusive findings [6]. This is due to concerns regarding availability and cost, along with the i.v. contrast and radiation exposure associated with use of CT urogram [6,29]. The more recent Canadian consensus document recommends CT urography for patients with visible haematuria or symptomatic microscopic haematuria, and states that the imaging method in patients with AMH may be decided on a case-by-case basis [7].

For patients with contraindications for CT urography, the AUA recommends including MRI with urography in the AMH evaluation [4]. If patients are ineligible for both MR urography and CT urography, the AUA recommends evaluating AMH via non-contrast CT imaging or renal ultrasonography with retrograde pyelography [4].

Urine cytology and molecular marker tests

The use of urine cytology or urine markers (e.g. NMP22, BTA-stat, UroVysion FISH) in the initial evaluation of patients with AMH is not recommended by any of the reviewed guideline statements [4–9,14–16] as they lack demonstrable efficacy [30], and may lead to emotional stress and unnecessary biopsies in the case of false-positive results [4]. The AUA guidelines do note that urine cytology may be useful in cases of persistent AMH after negative evaluation or those with risk factors for carcinoma *in situ* [4], while the Canadian Consensus Statement recommends cytology only for those with visible or symptomatic microscopic haematuria [6]. Notably, the EAU guidelines acknowledge the high sensitivity of cytology for the investigation of urothelial malignancy in high-grade tumours and carcinoma *in situ*, recommending it as an adjunct to, but not in place of, cystoscopy [15].

Follow-up after Negative Evaluation

Because of the low risk/burden of obtaining a urine analysis and the potential for a developing, as-yet not identified urological pathology, the AUA, Canadian consensus, ACP and joint BAUS/RA statement recommend ongoing follow-up after a negative initial AMH evaluation [4–8]. The AUA recommends annual subsequent urine analyses, stopping if negative for 2 consecutive years [4,31,32]; however, if AMH persists, the guidelines suggest yearly urine analysis should continue and repeat evaluation should be considered within 3–5 years [4].

The updated Canadian Consensus Statement notes that, after a negative evaluation, patients should be monitored by their primary care physician for LUTS, visible haematuria, significant or increasing proteinuria, declining renal function, or hypertension [7]. Furthermore, the statement recommends that a urine analysis be obtained for 3 years, and, if a patient has two consecutive negative tests, no further urine analyses are needed [7]. Notably, cytology is recommended yearly for 3 years in patients who have risk factors for bladder cancer. Additionally, the Canadian Consensus Statement recommends that, for persistent AMH, a repeat evaluation should be considered within 3–5 years, while a change in the patient's clinical status (e.g. substantial increase in the degree of microscopic haematuria, dysmorphic RBCs with concomitant hypertension, proteinuria, visible haematuria, pain or other new symptoms) may warrant earlier re-evaluation and/or referral to a nephrologist [7].

In addition, the BAUS/RA consensus statement recommends that, for patients in whom the criteria for referral to urology or nephrology are not met, or in whom investigations have been unremarkable, long-term monitoring should be undertaken because of the uncertainty of the underlying cause [8]. In particular, the guidelines recommend patients be monitored for the development of voiding LUTS, visible haematuria, significant or increasing proteinuria, falling estimated GFR and hypertension [8]. The NICE guidelines do not make any specific recommendation in this regard [9].

Conclusions

Significant variation exists among current guidelines for AMH with respect to who should be evaluated, in what manner, and in what timeframe. Moreover, while the NICE, BAUS, BAUS/RA and ACP statements aim to guide referring physicians, other guidelines, such as the AUA guidelines, more closely target urologists and urological healthcare providers. Importantly, the variations in the existing guidelines reflect the absence of level 1 evidence on the subject, as well as differences in relative prioritization across healthcare systems of diagnostic certainty vs fiscal control. As such, given the patient and health system implications of balancing appropriately focused and effective diagnostic evaluation, AMH represents a valuable future research opportunity, for example through the development and validation of improved risk stratification for pursuing evaluation.

Conflict of Interest

Dr Linder is involved in haematuria research for MDxHealth; no compensation or financial interest to disclose.

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Abbreviations: ACP, American College of Physicians; AMH, asymptomatic microscopic haematuria; CUA, Canadian Urological Association; EAU, European Association of Urology; NICE, National Institute for Health and Care Excellence; PPV, positive predictive value; RA, Renal Association; RBC, red blood cell.