The prevention and management of hospital admissions for urinary tract infection in patients with multiple sclerosis

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Abbreviations: urinary tract infections (UTIs), patients with MS (PwMS) multiple sclerosis (MS), health episode statistics (HES), emergency department (ED), Extended Disability Status Score (EDSS), standard deviation (SD), indwelling catheter (IDC), secondary progressive MS (SPMS), primary progressive MS (PPMS), suprapubic catheter (SPC), intermittent self-catheter (ISC)

Abstract

Introduction: Urinary tract infections (UTIs) are one of the commonest reasons for patients with multiple sclerosis (PwMS) presenting to hospital. Management of recurrent UTIs in PwMS can be challenging and characteristics of such patients are not well described.

Aims: To describe the neurological and urological features of PwMS presenting to hospital for UTIs and identify areas of management that could be improved to reduce UTI frequency.

Methods: Health episode statistics data were used to identify PwMS presenting to a tertiary hospital with UTI over a 5-year period. Medical records were reviewed for demographic, MS and urological history. The seven PwMS with the highest numbers of encounters were seen in a multidisciplinary clinic to enable detailed assessments.

Results: 52 PwMS (25 female, 27 male) with mean age of 60 had 112 emergency department presentations and 102 inpatient admissions for UTI. 24 presented multiple times and were more likely to be older and male with progressive MS. Almost two-thirds were using a urinary catheter. Less than half were under current urological and neurological follow-up. *Escherichia coli* and *Pseudomonas spp* were the commonest organisms cultured. Resistance to antibiotics was more frequent in patients with multiple presentations.

Conclusions: PwMS presenting to hospital for UTIs are more often male, older, with progressive MS and high levels of disability. A small group of PwMS accounted for a large number of encounters. Preventative and management strategies can be applied in primary and secondary care settings, with an emphasis on bladder, catheter and general physical care.

Introduction

Urinary tract infections (UTIs) are common in people with multiple sclerosis (PwMS). Estimates of prevalence vary but has been reported to be between 13% and 80%. They are one of the most frequent reasons for emergency attendances and admissions amongst PwMS, have a major impact on morbidity and quality of life, increase mortality risk and add considerable cost to the health system[1]. UTIs had the strongest association with MS as the cause of death in a recent study that reviewed death certificate data[2].

Previous work by the University College London Partners MS Service Group which collected health episode statistics (HES) data from the University College Hospitals London NHS Foundation Trust, Royal Free London NHS Trust, Bart's Healthcare NHS Trust and other hospitals and clinical commissioning groups across the regional National Health Service community services, found that UTIs accounted for by far the greatest number of non-elective and total admissions in PwMS. The total cost across the 2012/2013 one-year period was over £800,000 and had increased to over £930,000 in 2016/2017[3].

The causes of UTIs in PwMS are multifactorial, including: presence of lower urinary tract dysfunction such as detrusor overactivity and detrusor-sphincter dyssynergia; detrusor hypocontractility leading to incomplete bladder emptying and high post-void residual volumes; introduction of urinary catheters; use of immunomodulatory disease-modifying therapies; and physical disabilities that make personal hygiene and toileting more difficult[1]. The epidemiology and characteristics of PwMS who experience recurrent UTIs and risk factors for those with very frequent unplanned hospital admissions are not well described. This group of patients can be challenging to manage for both primary and secondary care health practitioners.

We aimed to characterise the neurological and urological features of PwMS with unplanned hospital encounters for UTI and identify patient-specific and systemic areas of management that could be improved to reduce UTI frequency. Based on this, as well as existing management guidelines[4–6], we propose an algorithm for assessing and managing PwMS with frequent hospital presentations for UTI targeted for both primary and secondary care settings.

Methods

HES data were audited to identify PwMS with Emergency Department (ED) presentations and inpatient admissions for UTI as the primary diagnosis (code N390) to University College London Hospitals NHS Trust over 5 years (April 1, 2014-March 31, 2019). Records were reviewed for data including demographics, MS history (subtype, duration, Extended Disability Status Score [EDSS]), urological symptoms and interventions and admission(s) for UTI (duration, frequency, microbiology, treatment). Patients, their carers and GPs were contacted directly to obtain additional missing information. Patient data was anonymised and analysis performed in IBM SPSS Statistics 25. Clinical and demographic characteristics were summarised using frequency (%), mean (standard deviation [SD]) or median (range). T-

test was used when comparing mean of two independent groups and $p<0.05$ was considered to be statistically significant.

Subsequently, seven PwMS accounting for the highest numbers of encounters were seen in person in a multidisciplinary clinic with MS, urology and specialist nurse input to assess current neurological and urological management and identify strategies to reduce the frequency of future UTIs, guided by the national recommendations on management of neurogenic bladder.

The Queen Square Clinical Audit Committee approved this research as an audit study with a waiver of informed consent as assessments were conducted as part of routine clinical management.

Results

Characteristics of patients with multiple presentations

Demographics

Over the audited time period, 52 PwMS (25 female, 27 male) with mean age of 60 years (SD 13, range 27-84) had presented to ED and/or been admitted to hospital for UTI. Median EDSS was 8.5 (restricted to bed much of day but retains some use of arms and self-care functions). Six met the European Association of Urology criteria for recurrent UTIs (i.e. ≥3 in last 12 months or ≥2 in last 6 months)[7] and 18 had multiple presentations not meeting these criteria. 28 had only single presentations (Table 1). Those with multiple presentations were more likely to be older, male with progressive forms of MS and therefore less likely to be on current disease-modifying therapy. Frequently there were other associated comorbidities such as spasticity (n=6), cognitive impairment (n=3), visual impairment (n=3), pressure areas (n=3) and dysphagia (n=2).

