Microscopic Hematuria as a Screening Tool for Urologic Malignancies in Women

Developed by the American Urogynecologic Society Systematic Review Committee

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Introduction: Most causes of microscopic hematuria (MH) are benign but may indicate an underlying malignancy. Current MH evaluation guidelines are reflective of male urologic malignancy risks. The objective of this systematic review was to evaluate whether the finding of MH predicts subsequent urologic malignancy in women.

Methods: MEDLINE was searched between January 1990 and June 8, 2018. The positive predictive value (PPV) of MH as a screening tool for urologic malignancy was calculated for each study individually and collectively. The pooled relative risk of urologic malignancy associated with MH was calculated.

Results: Seventeen studies were included. Eight studies included only women. In total, 300 urinary tract cancers were identified in 110,179 women with MH. The PPV of MH as a screening tool for cancer ranged from approximately 0.6% to 2.8%; confidence intervals (CIs) suggested this is a relatively unstable performance indicator because of small sample sizes. Average PPV across all studies was 2.13%, but the weighted average PPV was 0.24%. The risk of urologic malignancies among women with relative those without MH was 2.01 (95% CI, 1.61–2.51). Based on these limited data, we estimate that 859 (95% CI, 654–1250) women with MH would require complete evaluation to identify 1 urinary tract malignancy.

Conclusions: A very small proportion of women with MH are likely to have a urologic malignancy. Approximately 859 women require full screening to identify 1 malignancy. Current evidence is limited, and further studies, specifically in women, are needed.

Key Words: female urologic malignancy, hematuria, microscopic hematuria

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Urinalyses are obtained in clinical practice for a variety of indications.[1] If hematuria is identified, follow-up urine microscopy is recommended.[2] Although the underlying causes of microscopic hematuria (MH) are often benign, malignancy cannot be excluded without appropriate evaluation. There are various recommendations regarding what constitutes a complete evaluation, but in simple terms, both the upper (kidneys and ureters) and lower (bladder and urethra) urinary tracts should be included. Recommendations regarding when to initiate an evaluation for MH depend on how MH is defined, with various guidelines ranging between 2 and 25 red blood cells per high-power field (RBCs/HPF).[1–3]

In 2012, the US Preventive Services Task Force (USPSTF) updated a targeted literature search to evaluate the benefits and harms of screening for bladder cancer.[4] Based on the USPSTF review, there was insufficient evidence to recommend for or against bladder cancer screening in asymptomatic adults. However, because of the concern for cancer, many medical societies including the American Urogynecologic Society (AUGS), the American College of Obstetrics and Gynecology (ACOG), the American Urological Association (AUA), and the Canadian Urological Association (CUA) recommend evaluation of upper and lower urinary structures.[1,2,3]

Current guidelines are based on the best available research, which is primarily based on male subjects, despite known gender disparities for urologic malignancies.[2,3] In the United States, the age-adjusted incidence of bladder cancer is 4-fold higher, and renal cancer is 2-fold higher in men than in women, with reported rates of 34.9/100,000 versus 8.4/100,000 and 21.4/100,000 versus 10.7/100,000, respectively.[5] In addition to non–gender-specific causes such as infection and urinary calculi, women have other known benign causes of MH, such as menstruation and vaginal atrophy.

Because of the distinct differences in cancer rates between women and men, specific recommendations for evaluation of women with MH would be valuable. The AUGS and the ACOG issued a joint statement encouraging organizations producing future MH guidelines to perform gender-specific data analysis and produce gender-specific recommendations.[1] Therefore, the purpose of this study was to conduct a systematic review of the published literature regarding the use of MH as a screening tool for urologic malignancy in women. Secondary goals of this analysis were to systematically and critically assess other medically important, benign conditions identified in the workup of MH and to assess harms associated with screening in women.

