



Clinical trial

The prevalence and utility of screening for urinary tract infection at the time of presumed multiple sclerosis relapse

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A B S T R A C T

Background: Methods of screening for infections at the time of suspected relapse in people with multiple sclerosis (MS) vary across physicians. People with multiple sclerosis (MS) are at an increased risk of urinary tract infection (UTI). Data evaluating the utility of screening for potential UTI at the time of suspected relapse and whether there are key subgroups of patients in which screening would be most effective are sparse.

Objectives: To evaluate demographic and clinical predictors of UTI in the context of a suspected acute relapse in (1) a retrospective hospital admission cohort and (2) a prospectively-enrolled, ambulatory care-based cohort, and to determine an approximate number needed to screen to detect one UTI in both healthcare settings.

Methods: For the hospital admissions cohort, we included individuals with a known or new diagnosis of MS or clinically isolated syndrome who were admitted at least once to the Johns Hopkins Neurology Inpatient Service (March 2012 to December 2014). We considered those screened via urinalysis. Possible UTI was defined as leukocyte esterase OR nitrite positive. For the ambulatory population, we enrolled a cohort of RRMS patients aged 18–65 who were suspected of suffering from an acute MS relapse who either called or came into clinic. Participants were screened via urinalysis; possible UTI was similarly defined. Participants also completed questionnaires (disability, history of Uhthoff's-type phenomenon, recent sexual intercourse, and new urologic symptoms). For both cohorts, we calculated an approximate number needed to screen, and tested if demographic and patient characteristics were associated with possible UTI using logistic regression models.

Results: For the hospital admissions cohort, we included 158 individuals; 48 (30.4%) were identified as possibly having a UTI. For possible UTI, the approximate number needed to screen in order to detect 1 possible UTI is 3 (95% CI: 2, 6). Female sex was the only factor associated with increased odds of UTI (odds ratio [OR]: 3.90; 95% CI: 1.59–9.61; $p = 0.003$). For the ambulatory cohort, we included 50 participants; 10 (20.0%) with possible UTI. The approximate number needed to screen in order to detect 1 possible UTI was 5 (95% CI: 3, 11) in this cohort. Foul-smelling urine was positively associated with UTI (OR: 5.36; 95% CI: 1.10, 26.17; $p = 0.04$); no men had a possible UTI in this cohort, so we could not estimate odds ratios associated with sex.

Conclusion: UTIs at the time of a suspected MS relapse are relatively uncommon. Female sex is a strong risk factor for UTI in people with MS; foul-smelling urine is a potential predictor of UTI in people with MS. Larger studies are needed to comprehensively evaluate the utility of screening and risk factors for UTI at the time of suspected MS relapse.

1. Introduction

One of the hallmark characteristics of multiple sclerosis (MS) is a subacute period of neurologic disease worsening (e.g. a relapse). (Reich et al., 2018) However, some episodes of neurologic disease worsening may be pseudo-relapses, which are considered to be unrelated to new central nervous system demyelinating activity and are instead old symptoms unmasked by systemic stresses such as infections, ambient temperature changes, or fever (Buljevac et al., 2002). In clinical trials, MS relapses require new symptoms to be accompanied by Expanded Disability Status Scale (EDSS) change “in the absence of fever or signs of an infection” and often necessitate a study visit to confirm or refute the suspected relapse (Schumacher et al., 1965). This is in contrast to routine clinical practice where, when people with MS report symptoms

concerning for relapse, decisions about whether symptoms truly represent a relapse are often made over the phone.