Table 1. Demographics, MS and urological history of patients with unplanned hospital presentations for UTI.

	Total (n=52)	Multiple (n=24)	Single (n=28)
Demographics			
Age (years), mean (SD)	60 (13)	64 (9)*	56 (14)*
Male	27 (52%)	14 (58%)	13 (46%)
MS history			
MS subtype			
RRMS	12	1 (5%)*	11 (37%)*
SPMS	25	14 (64%)	11 (37%)
PPMS	11	6 (27%)	5 (17%)
Unknown	4	1	3
Duration of MS (mean, SD)	22 (10)	23 (11)	20 (9)
EDSS (median, range)	8.5 (4-10)	8.5	8.5
Currently on DMT	11 (21%)	1 (4%)*	10 (36%)*
Urological history			
Catheter (total)	33 (63%)	20 (83%)*	13 (46%)*

Suprapubic catheter (SPC)	18 (55%)	11 (44%)	7 (25%)
Indwelling catheter (IDC)	9 (27%)	8 (33%)*	1 (4%)*
Intermittent self-catheter (ISC)	6 (18%)	1 (4%)	5 (18%)
No catheter	15	2 (8%)*	13 (46%)*
Penile sheath	4	2 (8%)	2 (7%)
History of renal tract stones	7 (13%)	7 (100%)*	0 (0%)*
Detrusor overactivity on urodynamics	12/13 (92%)	5/5 (100%)	7/8 (88%)
Treatment for overactive bladder symptoms			
Antimuscarinic, β3-agonist	30	17 (71%)*	13 (46%)*
Intradetrusor botulinum toxin	10	5 (21%)	5 (18%)
Length of inpatient stay (days), mean (SD)	8.6 (17)	9.6 (19)	5.9 (11)

Abbreviations: SD – standard deviation, MS – multiple sclerosis, RRMS – relapsing remitting multiple sclerosis, SPMS – secondary progressive multiple sclerosis, PPMS – primary progressive multiple sclerosis, EDSS – extended disability status scale, DMT – disease-modifying therapy; *p-value <0.05

Urological history

Overall 33 (63%) patients were using a catheter (Table 1). PwMS with multiple presentations were more likely to be using a catheter, in particular a urethral indwelling catheter (IDC). 7 (13%) patients had a history of renal and/or bladder stones, all of whom had multiple UTI presentations. More PwMS with multiple UTI presentations had a history of catheter bypassing and blockages (n=5 and 3 respectively out of 20 patients using catheters [40%]) compared to those with single presentations (n=3 and 1 respectively out of 13 [31%]).

The majority of PwMS (16 of 24 [67%] with multiple presentations and 23 of 28 [82%] with single presentations) had not had renal tract imaging within the prior 12 months. Of the 33 patients using a catheter, 17 (52%) had undergone cystoscopy in the prior 5 years. Of the 13 patients who had urodynamic study results on record, detrusor overactivity was the most common finding (n=12 [92%]).

10 patients had received intradetrusor botulinum toxin and 30 had been on pharmacological therapy (antimuscarinics or β3-agonist) for overactive bladder symptoms. 22 patients (42%) were taking a form of UTI prophylaxis (11 antibiotics, 8 D-mannose, 5 methenamine, 4 cranberry). Only 21 (40%) were under current urology/uro-neurology and 20 (38%) under MS/neurology follow-up, although a small number had declined appointments due to poor mobility.

UTI presentations and microbiology culture results

In total there were 112 presentations to ED (range 1-11 per patient) resulting in 102 inpatient admissions (range 1-9 per patient) (Figure 1). Mean length of stay per admission was 8.6 days (SD 17, range 0-108) (9.6 days for those with multiple encounters compared to 5.9 days for those with single encounters). The ten most frequently presenting PwMS accounted for 50% of ED attendances and hospital admissions respectively (red box). PwMS who used a catheter had a greater mean number of ED attendances than those not catheterising (2.6 vs. 1.3, mean difference 1.3 [95% CI 0.3-2.5], p=0.045). There was a trend towards a higher mean number of ED presentations in male than female PwMS who used an IDC (6 vs. 1.8), but the difference did not reach statistical significance.

53 episodes required treatment with intravenous antibiotics and mean duration of antibiotic treatment was 6.8 days (SD 3.3, range 3-28). Infectious complications of UTI included urosepsis (n=7, 6.3%), epididymo-orchitis (n=1, 0.9%), prostatitis (n=1, 0.9%) and *Clostridium difficile* infection (n=1, 0.9%). Non-infectious complications included delirium (n=27, 24%) and acute kidney injury (n=6, 5.3%).