MATERIALS AND METHODS

The AUGS Systematic Review Committee consists of board-certified or board-eligible female pelvic medicine and reconstructive surgeons and individuals with expertise conducting systematic reviews. Consistent with how MH findings are used in clinical practice, the committee focused on (1) the extent that

a finding of MH predicts subsequent urologic malignancy and (2) the presence of clinical or other risk-stratification characteristics that influence the probability of identifying urologic cancers among women with MH. This study was exempt from institutional board review and is registered with PROSPERO (ID CRD42015020038).[6]

In collaboration with a medical librarian, MEDLINE was searched using the key words *hematuria* or *microhematuria* in English between January 1990 and June 8, 2018. The complete search algorithm is available online (Appendix 1, Supplemental Digital Content 1, http://links.lww.com/FPMRS/A77). Citations were screened for eligibility by 10 reviewers using Abstrackr (http://abstrackr.cebm.brown.edu/account/login), a public-use software platform that facilitates team-based systematic reviews.[7]

For quality-control purposes, 50 abstracts were initially evaluated by all reviewers. Additional abstracts were evaluated until consensus was achieved, and all remaining abstracts were then independently screened by 2 reviewers with discrepancies adjudicated by a third reviewer. Full-text manuscripts of abstracts that met inclusion/exclusion criteria (Table 1) were independently evaluated by 2 reviewers. Adult women with MH were the population of interest for this study; therefore, data were included from all studies that either reported gender-stratified results or included at least 90% women. All women needed to have MH defined as 3 or more RBCs/HPF and an assessment of urinary tract malignancy. Women with gross hematuria were excluded from this review. References of the included studies were manually reviewed, and any additional manuscripts that met inclusion criteria were also included in the review.

Data were extracted in duplicate using a database containing a combination of drop-down response options and free-text fields. Any discrepancies identified following full-text review were discussed with a third physician (P.C.J.) and a clinical epidemiologist (H.E.R.) to achieve consensus.

Extracted data included information such as (1) study design, (2) single or mixed-gender population, (3) geographic location, (4) exclusively MH-positive (MH^+) patients or a combination of MH^+ and MH-negative (MH^-) patients, (5) definition of MH, (6) number of women with MH, and (7) number of urinary tract malignancies. If available, information was also extracted regarding the utility of MH as a screening tool in relation to risk-stratification variables such as age, tobacco use, parity, exposure to pelvic radiation, pelvic organ prolapse, and other factors. We were specifically interested in data regarding cancer evaluation of both the bladder and upper urinary tracts based on current AUA guidelines,[2] although information from studies that did not report this information was still included.

Categorical data were tabulated. The positive predictive value (PPV) of MH as a screening tool for urologic malignancies was calculated for each study individually and all studies collectively, including a PPV weighted by each study's sample size. When available, the number of women without MH in each study was recorded, and that information was used to calculate a pooled relative risk (RR) of urologic malignancy associated with MH and number of women with MH needed to screen (NNS) to identify 1 case of urologic cancer. Where data permitted, the utility of MH to screen for cancer based on other potential risk-stratification variables was examined. Finally, the potential bias among included studies with criteria developed by the GRADE Working Group for use in systematic reviews of screening tools was assessed.[8]

TABLE 1. Inclusion and Exclusion Criteria and Bias Assessments for AUGS Systematic Review MH as a Screening Tool for Urologic Malignancies in Women

Inclusion Criteria
MH defined as ≥3 RBCs/HPF in the absence of obvious benign cause
Assessment of bladder and/or upper urinary tract
Women aged ≥18 y
Results stratified by gender in mixed-gender studies or included ≥90% women
Exclusion Criteria
Exclusively pediatric study population
Hematuria assessed with dipstick or urinalysis without microscopy
Gross hematuria
Prior urologic cancer
Exclusively inpatient study population
Renal transplant
Case reports

RESULTS

The search algorithm yielded 1809 unique citations, with 168 of these articles reviewed in full text. Seven additional articles were included that were identified by reference review. Of these 175 studies (Fig. 1), this report includes the results from 17 studies that met inclusion criteria.[9–25] Of the included studies, 16 studies were observational (7 case series,[11,14,15,19,22,24,25] 7 cohort studies,[9,12,16–18,20,21] 2 case-control studies[10,13]), and 1 study was a 1-arm, preintervention-postintervention design[23] (Table 2). Eight studies included only women, with the remaining mixed-gender reports providing gender-stratified data suitable for inclusion in this review. Eleven studies included 3 or more RBCs/HPF as 1 element of the definition for MH,[9–15,18,19,21,24,25] 3 studies had absent or ambiguous MH definitions,[17,20,23] and the remaining studies used other definitions for MH.