People with MS are at increased risk for urinary tract infections (UTIs), but because they may have sensory impairments and baseline urologic dysfunction due to the disease itself, UTIs may be asymptomatic (Mahadeva et al., 2014; Phé et al., 2016). The “absence of infection” due to UTI may be determined differently between physicians; some systematically assess for evidence of UTI, while others prescribe corticosteroid treatment without ruling out infections except by questioning patients regarding symptoms thereof. This situation produces a dilemma, as giving corticosteroids to a person with an active untreated bacterial infection may lead to worsened infection and complications such as pyelonephritis and urosepsis (Fardet et al., 2016). On the other hand, the yield of routinely screening for UTI in the entire relapsing-

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remitting MS (RRMS) population presenting with possible relapse symptoms is unknown, and the costs (clinic time, laboratory fees, and delay in treating the underlying relapse) may not be justified, especially given the unknown yield. It may be possible to eliminate UTI as a diagnostic consideration based on a patient's history of urologic and other MS symptoms, both of which can be assessed at home over the phone.

Thus, to address these existing, highly relevant clinical questions, we systematically evaluated the frequency and utility of UTI screening at the time of suspected relapse in two complementary populations of people with MS. Specifically, our aims were to (1) evaluate potential demographic and clinical predictors of UTI at the time of hospitalization for a suspected MS relapse and (2) to determine, at the time of new symptoms, whether specific patient-reported characteristics (including characteristics predictive of UTI in the general population) were associated with UTI in a prospective ambulatory care setting. Finally, for both cohorts, we determined an approximate number need to screen to detect a confirmed UTI.

2. Methods

2.1. Aim 1: frequency of UTI at the time of hospitalization

2.1.1. Study population

We included individuals with a known or new diagnosis of MS or clinically isolated syndrome (CIS) who were admitted to the Johns Hopkins Hospital Neurology Inpatient Service between March 2012 and December 2014. All individuals with MS were evaluated for inclusion. We excluded individuals who were admitted for other reasons than suspected MS relapse: seizures, cognitive decline, chronic inflammatory demyelinating polyneuropathy flare, hypertension, meningitis, infection, other neurological disorder, and other musculoskeletal complaints. We also excluded individuals who were transferred from another hospital and received treatment at that institution as well as those who had the presenting suspected relapse < 30 days from prior relapse onset. For patients admitted multiple times over the study period, we included only the first admission for suspected relapse. We included only the first admission to be conservative, as we reasoned that the first admission was most likely to be a true relapse and that repeated admissions occurring over our study period were more likely to be pseudo-relapses and would thus introduce bias in the analyses. This study was approved by the Institutional Review Board at the Johns Hopkins School of Medicine.

2.1.2. Outcomes

For each patient, we initially considered whether urinalyses were performed. Among patients who were screened, we considered the frequency of urinalyses which were consistent with a “possible” UTI (leukocyte esterase OR nitrite positive); this definition of UTI was derived using results of several meta-analyses suggesting that positive results for either leukocyte esterase or nitrate could be suggestive of an UTI (Devillé et al., 2004; Hurlbut and Littenberg, 1991). Among those classified as a “possible” UTI, we evaluated the prevalence of completion of urine culture and whether possible results were confirmed. We considered a confirmed-by-culture UTI as those with at least 100,000 colony-forming units/milliliter (cfus/mL) in women and at least 10,000 cfus/mL in men who did not have evidence of contamination (i.e. mixed flora, unclean catch).

2.1.3. Candidate predictors of possible UTI

We collected demographic, clinical and magnetic resonance imaging information at the time of suspected relapse. Specific predictors of interest included: age, sex, MS subtype (CIS, RRMS, progressive), disease duration, current MS disease-modifying therapy use (no therapy, injectable therapy, oral/infusion therapy), use of cane (e.g. Expanded

Disability Status Scale [EDSS] scores ≥ 6), gadolinium-enhancing lesion (yes, no), history of UTI, history of bladder dysfunction, and bladder symptoms, as recorded at time of hospital admission.