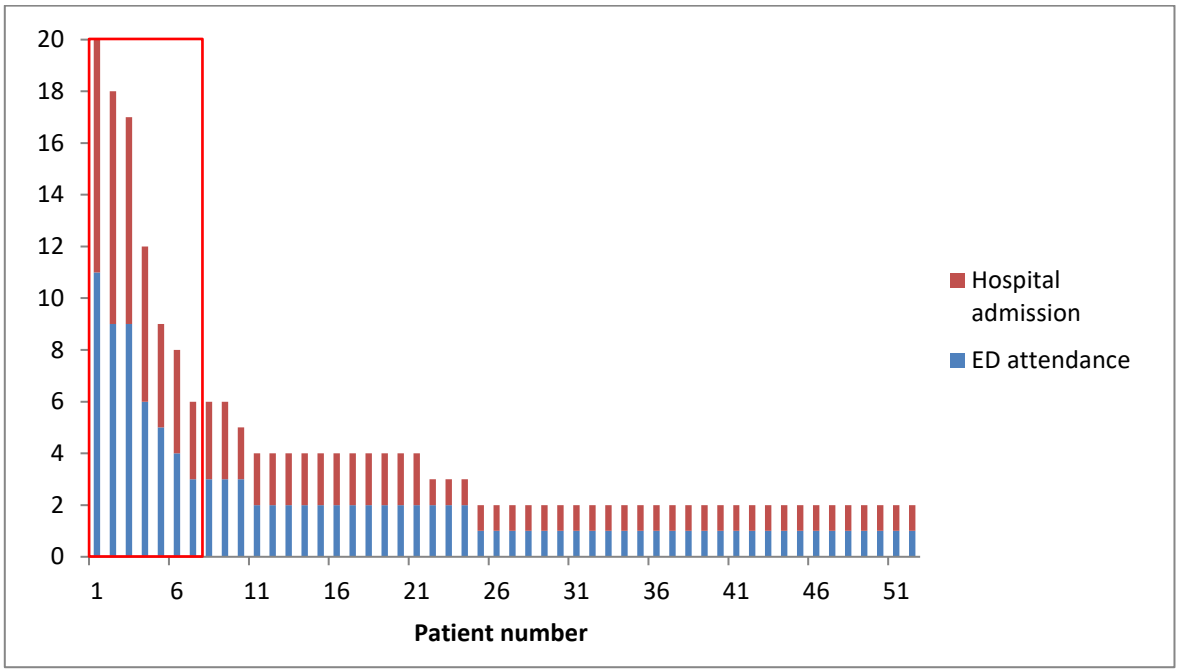

Figure 1. Numbers of ED attendances and hospital admissions for UTI.

During the period studied, results of 156 urine culture samples were available, comprising 112 (70%) samples from patients with multiple encounters and 47 (30%) from those with single encounters. 92 (59%) were catheter specimens, 65 (42%) were mid-stream urine specimen and 2 (1.3%) were taken from a nephrostomy. Excluding 48 samples (31%) which were reported as having no growth, the most common organism isolated was *E. coli* (23%) followed by *Pseudomonas spp* (22%) and *Klebsiella spp* (12%). However, relative proportions of organisms differed between samples taken from patients with a history of multiple versus single presentations for UTI (Figure 2) and those from catheter versus mid-stream urine. *Pseudomonas spp* was more common in catheter specimens whilst *E. coli* was more common in non-catheter specimens overall.

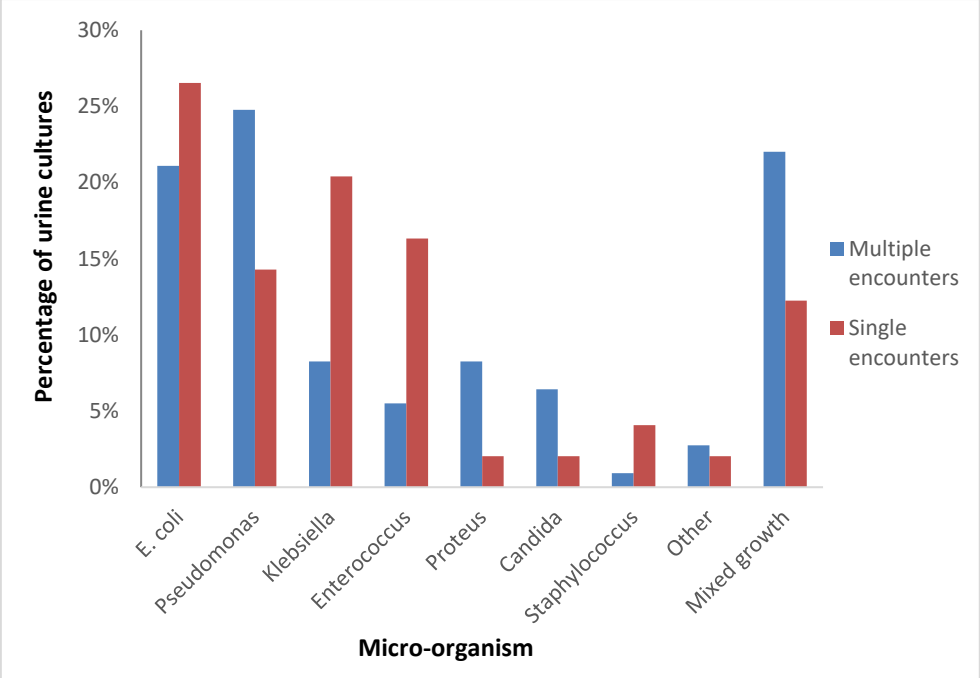

Figure 2. Range of organisms isolated from urine samples of patients with multiple and single encounters. 'Other' category included *Enterobacter spp.*, *Achromobacter insolitus*, *Stenotrophomonas maltophilia* and *Acinetobacter baumanii*.

Across all organisms, there was resistance to a greater number of antibiotics amongst PwMS with multiple encounters than single encounters. In the multiple encounters group, a higher number of specimens cultured organisms that were resistant to the antibiotics amoxicillin, trimethoprim, ciprofloxacin, gentamicin and cephalexin than were sensitive, whereas in the single encounters group, this was only the case for amoxicillin. In both groups, fewer specimens cultured organisms that were resistant to nitrofurantoin than were sensitive. This pattern was observed in the relative proportions of two of the three most common organisms (*E. coli* and *Klebsiella spp*) that were sensitive and resistant to several commonly prescribed antibiotics. *Pseudomonas aeruginosa* is intrinsically resistant to amoxicillin, nitrofurantoin and trimethoprim, so only data on ciprofloxacin and gentamicin are applicable (Figure 3).