Methods for the ascertainment of urologic malignancies varied across studies. Some reports identified cancers from electronic databases with little or no description of how these cancers were identified, whereas others provided extensive detail on abdominal radiography, renal ultrasound, and cystoscopy (Table 2).

In total, included studies identified 300 urinary tract cancers out of 110,179 women with MH (Table 3). The number of included women with MH from each study ranged from 15 to 104,373, and the number of urologic malignancies ranged from 0 to 217. Five of the 17 studies contributed no malignancies. Notably, 1 study[21] contributed 94.7% of all women with MH and 72.3% of all urologic cancers examined in this review. Among the studies in which 1 or more urologic malignancies were identified, the PPVs of MH as a screening tool for these cancers ranged from 0.21% to 13.33%, with most PPVs ranging from approximately 0.6% to 2.8%. Large confidence intervals (CIs) around the PPVs suggested that the estimate of this performance indicator was relatively unstable in many of the studies included in this review because of small sample sizes. Importantly, in 4 studies, the lower boundary of the 95% CI was less than zero, indicating that MH as a screening tool for urologic malignancies had no value. In the study with the largest PPV (Linder et al,[19] N = 15), the CI ranged from −3.87% to 30.54%, a clear reflection of the instability of the PPV in this report. The average PPV across all studies in this review was 2.13%, but the weighted average PPV was 0.24%, and this was driven largely by the considerable sample size reported by Jung et al.[21]

Several articles reported urologic malignancies in women without MH.[17,18,21,23] In these studies, the risk of urologic

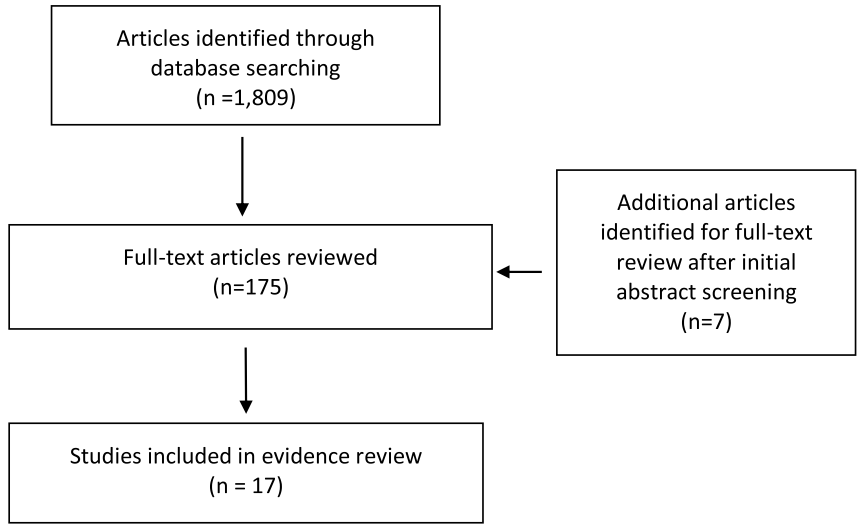

FIGURE 1. Identification of articles for inclusion in evidence review of microhematuria as a screening tool for identification of urogynecologic malignancy.

malignancies among women with MH relative to those without MH was 2.01 (95% CI, 1.61–2.51). Based on data from this limited subset of reports, we estimate that 859 women (95% CI, 654–1250) with MH would require complete evaluation to identify 1 urinary tract malignancy.