2.1.4. Statistical analysis

Initial analyses calculated the frequency of possible UTI as well as the percentage of patients in which UTI was confirmed by urine culture. We also fit univariate and multivariable logistic (adjusting for all potential predictors) models to assess the association between candidate UTI predictors and odds of probable/possible UTI. Because of the relative infrequency of confirmed by culture UTI (and potential lack of power), we assessed possible risk factors for possible UTI, as this was the most commonly observed outcome and included the broadest definition of UTI (in an attempt to make as few assumptions as possible). We calculated an approximate “number needed to screen” in this context as the reciprocal of the number of patients who screened positive for the given test of interest. Both urinalysis and urine culture assessment were not tested sequentially in this cohort. As a result, we calculated independent approximate number needed to screen values for possible UTI and confirmed-by-culture UTI. All statistical analyses were conducted in R Version 3.2.2 (<https://www.r-project.org>).

2.2. Aim 2: self-reported predictors of possible UTI in prospective cohort

2.2.1. Study population

We prospectively enrolled a cohort of RRMS patients aged 18–65 who were suspected of suffering from an acute MS relapse. We did not include participants who were older than 65 as the frequency of relapses in people with MS decreases with age, and those aged > 65 who were experiencing symptoms of a potential relapse were more likely to be pseudo-relapses. Initially, participants called in or were enrolled directly following clinical follow-up visits, where for either case he or she reported symptoms concerning for a relapse (as determined by study team members) and did not live ≥ 100 miles from Johns Hopkins (e.g. patients with milder symptoms who live further away may be less likely to participate). We asked these enrolled patients to complete a urinalysis via a clean-catch sample at Johns Hopkins and self-administer a urine dipstick; urine samples were then sent to Johns Hopkins Clinical Laboratory for formal urinalysis and urine culture with antibiotic sensitivities. However, recruitment for this portion of the study lagged as eligible patients were largely unwilling to participate in the on-site study visit. Thus, in order to facilitate increased enrollment, we modified the protocol to allow the study to be completed remotely in entirety; participants provided a clean-catch urine sample (that was analyzed in a clinical laboratory for urinalysis and urine culture) and completed all relevant questionnaires by phone. All participants were required to have not had a diagnosed UTI or relapse within 30 days prior to the onset of the currently reported symptom. Patients with an indwelling bladder catheter were also ineligible; relatively few participants had an indwelling catheter, and the baseline risk of UTI may be different in this population rather than the general MS population.

2.2.2. Outcomes

For this prospective cohort, we asked all enrolled patients to complete a urinalysis via a clean-catch urine sample; urine samples were sent to a clinical laboratory for formal urinalysis and urine culture with antibiotic sensitivities for both in-person and remote visits. We evaluated the frequency of “possible” (leukocyte esterase OR nitrite positive) UTI as well as the prevalence of potential contamination, as reported by laboratory testing. Urine culture was also performed systematically in this cohort. Among those classified as a “possible” UTI, we evaluated whether possible results were confirmed on culture (> 100,000 CFUs/mL in women; > 10,000 CFUs/mL in men) without evidence of contamination.

2.2.3. Candidate predictors of possible UTI

In addition to demographic and clinical predictors described in Section 2.1.3, participants also completed questionnaires assessing current neurologic function and urinary symptoms at the time of relapse. These questionnaires included assessment of baseline disability (Patient-Determined Disease Steps [PDDS]), history of Uhthoff's-type phenomenon (transient worsening of neurologic symptoms in the context of fever, exertion, fatigue or heat), history of sexual intercourse ≥ 6 times in the past month, new urologic symptoms predictive of UTI (e.g. the self-reported Bladder and Bowel Control Scales which includes assessment of symptoms of urgency, dysuria/pain while urinating, back pain, cloudy urine, hematuria, foul-smelling urine, and history of UTI).