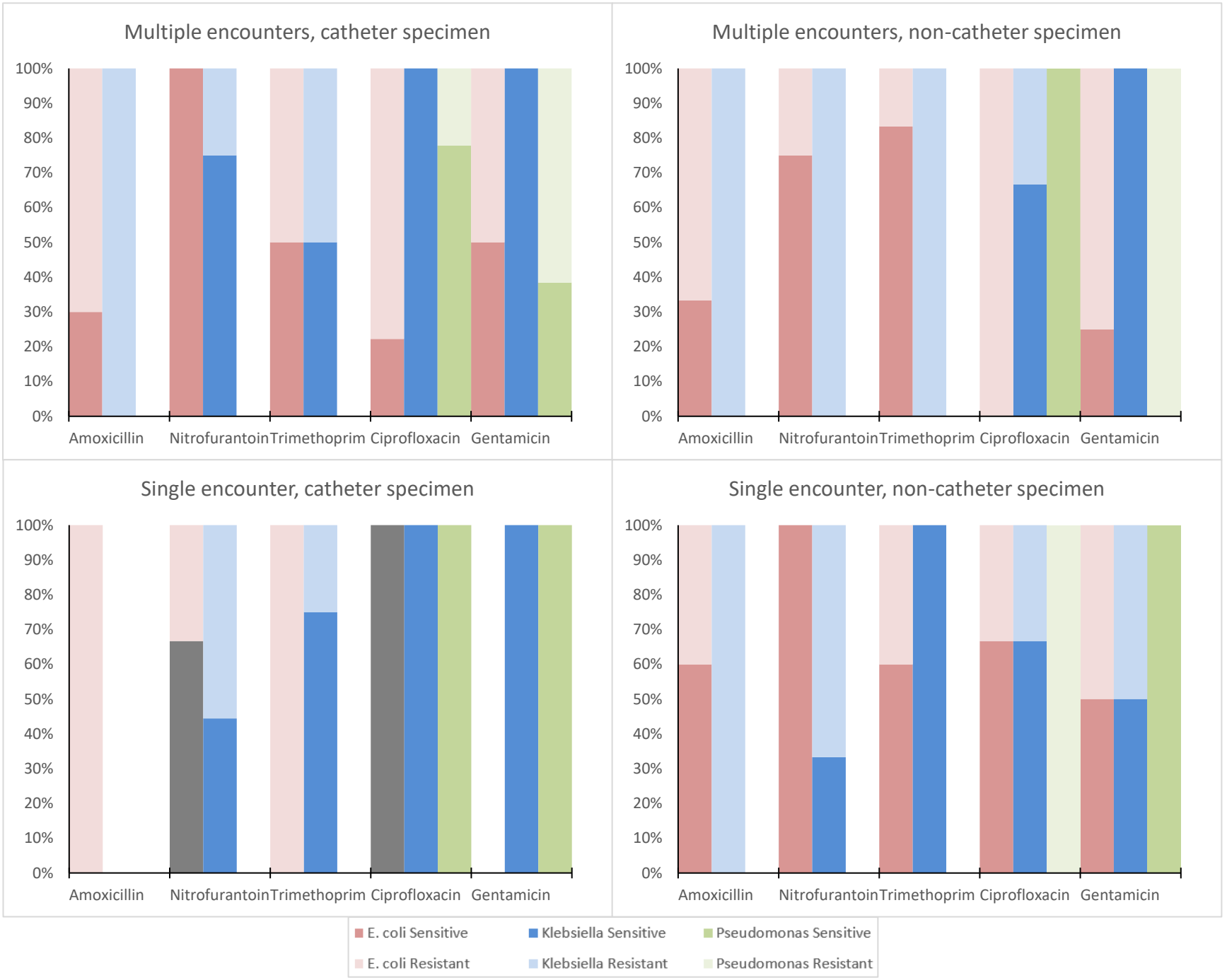

Figure 3. Relative sensitivity and resistance of *E. coli*, *Klebsiella spp* and *Pseudomonas spp* to selected antibiotics in patients with multiple and single encounters and from catheter and non-catheter specimens, noting that *Pseudomonas spp* is intrinsically resistant to amoxicillin, nitrofurantoin and trimethoprim.

Multidisciplinary clinic review

As an initial pilot, the PwMS accounting for the 7 (5 males) highest numbers of encounters (41% of ED presentations, 38% of admissions [red box, figure 1]) were reviewed in a multidisciplinary clinic with collaborative input from an MS neurologist, specialist nurse and urologist to assess current management and identify areas that could be improved.

Mean age was 62 (SD 13), mean MS duration was 18.7 years (SD 6.2) and median EDSS was 8 (range 7-9). All but one had progressive forms of MS (4 SPMS, 2 PPMS). Patients had a number of MS-related symptoms included spasticity (n=6), cognitive impairment (n=3), visual impairment (n=3), pressure areas (n=3) and dysphagia (n=2). 4 patients had SPCs, 2 had IDCs and 1 was using a penile sheath due to preference despite previously elevated post-void residual volumes. A history of catheter bypassing and/or blocking was reported by all 6 patients who had a catheter. 2 patients had a previous history of renal tract stones.

As part of the review, all patients received up-to-date renal tract ultrasound if they had not been imaging performed within the last 12 months. Reassuringly, there was no evidence of any upper renal tract abnormality in any of the patients and no focal structural abnormalities or stones were identified. Flexible cystoscopy was performed on 5 of the patients who had not had this within the last 12 months. The bladder was trabeculated in 4 cases and in 1 patient a bladder stone was identified.