A secondary objective of this review was to assess whether patient characteristics or risk factors impacted the ability of MH to predict urologic malignancy. Of the 9 characteristics identified a priori by the review committee (Table 4), informative data were identified for 3. These included (1) age (6 studies), (2) tobacco use (2 studies), and (3) degree of MH (2 studies). For each of these 3 variables, cancer risk increased in parallel with the risk factor. That is, urologic malignancies were more common among older women with MH, smokers with MH, and women with higher degrees of MH (Table 5). It should be noted that even among studies that assessed these variables in relation to cancer risk among women with MH, there was no standardization in how the variables were analyzed, which inhibited cross-study comparisons. There were not enough data to assess the remaining 8 variables including (1) irritative voiding symptoms, (2) pelvic radiation exposure, (3) chemical exposure, (4) pelvic organ prolapse, or number of (5) pregnancies and (6) live births. Included studies provided essentially no information concerning the balance of benefits and harms associated with MH screening and subsequent evaluation including what would constitute the optimal "workup."

Included studies were evaluated for quality and bias with mixed findings. The overall quality of the literature with respect to the evaluation of MH for women was poor. Microscopic hematuria was not uniformly classified across studies, nor was follow-up standardized or consistent. In addition, only a small sample of enrolled subjects had both MH screening and complete workup, resulting in only a fraction of the data being suitable for inclusion in this review. In most studies, MH screening was independent of subsequent urologic evaluations. However, because most articles were based on data from referral practice settings, when evaluations were conducted, they were done because of a prior MH finding. Finally, few of the articles included in the review reported information on uninterpretable findings or withdrawals from the study. In addition to these concerns, the committee noted that the study by Jung et al[21] was not only considerably larger than the other reports, but also the population-based managed-care database that provided its data is qualitatively different from data in smaller studies conducted in specialty urology clinics based in academic medical centers.

DISCUSSION

Data from 17 eligible studies regarding the utility of MH as a predictor for urologic malignancies in women suggest that a very small proportion of women with MH will have a urologic malignancy. The low PPVs observed among women—ranging in most studies from 0.21% to less than 5% with a weighted average of 0.24%—are lower than other PPVs for other screening tools. For example, a recent study showed that using diagnostic digital mammography to screen for breast cancer has a PPV of 27.5%.[26]

Although the studies of women included in this review differed in terms of MH definition, cancer ascertainment methods, follow-up time, and sample size, the consistent and relatively small PPVs observed across most studies are notable. In addition, PPV CIs dropped below zero for some studies, indicating that MH had essentially no value in predicting urologic cancer among the women in those studies.

It is important to emphasize that a low PPV is consistent with data from a subset of the included studies that indicated an RR of 2.0 for the association between MH and urinary tract cancer. Although women with MH were twice as likely to have a urinary tract cancer identified relative to those without MH, the data also show that the absolute risk of urinary tract cancer among women with MH is extremely low. The small absolute risk of urinary tract malignancy among women with MH relative to those without also contributed to the finding that approximately 859 women with MH would need a full workup to identify a single urinary tract malignancy. Not only would considerable health care resources need to be expended to identify 1 malignancy, but also the hundreds of women with MH in whom no tumors are identified would be subjected to needless anxiety, unnecessary out-of-pocket health care expenses, and risks inherently associated with cystoscopy and imaging. Although we did not specifically search for cost analyses, we did not identify any studies that evaluated the costs associated with screening.

Several medical groups offer guidelines on the definition of MH and what to do for patients, regardless of gender, found to have MH. The AUA updated its recommendations in 2012[2] to define MH as a single positive, properly collected, specimen

TABLE 2. Selected Characteristics of Studies Included in the AUGS Systematic Review of MH as a Screening Tool for Urologic Malignancies in Women