2.2.4. Statistical analysis

We evaluated the association between demographic, clinical and additional outcome measures collected as a part of this study (e.g. PDDS, Bladder and Bowel FSS, Uhthoff's-type phenomenon, sexual intercourse, self-reported Bowel Control Scale components, and positive urine dipstick) and possible/probably UTI using univariate and multivariable logistic regression models. As in the inpatient cohort, we calculated an approximate number needed to screen in this context was calculated as the reciprocal of the number of patients who screened positive for the given test of interest. As both urinalysis and urine culture assessment were intended to be performed systematically in this cohort, we did not adjust for the calculation for the approximate number needed to screen to account for sequential testing.

All analyses additionally adjusted for whether the participant completed the study visit in-person or over the phone.

3. Results

3.1. Aim 1: frequency of UTI at the time of new symptoms

Of the 237 admissions to the Johns Hopkins Neurology Service between March 2012 and December 2014 for MS relapse we screened, we excluded individuals ($n = 22$ admissions) who were admitted for other reasons than suspected MS relapse (e.g. progressive multifocal leukoencephalopathy, neuromyelitis optica, transverse myelitis, delirium, viral infections, psychosis, hypertension, meningitis, among others). We included the first admission for suspected relapse among patients with multiple admissions over the study period and excluded second or third admissions ($n = 57$ admissions); there were 158 individuals/admissions eligible for the analysis. For the included cohort, individuals were aged 39.2 years (Table 1; standard deviation [SD]: 12.3 years), were 69% female, had predominantly RRMS, were of

Table 1
Baseline characteristics of study populations.

	Patient population	
	Inpatient (Aim 1)	Prospectively enrolled ambulatory (Aim 2)
N	158	63
Age (SD), years	39.2 (12.3)	36.9 (9.9)
Male sex, n (%)	49 (31.0%)	5 (7.9%)
MS subtype		
CIS*, n (%)	14 (8.9%)	0 (0.0%)
RRMS, n (%)	126 (79.7%)	63 (100.0%)
Progressive, n (%)	17 (10.8)	0 (0.0%)
Unknown, n (%)	1 (0.6%)	0 (0.0%)
Use of walking aid, n (%)	53 (33.5%)	8 (12.7%)
MS disease modifying therapy		
No therapy, n (%)	105 (66.5%)	19 (30.2%)
Injectable, n (%)	36 (22.8%)	24 (38.1%)
Oral/infusion, n (%)	17 (10.8%)	17 (26.0%)
History of UTI, n (%)	16 (10.1%)	46 (73.0%)

* CIS: clinically isolated syndrome; RRMS: relapsing remitting MS.

moderate disability (33.5% needed a walking aid), 147 (93.3%) had received a brain MRI with contrast, and 13 (8.2%) received treatment with antibiotics. Approximately 10% of patients had a documented history of UTI. Of the 158 eligible individuals, 48 (30.4%) were identified as possibly having a UTI (leukocyte esterase or nitrite positive urinalysis). Four (2.5%) individuals were identified as leukocyte esterase and nitrite positive urinalysis (Table 2). Fifty (31.6%) individuals had a formal urine culture performed; 9 of the 50 (18.0%) indicated evidence of contamination and were excluded. Of the 41 eligible urine cultures, 7 (17.1%) were identified as having a confirmed UTI, 6 (14.6%) were leukocyte esterase positive, 2 (4.9%) were nitrite positive, 2 (4.9%) were both leukocyte and nitrite positive, and 1 (2.4%) was neither leukocyte nor nitrite positive. The sensitivity and specificity of possible UTI determined by urinalysis for confirmed by culture UTI were 85.71% (42.13%, 99.64%) and 39.39% (22.91%, 57.86%). For possible and confirmed-by-culture UTI, the approximate number needed to screen in order to detect 1 positive possible or confirmed-by-culture UTI is 3 (95% CI: 2–6) and 6 (95% CI: 4–18) patients, respectively. In sensitivity analyses excluding patients with enhancing lesions, 20 of the 61 had possible UTI (32.7%) and 21 of these individuals had a formal culture performed (4 demonstrated evidence of contamination). 4 of the 17 (23.5%) eligible cultures were identified as having a confirmed UTI.