Management recommendations included changing those with IDCs to SPCs (n=2), consideration of intradetrusor botulinum toxin to treat detrusor overactivity and reduce catheter bypassing (n=4), SubyG bladder instillations to reduce debris (n=2), topical oestrogen for vulvovaginal atrophy (n=1) and liasing with district nurses and carers to optimise catheter care, perineal hygiene and hydration (n=3). All patients had ongoing urological and neurological follow-up arranged.

Discussion

Identifying PwMS at increased risk of frequent UTIs

Based on our findings, we propose the following as high risk factors for UTIs resulting in unplanned hospital attendances in PwMS (Table 2). The male predominance amongst this cohort is notable, compared to community acquired UTIs which affect significantly more females[8]. Use of catheters, older age and the presence of neurogenic lower urinary tract dysfunction may explain this finding in PwMS. A history of UTIs that are recurrent and/or severe enough to result in hospital presentation or presence of the below risk factors in PwMS should prompt consideration of preventative strategies (Figure 4).

Table 2. Characteristics of PwMS with frequent UTIs.

Demographics	• Older age >60 • Male sex
MS factors	• Progressive MS
Urological factors	• Use of urinary catheter, particularly urethral indwelling catheter • Frequent catheter blockages (catheters blocking within 6 weeks of being changed) or bypassing

	• History of renal tract stones • Urine pH alkaline, history of *Proteus* infections

Prevention

According to existing guidelines on management of neurogenic bladder[4–6], key recommendations applicable to this cohort include:

- Measurement of post-void residual volume and catheterisation (ideally by ISC) if consistently >100ml;
- Optimisation of catheter type (i.e. changing from IDC to ISC or SPC, use of a catheter valve as opposed to continuous drainage into a leg bag in risk-assessed cases without elevated detrusor pressures or risk of upper renal tract damage);
- Adequate treatment of lower urinary tract symptoms;
- Periodic review by trained health care professional;
- Cystoscopy and ultrasound must be performed to exclude underlying abnormalities such as bladder and renal stones;
- Use of appropriate prophylactic agent if no alternative causes of recurrent UTIs are identified or significant complications from UTI.

Based on our findings as well as the above guidelines[4–6], we propose the following algorithm of prevention strategies for PwMS at high risk of UTIs (Figure 4).

Long-term prophylactic antibiotics are not routinely recommended due to concern about development of antimicrobial resistance and potential adverse effects[9,10]. The spectrum of organisms in complicated UTIs is greater than with uncomplicated UTIs and bacteria are more likely to be antibiotic-resistant[7]. This was the case in our cohort particularly for those who had multiple UTI presentations, where resistance to common first-line antibiotics was prevalent. As such, use of a single antimicrobial for prophylaxis is unlikely to be effective against the heterogeneous range of causative organisms. They should only be given routinely in specific situations such as before an invasive urological procedure.

Topical oestrogen may be of benefit in postmenopausal women with no contraindications to use. A Cochrane review concluded that based on two studies comparing vaginal oestrogens to placebo, vaginal oestrogens reduced the number of UTIs in postmenopausal women with recurrent UTIs[11].

Urinary retention and incomplete bladder emptying increase the risk of UTIs due to stagnation of urine and subsequent multiplication of bacteria[12]. UK guidelines recommend screening for voiding dysfunction by ultrasound or single in-out catheterisation and consideration of ISC in those with high post-void residual volumes of >100ml[4,6]. However, ISC while preferred may not be physically possible in the highly disabled group of PwMS as seen in our cohort and a long-term catheter is often required. Use of a long-term catheter itself is associated with risk of UTIs as a biofilm can form over the surface of catheters, acting as an environment where bacteria can grow relatively protected from antimicrobials and host defence mechanisms[13]. In these cases, SPC is preferred to urethral IDC[7]. To minimise catheter-associated UTIs, insertion should be performed under aseptic conditions with regular changes. A sufficiently large catheter (at least 16 French) should be used to reduce the risk of blockages. Closed catheter urinary drainage systems are designed to limit

the development of bacteriuria. A flip-flow valve attached to the catheter is preferred in patients with large capacity, low-pressure bladders who can manage this, thereby avoiding a drainage bag.

PwMS with higher levels of disability, especially those who are reliant on carers for personal activities of daily living, experience greater difficulties with maintaining adequate hydration, regular bathing and perineal hygiene and are more prone to constipation and pressure areas. These can increase the risk of UTIs and routine general physical review by a trained health care professional, in either primary or secondary care, to identify and address these issues is important for overall management of PwMS as well as to reduce UTIs.

In patients with recurrent UTIs, renal tract imaging should be performed to exclude underlying abnormalities such as stones[1]. Ultrasound can be used as a screening tool but non-contrast CT may be required if the index of suspicion is high. Other risk factors for stones that should particularly prompt consideration of imaging include a history of prior nephrolithiasis, infection due to urease-producing bacteria, such as *Proteus mirabilis*, and alkaline urine pH produced by formation of ammonia from urea. As urine pH rises, calcium and magnesium phosphate crystals can precipitate in the urine and catheter biofilm, eventually leading to encrustation, and complications such as catheter blockage, bypassing of urine and bladder stone formation[13]. Urine pH >7 was also identified as a risk factor based on a recent retrospective study that used multivariate logistic regression analysis to develop a risk prediction nomogram for UTIs in patients with neurogenic bladders[14]. Acidification of urine using bladder instillations such as SubyG solution may reduce encrustation and subsequent stone formation[15]. Administration of oral L-methionine has been shown to decrease urinary pH and the risk of struvite and calcium phosphate stone formation in healthy subjects[16].