Authors, Year of Publication	Location	Study Design	Study Population	Definition of MH	Malignancies Ascertained/identified	Method(s) to Ascertain Malignancy
Abbaszadeh et al,[25] 2009	Iran	Case series	Outpatient clinic; referred for evaluation of MH	≥3 RBCs/HPF on at least 2 occasions; minimum gap of 2 wk	Bladder	Cystoscopy and pathological assessment of biopsy specimen in all cases
Bradley et al,[24] 2016	United States	Case series	Electronic medical records used to identify women who were evaluated by urogynecology or urology	≥3 RBCs/HPF	Bladder, kidney	Laboratory results, cystoscopy findings and imaging results extracted from medical records
Hung et al,[23] 2012	Taiwan	Single-arm intervention	Interstitial cystitis patients	Unclear	No malignancies identified	Cytological examinations, cystoscopy, renal and bladder ultrasonography
Jaffe et al,[22] 2001	United States	Case series	Consecutive patients who presented with asymptomatic MH to division of urology	≥3 RBCs/HPF	Bladder, kidney	Urine cytology, renal ultrasound, cystoscopy, intravenous urography
Jung et al,[21] 2011	United States	Cohort	Retrospective cohort study of patients who underwent microscopic urinalysis in a large managed-care organization	≥3 RBCs/HPF	Bladder, kidney and renal pelvis, ureter, or other urinary structure	Cases identified from cancer registry
Khadra et al,[20] 2000	United Kingdom	Cohort	Patients enrolled from a hematuria specialty clinic	Not defined	Not reported by gender	Abdominal radiography, renal ultrasound, intravenous pyelogram, and flexible cystoscopy
Linder et al,[19] 2017	United States	Case series	Charts of pelvic organ prolapse (POP) patients evaluated in a urogynecology clinic	≥3 RBCs/HPF on 1 sample	Bladder, urothelial	Renal function testing, office cystoscopy, and upper urinary tract imaging, with CT urogram
Lippmann et al,[18] 2017	United States	Cohort	Retrospective cohort in an integrated health care system database; women who were referred for urologic evaluation were entered into a prospective database	>3 RBCs/HPF	Bladder, kidney, ureteral	Urinary tract imaging results, cystoscopy findings, and cause of hematuria recorded voluntarily by urologists
Lotan and Shariat,[17] 2008	United States	Cohort	Patients at elevated risk of bladder cancer at multiple sites	Not defined	No malignancies identified	Cystoscopy, endoscopy
Miyanaga et al,[16] 1999	Japan	Cohort	Patients diagnosed with MH by health examination and who consulted urologists	"Patients who had been diagnosed as having MH by health examination"	Bladder, renal and ureteral	Ultrasonography, intravenous urography, cystoscopy
Pichler et al,[15] 2013	Austria	Case series	Asymptomatic MH who were low risk due to prior workup	≥3 RBCs/HPF	No malignancies identified	Cystoscopy with ultrasound
Pillalamarri et al,[14] 2015	United States	Case series	Women with POP presenting to a single outpatient urogynecology provider	≥3 RBCs/HPF with concurrent negative urine culture	No malignancies identified	Cystoscopy, cytology, and imaging with ultrasound, intravenous urography, or CT urography

Richter et al,[13] 2016	United States	Case-control	Patients enrolled through multicenter urogynecology clinics	≥3 RBCs/HPF on a single properly collected noncontaminated specimen in the absence of infection	Bladder	Cystoscopy and imaging by CT urography, renal ultrasound, retrograde pyelogram, renal ultrasound, or magnetic residence imaging
Sagnak et al,[12] 2011	Turkey	Cohort	Incidental, asymptomatic MH from outpatient clinics	≥3 RBCs/HPF on at least 2 different occasions; minimum gap ≥2 wk	Bladder	Ultrasonography, cystoscopic biopsies
Sugimura et al,[11] 2001	Japan	Case series	Retrospective study of renal cell cancer patients who presented at urology department	≥2 RBCs/HPF	Bladder	Choice of the urologist managing the patient
Töz et al,[10] 2015	Turkey	Case-control	POP patients identified from hospital database	≥3 RBCs/HPF	Bladder and upper urinary tract malignancies	Not reported
Turkeri et al,[9] 2014	Turkey	Cohort	MH patients presenting to 7 medical centers	≥3 RBCs/HPF	Bladder	Choice of radiological examination at discretion of referring physician

with 3 or more RBCs/HPF without obvious benign cause. This guideline also decreased the suggested age at which to initiate a workup for MH from 40 to 35 and recommended cystoscopy and computed tomography (CT) urography to evaluate both the upper and lower urinary tracts. Published in 2009, the CUA[3] also defines MH as 3 or more RBCs/HPF, but it requires 2 positive results on separate occasions. The CUA recommends initiating an evaluation for patients 40 years or older with cystoscopy, renal ultrasound, and urine cytology.