Of the potential candidate predictors of UTI, only female sex was associated with an increased odds of possible UTI (odds ratio [OR]: 3.90; 95% CI: 1.59–9.61; $p = 0.003$; Fig. 1) in univariate models. We observed a trend toward an increased risk of UTI among individuals with a previous history of UTI (OR: 2.51; 95%CI: 0.85–7.41; $p = 0.09$) as well as those who were currently walking impaired (OR: 1.74; 95% CI: 0.85–3.58; $p = 0.13$). We did not observe evidence of potential effect modification among the three potential risk factors (p for interaction = 0.40). In multivariable models mutually adjusting for all potential candidate predictors, only female sex was independently associated with an increased odds of possible UTI (OR: 4.12; 95% CI: 1.51–11.26; $p = 0.006$).

3.2. Aim 2: self-reported predictors of possible UTI in prospective cohort

We prospectively enrolled 63 people with RRMS who were suspected of suffering from an acute MS relapse. Participants were on average aged 36.9 years (SD: 9.9 years), were largely female (92.1%), were generally mildly disabled (12.9% reported needing a walking aid), and most (73.3%) had a positive history of UTI (Table 1). Of the 63 participants, 55 (87.3%) completed a formal urinalysis; 5 of the 55 (9.8%) indicated evidence of contamination and were excluded. Of the 50 eligible urinalyses, 10 (20.0%) were identified as possibly having an UTI (e.g. leukocyte esterase or nitrate positive); 1 participant was leukocyte esterase and nitrate positive. Of the 5 confirmed-by-culture UTI's, 1 of the 5 was leukocyte esterase positive and 1 of the 5 was nitrite positive. In this cohort, for possible and confirmed-by-culture UTI, the number needed to screen in order to detect 1 positive UTI is 5 (95% CI: 3–11) and 10 (95% CI: 5–59) patients, respectively.

Of the 50 individuals who completed a formal clean-catch urinalysis, 24 (48.0%) additionally completed a self-administered urine dipstick; 8 (33.3%) were identified as possibly having an UTI and 2 (8.3%) were identified as probably having an UTI using the self-administered dipstick. The sensitivity and specificity of identifying a possible UTI by urinalysis using a self-administered dipstick are 86.1% (95% CI: 72.1–94.7%) and 57.1% (95% CI: 18.4%–90.1%), respectively.

To be consistent with analyses of our hospital inpatient population, we evaluated candidate predictors of possible UTI as determined by urinalysis. Of the potential candidate self-reported predictors of urinalysis-confirmed possible UTI, only foul-smelling urine was associated with an increased odds of possible UTI by urinalysis (OR: 5.36; 95% CI: 1.10–26.17; $p = 0.04$; Fig. 2B) in univariate models. Since no men had

Table 2
Results of urinalysis in inpatient and ambulatory study populations.