Detrusor overactivity is common in PwMS and was the most frequent urodynamic finding amongst our cohort. Typically detrusor overactivity presents with overactive bladder symptoms of urgency, frequency, urge incontinence and nocturia. However, in patients with catheters, it can manifest as bladder spasms, recurrent catheter blockages or urine bypassing around the catheter. PwMS experiencing these symptoms along with frequent UTIs should be referred to a urologist to consider treatments such as antimuscarinic agents or intradetrusor botulinum toxin injections. Whilst the latter is usually administered to those with urodynamically-proven detrusor overactivity, empirical treatment may be considered in PwMS with the above symptoms who are too disabled to undergo invasive urodynamic studies. Intradetrusor botulinum toxin has been found to reduce the incidence of symptomatic UTIs. The mechanism for this is uncertain, but may be due to improvement in urodynamic parameters including bladder capacity at low pressure[17]. Whilst we found antimuscarinic or β3-agonist use was higher amongst PwMS with multiple UTI presentations, this may be due to those with more severe neurogenic bladder being both more likely to develop UTIs and to need medical management of detrusor overactivity. Of note, only a minority of PwMS in this cohort had undergone urodynamics. Although this may be partly due to the greater difficulty in performing invasive studies in patients with higher levels of disability, it also suggests that urological review may not currently be entrenched in management of a PwMS with lower urinary tract symptoms and recurrent UTIs.

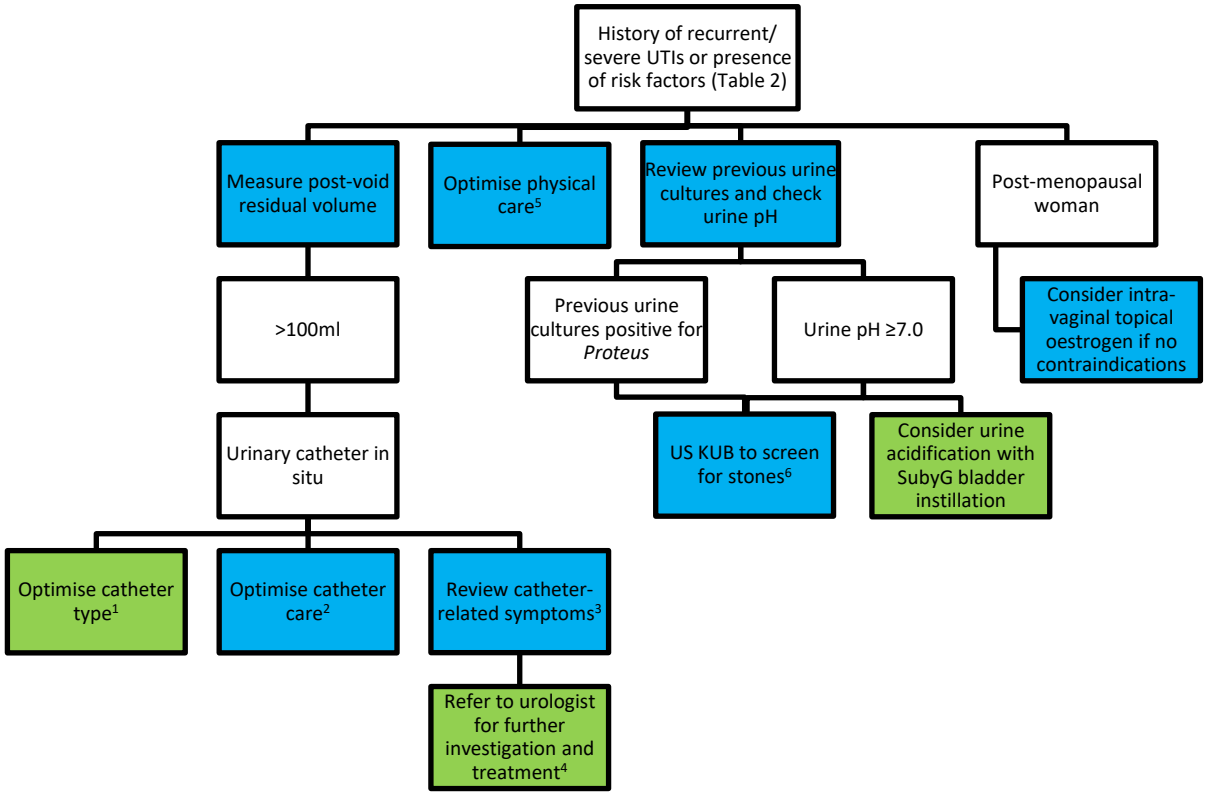

Figure 4. Algorithm for prevention strategies in PwMS at high risk of UTIs. Blue shading indicates measures that could be initiated in primary care; green shading indicates measures that may require specialist referral. US KUB – ultrasound kidney ureters bladder.

1. Clean ISC or SPC preferred to IDC, use size ⩾16Ch.
2. Regular assessment of hygiene, regular catheter changes, flip-flow valve attached to catheter rather than drainage bag in appropriate patients.
3. Including blockages and bypassing.
4. Including cystoscopy and antimuscarinics or intradetrusor botulinum toxin.
5. Hydration and nutrition, perineal hygiene, pressure areas, constipation.
6. If US KUB shows findings suspicious for stones, CT kidney ureters bladder should be performed to confirm the findings and the patient referred to a urologist for further investigation (including sending stone fragments for stone biochemistry) and treatment.

Management

Management of PwMS with UTI has been previously reviewed[1] and the key points are summarised in Box 1.