In contrast, recently published joint guidelines from ACOG and AUGS[1] recommend that asymptomatic, low-risk women between the ages of 35 to 50 years without a history of smoking undergo further evaluation only if they have 25 or more RBCs/HPF noted on urinalysis. Importantly, the AUGS/ACOG recommendations are primarily based on data from Jung et al,[21] which (1) also accounted for approximately 94% of all women with MH who were included in this review and (2) had the lowest overall PPV of 0.21%. Nonetheless, Jung and colleagues' data for women older than age 40 years show that cancer risk increases with degree of MH, ranging from 0.16% among those with 0 to 2 RBCs/HPF to 0.87% among those with 25 to 99 RBCs/HPF, data that support the role of changing the definition of MH as a risk factor for urinary tract malignancy.

The relatively small number of studies that met inclusion criteria for this review highlights the paucity of quality information available to guide recommendations for women with MH. This supports the AUGS/ACOG position that additional data are needed to help inform guidelines specifically for women.[1] This report summarizes findings from a systematic review; it does not provide updated practice guidelines. Again, the purpose of this study was to systematically review and compile currently available data from the medical literature. Creation of guidelines is a separate process that uses medical literature when available and combines that with expert opinion to make recommendations. This systematic review could be used to help create future guidelines and recommendations. The findings of this systematic review are consistent with the 2011 USPSTF review that found insufficient evidence to adequately assess the balance of benefits and harms of screening for bladder cancer in asymptomatic adults.[4]

This review has important limitations. First, the overall quality of the literature that met inclusion criteria was poor, and most included studies were not specifically designed to address the primary research question concerning MH screening in asymptomatic women. As a result, numerous sources of potential bias were identified, including variability in both the MH definition and the methods used to assess urinary tract malignancies. This variability could lead to misclassification of both MH exposure and cancer outcomes, ultimately impacting the accuracy of PPV, RR, and NNS. Another limitation is that approximately 95% of the data in this review comes from 1 report, which drew from a large managed-care population.[21] The sample size for that study was 42 times larger than the second-largest study in this review. The contribution of data from a managed-care population, presumably mostly community-based clinics, is inherently different than data obtained from specialty referral clinics. These differences could generate cross-study differences in both MH and cancer ascertainment, potentially introducing bias into the findings of this review. It was also unclear if all MH patients in the Jung report[21] underwent a full evaluation for cancer. Given that the PPV in the study of Jung et al[21] was by far the smallest of all studies included in this review, it is tempting to speculate that underlying malignancies were not ascertained. This should be carefully considered given the emphasis that study has had on current recommendations. A related issue involves which cancers were

TABLE 3. Overall and Study Specific PPV of MH as a Screening Tool for Urologic Malignancies in Women