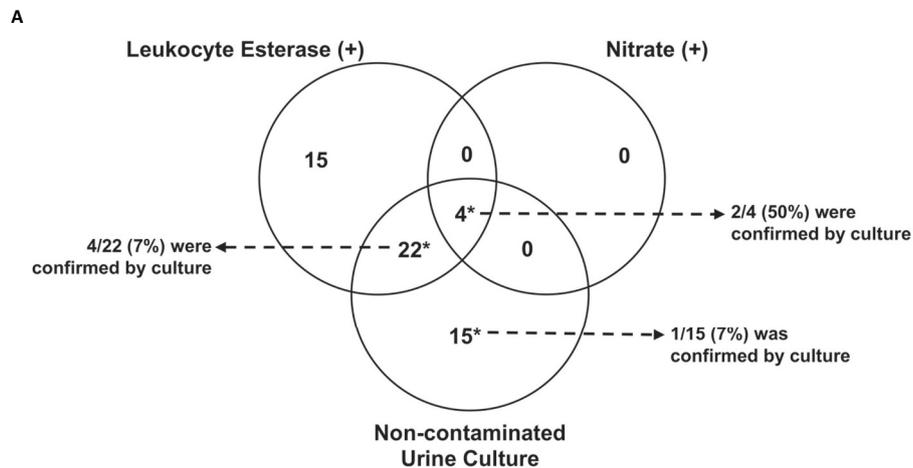
Inpatient Population (n=158)			
	All patients	Women	Men
Eligible for analysis	158	109	49
Possible UTI / total eligible	48 / 158	41 / 109	7 / 49
Leukocyte esterase positive / total eligible	48 / 158	41 / 109	7 / 49
Nitrite positive / total eligible	4 / 158	4 / 109	0 / 49
Leukocyte esterase positive and nitrite positive / total eligible	4 / 158	4 / 109	0 / 49
Completed urine culture / total eligible*	50 / 158	38 / 109	12 / 49
Completed urine culture without evidence of contamination / total eligible	41 / 158	29 / 109	12 / 49
Confirmed UTI by culture / total eligible**	7 / 158	5 / 109	2 / 49

Prospectively Enrolled Ambulatory Population (n=63)			
	All patients (n=63)	Women (n=58)	Men (n=5)
Completed urinalysis without evidence of contamination / total ambulatory population	50 / 63	45 / 58	5 / 5
Completed urine culture without evidence of contamination / total ambulatory population	56 / 63	47 / 58	5 / 5
Possible UTI by urinalysis / total completing urinalysis and culture without evidence of contamination	10 / 50	10 / 50	0 / 50
Leukocyte esterase positive / total completing urinalysis	9 / 50	9 / 50	0 / 50
Nitrite positive / total completing urinalysis	2 / 50	2 / 50	0 / 50
Leukocyte esterase positive and nitrite positive / total completing urinalysis	1 / 50	1 / 50	0 / 50
Confirmed UTI by culture / total completing urine culture**	5 / 56	5 / 47	0 / 5

* We excluded urine cultures which demonstrated evidence of contamination; we excluded results of 9 urine cultures leaving n = 41 for this analysis.

** We considered confirmed UTI as urinalysis results men with > 10,000 colony forming units/millileter (cfus/mL) or women with > 100,000 cfus/mL; 9 participants did not provide a clean catch and sample was marked as contaminated in the inpatient cohort.

*** Of the 63 participants in the ambulatory population, 55 completed formal urinalysis and culture.



*7 individuals were leukocyte esterase positive and nitrate negative and had a contaminated urine culture;
0 individuals were leukocyte esterase and nitrate positive and had a contaminated urine culture;
2 individuals were leukocyte esterase and nitrate negative and had a contaminated urine culture;

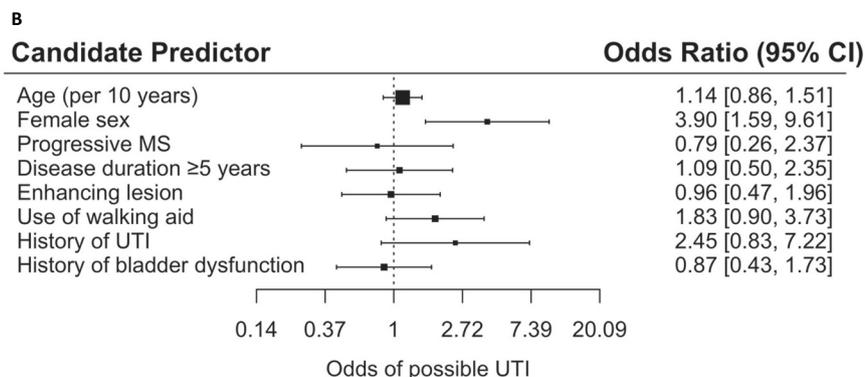


Fig. 1. (A) Prevalence of leukocyte esterase and nitrate positivity with results of urine culture. (B) Evaluation of candidate predictor of possible UTI in inpatient study population from univariate analyses.