1. Distinguish between asymptomatic bacteriuria, which is almost universal in patients with long-term catheters and does not require antimicrobial treatment, and symptomatic infection.
2. Symptoms of UTI may differ in PwMS, who can have urological, neurological or systemic manifestations.
    - Urological – change in odour or appearance (e.g. cloudiness, haematuria, increased sediment) of urine, dysuria, increased frequency, urgency, incontinence, catheter blockages, bypassing of urine around catheter;

- Neurological – delirium, reduced level of consciousness, flare of existing neurological conditions (e.g. spasticity, weakness, mobility, balance, neuropathic pain);
- Systemic – fever, malaise, lethargy.

3. If symptomatic infection is suspected, obtain a urine specimen ideally in a boric acid container, which can reduce mixed growth results from contaminants without the need for prompt refrigeration of the sample in order to produce a dominant organism[18].
    - In the presence of a catheter, the specimen should be obtained from the sampling port or catheter valve and not from the drainage bag as this may contain contaminated urine.
4. Commence empirical antibiotics guided by the patient's previous urine culture results and local susceptibility data. This should ideally be as narrow-spectrum as possible, taking into account that micro-organisms causing UTIs in patients with neurogenic bladders are different to those in healthy individuals[19].
    - Results from this cohort suggest that of the commonly prescribed empirical oral antibiotics, organisms were more likely to be sensitive than resistant to nitrofurantoin, along with co-amoxyclav, cefuroxime and fosfomycin. On the other hand, organisms were more likely to be resistant to trimethoprim and amoxicillin. These findings to be interpreted with caution in the context of local data.
5. Depending on results of the urine culture, the original antibiotic may be continued or changed. The appropriate antibiotic should generally be given for 5 to 7 days, but can be extended up to 14 days depending on severity of infection[5].
6. PwMS with recurrent UTIs who recognise early symptoms of infection can be prescribed a course of self-start antibiotics to keep at home in order to reduce delay in initiating treatment and risk of developing a more severe infection.

Table 3. Clinical presentations of UTIs in PwMS.

Urological	• Change in odour of urine • Change in appearance of urine (e.g. cloudiness, haematuria, increased sediment) • Dysuria • Increased frequency, urgency, incontinence • Catheter blockages, bypassing of urine around catheter
Neurological	• Delirium, reduced level of consciousness • Flare of existing neurological conditions (e.g. spasticity, weakness, mobility, balance, neuropathic pain)
Systemic	• Fever, malaise, lethargy

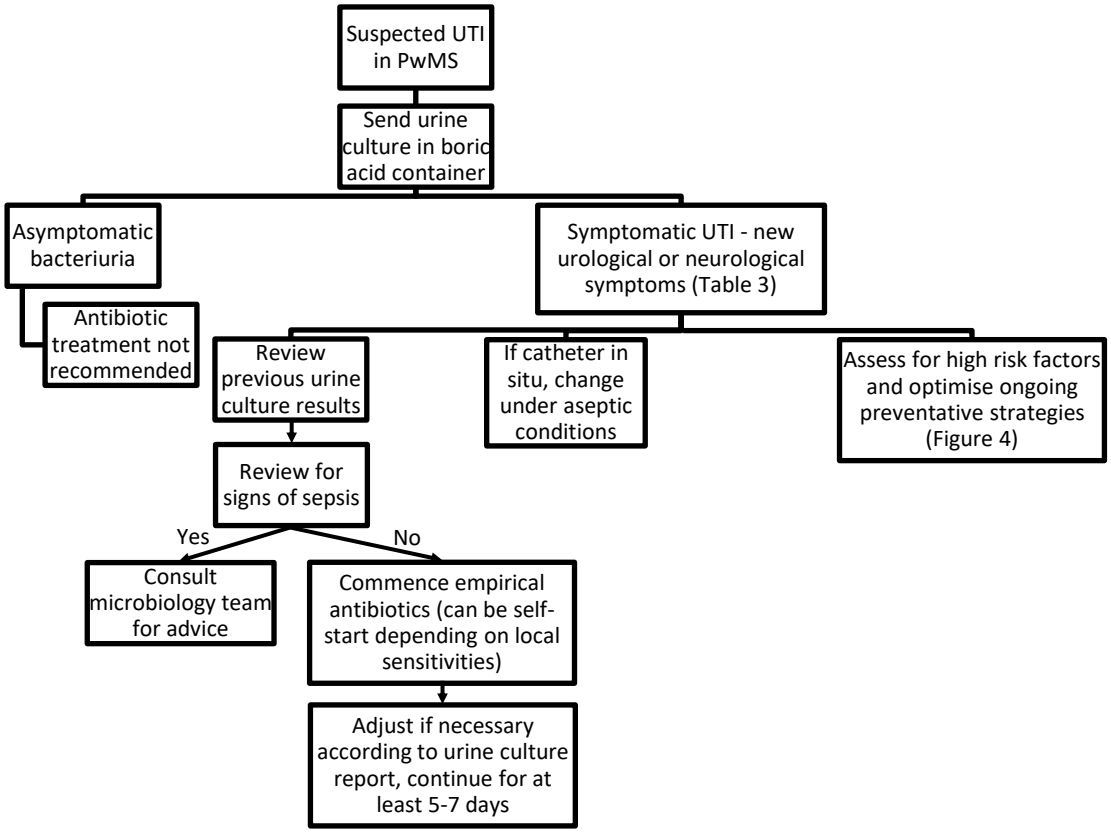

Figure 5. Algorithm for management of suspected UTI in PwMS.