Authors, Year of Publication	No. MH+ Women in Whom Urologic Malignancy Was Assessed (% of Total)	No. Women With Confirmed Urologic Malignancy (% of Total)	PPV of MH in Relation to Urologic Malignancy, %	95% CI
Total	110,179 (100.0)	300 (100.0)	0.27	0.24 to 0.30
Abbaszadeh et al,[25] 2009	249 (0.23)	7 (2.33)	2.81	0.76 to 4.86
Bradley et al,[24] 2016	151 (0.14)	2 (0.67)	1.33	−0.50 to 3.15
Hung et al,[23] 2012	28 (0.03)	0 (0)	—	—
Jaffe et al,[22] 2001	222 (0.20)	11 (3.67)	4.96	2.10 to 7.81
Jung et al,[21] 2011	104,373 (94.73)	217 (72.33)	0.21	0.18 to 0.24
Khadra et al,[20] 2000	484 (0.44)	17 (5.67)	3.51	1.87 to 5.15
Linder et al,[19] 2017	15 (0.01)	2 (0.67)	13.33	−3.87 to 30.54
Lippmann et al,[18] 2017	2,482 (2.25)	19 (6.33)	0.77	0.42 to 1.11
Lotan and Shariat,[17] 2008	467 (0.42)	13 (4.33)	2.78	1.29 to 4.28
Miyanaga et al,[16] 1999	164 (0.15)	4 (1.33)	2.44	0.08 to 4.80
Pichler et al,[15] 2013	56 (0.05)	0 (0)	—	—
Pillalamarri et al,[14] 2015	209 (0.19)	0 (0)	—	—
Richter et al,[13] 2016	493 (0.45)	0 (0)	—	—
Sagnak et al,[12] 2011	108 (0.10)	1 (0.33)	0.93	−0.88 to 2.73
Sugimura et al,[11] 2001	492 (0.45)	3 (1.00)	0.61	−0.08 to 1.30
Töz et al,[10] 2015	29 (0.03)	0 (0)	—	—
Turkeri et al,[9] 2014	157 (0.14)	4 (1.33)	2.55	0.08 to 5.01

ascertained in the studies that are reported here. The goal of this review was to evaluate MH as a tool to screen for several different urological cancers among women. However, some studies focused only on bladder cancer. Thus, in these studies, renal and ureteral cancer could not be ruled out, potentially contributing to more underestimation of pooled urologic malignancies.

This review also has a number of strengths. First, based on the literature review conducted for this study, it is the first systematic review that examines the MH workup specifically among women. Second, only studies that met a clear set of selection criteria were included and only studies published after 1990. The latter criterion helped minimize the impact that changes in imaging technology would have on the ascertainment of cancer. Finally, this review provides several MH statistics in relation to urinary tract malignancy. These included individual, pooled, and weighted PPV, as well as RR and NNS from a subset of studies with appropriate data.

This systematic review demonstrates that the ability of MH to correctly identify a woman with urologic cancer is very low. However, the evidence underpinning this conclusion is subject to multiple potential biases, a finding that underscores the importance of designing and implementing future studies specifically focused on identifying the circumstances under which women with MH should receive a full workup for urinary malignancy. Based on these findings, such a study should focus on women

TABLE 4. A Priori Risk Factors

Age
Irritative voiding symptoms (symptomatic vs asymptomatic MH)
Tobacco use (past, current, secondhand)
Chemical exposures such as cyclophosphamide
Pelvic organ prolapse
Interstitial cystitis/bladder pain syndrome
Degree of MH (ie, >25 RBCs/HPF)
Presence of MH on >1 occasion
Catheterized specimen
Prior pelvic radiation
Pregnancy

TABLE 5. Summary of Findings for Urogynecologic Risk Factors and Urogynecologic Malignancies Among Women With Microhematuria

Authors, Year of Publication	Direction of Effect
Age	
Abbaszadeh et al,[25] 2009	Increased
Jaffe et al,[22] 2001	Increased
Jung et al,[21] 2011	Increased
Khadra et al,[20] 2000	Increased
Lippmann et al,[18] 2017	Increased
Lotan and Shariat,[17] 2008	Increased
Irritative voiding symptoms	ND
Tobacco use	
Jaffe et al,[22] 2001	Increased
Lippmann et al,[18] 2017	Increased
Pelvic radiation exposure	ND
Chemical exposures	ND
POP	ND
Degree of MH	
Jung et al,[21] 2011	Increased
Lippmann et al,[18] 2017	Increased
No. pregnancies	ND
No. live births	ND

Abbreviation: ND, no data.

older than 40 years; should use a rigid, widely accepted definition of MH; and should employ consistent diagnostic testing modalities that will allow for identification of any of the various urinary tract tumors that might cause MH.

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This document reflects clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Its content is not intended to be a substitute for professional medical judgment, diagnosis, or treatment. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient.

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