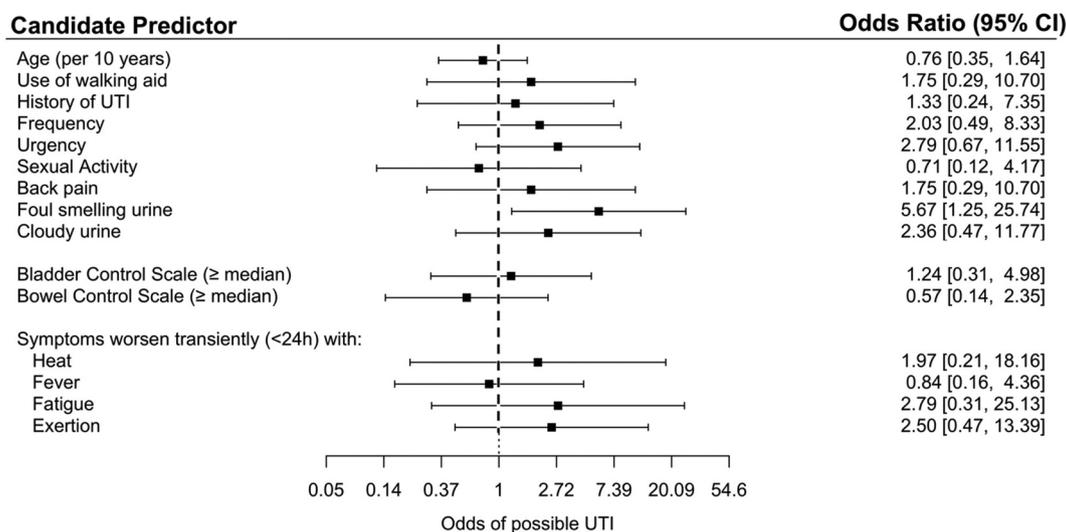


Fig. 2. Evaluation of candidate predictor of possible UTI in ambulatory care population from univariate analyses.

a possible UTI and no patients reported hematuria, we could not evaluate these variables as candidate predictors of UTI. We also observed a trend toward an increased odds of possible UTI by urinalysis for urgency, though results did not attain statistical significance (Fig. 2). Results were similar in preliminary multivariable models mutually adjusting for all potential candidate predictors; only foul-smelling urine was associated with a trend towards increased odds of possible UTI (OR: 7.62; 95% CI: 0.85–68.64; $p = 0.07$). History of Uththoff's-type phenomenon (e.g. transient worsening of neurologic symptoms in the context of fever, exertion, fatigue or heat) was not associated with possible UTI in univariate or multivariable-adjusted models. Again, sex could not be included in the models since no men had a UTI in this sample.

4. Discussion

We found that UTIs at the time of a suspected MS relapse were relatively uncommon; this finding was consistent in both a hospitalized as well as ambulatory patient population. In both cohorts, female sex was a strong risk factor for UTI. Other potential risk factors identified included a previous history of UTI, having a walking impairment and foul-smelling urine. Self-administered urine dipsticks were well-tolerated in the subgroup of patients who completed them; preliminary evidence suggests the dipsticks may maintain a high level of sensitivity but may lack specificity for detecting UTI. Notably, as our sample size was limited, larger studies are needed to calculate more reliable estimates of sensitivity and specificity.