PwMS with recurrent UTIs who recognise early symptoms of infection can be prescribed a course of self-start antibiotics to reduce delay in initiating treatment and risk of developing a more severe infection. Following onset of typical symptoms a pre-antibiotic urine sample should be obtained in a supplied boric acid container ideally prior to commencing antibiotics. The choice of self-start antibiotic depends on previous known sensitivities, selecting the narrowest spectrum agent available. Treatment adjustment may be required after results of the urine culture are known. The patient should seek further medical attention if symptoms do not improve by 48 hours or worsen. For patients with a febrile UTI, whether they have a catheter or not, the implication is that the upper urinary tract maybe at risk. Hence, clinical review for signs of sepsis, consultation with the microbiology team for advice regarding specific antibiotic prescription bespoke for the patient, based on meticulous review of their previous culture results, is recommended.

Community approach

To improve management of PwMS with UTI and reduce non-elective hospital encounters, it is important to engage with local and community partners as well as patients and their families or carers. Work by the UCLP MS Service Group to understand the impact of UTI and unplanned admissions on patients and families found that key issues included fragmentation of care, delays in accessing timely expert advice and treatment especially out-of-hours, difficulties in navigating health systems and lack of information sharing between different clinicians. PwMS would like support to self-manage where possible[3]. From this, a new model of care called NeuroResponse® (York Health Economics Consortium,

2018) was developed to improve the quality of life of people living with long-term neurological conditions including MS using technology and is currently being scaled across London[20].

A multidisciplinary approach involving clinicians in MS, urology and microbiology, patients, their families and GP is recommended. Our pilot UTI clinic to review PwMS with the most frequent hospital encounters efficiently identified management gaps and proposed individualised treatment strategies based on each clinician's area of expertise. A comprehensive one-stop clinic is more convenient to attend than separate appointments for PwMS with high levels of disability in whom transport is challenging. Telemedicine consultations have already been carried out with success in a small number of such patients and expansion of its use is feasible and should be considered in the future, given the mobility challenges associated with this patient group.

Limitations

This study was based on retrospective review of patient records identified using HES data. The code N390 refers to 'Urinary tract infection, site not specified' and depends on the accurate primary diagnosis being entered by the treating clinician. Due to clinician differences, there may be variability in how the diagnosis of UTI was made, for example whether it was based on suggestive symptoms and a positive urine dipstick at the point of ED presentation or only once a subsequent positive urine culture was obtained.

As this study only included PwMS who presented to hospital, the population has a high median EDSS, includes a relatively large proportion of PwMS with progressive disease. It is not necessarily generalisable to the overall population of PwMS who develop UTIs, most of whom would be managed in the community. However, we have focused on this group as UTIs resulting in hospital presentation are associated with significant morbidity and cost to the health system, as demonstrated by lengthy admissions and resultant complications. These cases are particularly challenging but successful management in a multidisciplinary environment can have a major positive impact. Whilst the sample size may not have had sufficient power to detect statistically significant differences in some of the variables compared, the algorithms we have recommended based on our findings are also supported by existing guidelines and prior studies. However, it would be important to validate these in prospective studies with a control group and other larger cohorts.

Conclusions

UTIs is a common cause of ED attendances and hospital admissions amongst PwMS. They are more often male (in contrast to female predominance in the general population), older, with progressive MS and high levels of disability. A small group of PwMS account for a large number of encounters. Compared to those with a single encounter, they were significantly older, more likely to have progressive MS and to use a catheter, though level of disability was similar in both groups. Presenting symptoms could be neurological, urological or systemic. Urine cultures produced a heterogeneous range of organisms with relatively high levels of antibiotic resistance, particularly in PwMS with a history of multiple UTI presentations. Based on our findings and existing guidelines, we propose a number of

preventative and management strategies in both primary and secondary care settings, with an emphasis on optimising bladder, catheter and general physical care.

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Figure and table legends

Table 1. Demographics, MS and urological history of patients with unplanned hospital presentations for UTI.
Abbreviations: SD – standard deviation, MS – multiple sclerosis, RRMS – relapsing remitting multiple sclerosis, SPMS – secondary progressive multiple sclerosis, PPMS – primary progressive multiple sclerosis, EDSS – extended disability status scale, DMT – disease-modifying therapy; *p-value <0.05

Table 2. Characteristics of PwMS with frequent UTIs.

Table 3. Clinical presentations of UTIs in PwMS.

Figure 1. Numbers of ED attendances and hospital admissions for UTI.

Figure 2. Range of organisms isolated from urine samples of patients with multiple and single encounters.

Figure 3. Relative sensitivity and resistance of *E. coli*, *Klebsiella spp* and *Pseudomonas spp* to selected antibiotics in patients with multiple and single encounters and from catheter and non-catheter specimens, noting that *Pseudomonas spp* is intrinsically resistant to amoxicillin, nitrofurantoin and trimethoprim.

Figure 4. Algorithm for prevention strategies in PwMS at high risk of UTIs. Blue shading indicates measures that could be initiated in primary care; green shading indicates measures that may require specialist referral.
[1.] Clean ISC or SPC preferred to IDC, use size $\geqslant$16Ch.
[2.] Regular assessment of hygiene, regular catheter changes, flip-flow valve attached to catheter rather than drainage bag in appropriate patients.
[3.] Including blockages and bypassing.
[4.] Including cystoscopy and antimuscarinics or intradetrusor botulinum toxin.
[5.] Hydration and nutrition, perineal hygiene, pressure areas, constipation.
[6.] If US KUB shows findings suspicious for stones, CT KUB should be performed to confirm the findings and the patient referred to a urologist for further investigation (including sending stone fragments for stone biochemistry) and treatment.

Figure 5. Algorithm for management of suspected UTI in PwMS.