While findings were not statistically significant in our study, we did observe a significant trend toward a positive association between a history of UTI and risk of possible UTI which is also consistent with the non-MS literature (Hu et al., 2004; Laupland et al., 2007; Scholes et al., 2000; Hooton et al., 1996). Furthermore, we also observed a marginal trend consistent with increasing disability and risk of UTI; this finding is also consistent with studies of non-MS older adults. In contrast to several existing studies of non-MS populations, we did not find an association between age and risk of UTI; it's possible that the age distribution in our studies was limited and we did not have sufficient power. However, in MS, relapses tend to diminish in frequency with age, so it's also possible that age may be a less relevant consideration at the time of suspected MS relapse. We also did not find an association between sexual activity and risk of UTI, which is in contrast to existing literature in non-MS populations (Hooton et al., 1996; Strom et al., 1987; Moore et al., 2008).

In our study, we evaluated possible UTI diagnosis using definitions

derived from results of urinalysis and urine culture to be as comprehensive as possible. Diagnosis of “uncomplicated” UTI in the general population is defined as having $> 10^5$ cfus/mL for women and $> 10^3$ cfus/mL for men. While widely applied, diagnostic thresholds among symptomatic individuals could potentially be much lower (Stamm et al., 1982; Smith et al., 1983). In the context of MS, interpretation of these results using standard thresholds may be challenging where symptomatic UTI may be masked by baseline urologic dysfunction.

Strengths of our study include its evaluation of prospectively-collected patient reported risk factor information in the outpatient portion; very few studies have determined whether common risk factors for UTI in the non-MS population could be similarly applied in people with MS. Furthermore, we also considered a set of additional potential risk factors that may be distinct in MS, as MS patients may have sensory impairments and baseline urologic dysfunction that may manifest as different UTI clinical presentations (Sliwa et al., 1996). Furthermore, our study had dual aims and was able to evaluate prevalence of UTI in two distinct clinical MS relapse populations.

Our study also has several noteworthy limitations. Sample sizes for both aims were relatively small, and we were unable to assess whether some patient characteristics were associated with possible UTI as few or no patients had them. For example, in the outpatient cohort, we could not evaluate whether sex or hematuria were associated with possible UTI. The small sample sizes and relatively limited number of probably/possible UTI also likely contributed to the wide confidence intervals for our estimated number needed to screen. Because of the limited sample size, we also did not perform analyses assessing risk factors for possible UTI separately or risk factors for confirmed-by-culture UTI; it's possible that risk factors themselves may differ or the strength of the association may differ by how strictly UTI is defined. Next, analyses of UTI risk factors in the hospitalization cohort were retrospective in nature; an absence of a history of UTI in the medical history or intake summaries does not necessarily imply a true lack of positive UTI history. Thus, potential misclassification could have impacted observed results. We also could not assess whether specific patient characteristics predictive of UTI in the general population were similar in the inpatient MS population nor could we evaluate whether MS or MS therapy-related (or lack thereof) characteristics (e.g. more detailed information on disability) could have impacted the results. Also, our study did not include a cohort of patients who presented to the Emergency Department with suspected relapse and only included the subset who were admitted. It's possible that the frequency and utility of assessing for potential UTI may differ when this population (e.g. those seen in the Emergency Department vs. those actually admitted) is also considered.

Furthermore, for the outpatient cohort we modified the design of the study due to slow recruitment. While this modification likely helped to facilitate recruitment, and we did not observe differences in results when adjusting for in-person versus remote assessments, it's possible patients willing to come in for a study visit may differ systematically from those who would not be willing to participate in an on-site study visit.

5. Conclusions

Results of our study suggest that UTI is relatively uncommon in people with MS presenting for a suspected relapse. Female sex, foul-smelling urine and potentially a previous history of UTI and current walking impairment are potential independent predictors of probably/possible UTI in people with MS with a suspected relapse. Future larger, prospective studies are needed to more robustly identify risk factors for confirmed UTI. The results of the larger studies may facilitate identification of targeted subgroups of patients in which screening for UTI at the time of a suspected MS relapse is most effective. Alternatively, follow-up studies may suggest a subgroup in which the likelihood of confirming a UTI is so low that routine screening for it, potentially delaying relapse treatment, is not necessary.

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