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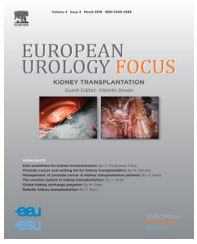

Guidelines

Evaluation and Treatment in Urology for Nocturia Caused by Nonurological Mechanisms: Guidance from the PLANET Study

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Abstract

Patients with nocturia are commonly referred to urology clinics, including many for whom a nonurological medical condition is responsible for their symptoms. The PLanning Appropriate Nocturia Evaluation and Treatment (PLANET) study was established to develop practical approaches to equip healthcare practitioners to deal with the diverse causes of nocturia, based on systematic reviews and expert consensus. Initial assessment and therapy need to consider the possibility of one or more medical conditions falling into the "SCREeN" areas of Sleep medicine (insomnia, periodic limb movements of sleep, parasomnias, and obstructive sleep apnoea), Cardiovascular (hypertension and congestive heart failure), Renal (chronic kidney disease), Endocrine (diabetes mellitus, thyroid disease, pregnancy/menopause, and diabetes insipidus), and Neurology. Medical and medication causes of xerostomia should also be considered. Some key indicators for these conditions can be identified in urology clinics, working in partnership with the primary care provider. Therapy of the medical condition in some circumstances lessens the severity of nocturia. However, in many cases there is a conflict between the two, in which case the medical condition generally takes priority on safety grounds. It is important to provide patients with a realistic expectation of therapy and awareness of limitations of current therapeutic options for nocturia.

Patient summary: Nocturia is the symptom of waking at night to pass urine. Commonly, this problem is referred to urology clinics. However, in some cases, the patient does not have a urological condition but actually a condition from a different speciality of medicine. This article describes how best the urologist and the primary care doctor can work

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together to assess the situation and make sensible and safe treatment suggestions. Unfortunately, there is sometimes no safe or effective treatment choice for nocturia, and treatment needs to focus instead on supportive management of symptoms.

1. Introduction

Nocturia may be present if the rate of urine production by the kidneys is increased, either at night or all the time. This can happen in endocrine, renal, cardiovascular, or neurological disease, associated with the following:

1. Daytime retention of salt and water, with night-time diuresis (eg, peripheral oedema).
2. Loss of solutes in the urine (eg, glucose in poorly controlled diabetes mellitus [DM]).
3. Night-time natriuresis or impaired urine concentrating mechanism in the renal medulla (eg, chronic kidney disease [CKD]).

Furthermore, a sleep or neurological disorder may increase arousals or cause an increase of the proportion of light sleep that will raise the likelihood of waking, and once wakened the patient may then pass urine. Thus, many medical conditions can be directly relevant to the symptom of nocturia [1,2].

Patients with nocturia are commonly referred to urology clinics, and potentially this includes cases where a medical condition is actually responsible, which lies outside the expertise available in the clinic. The wide-ranging and interactive effects of possible relevant factors mean that single specialities often need practical guidance on a suitable way to proceed if a particular condition is suspected, which is not part of their normal practice.

The PLanning Appropriate Nocturia Evaluation and Treatment (PLANET) study was established to develop practical approaches to equip healthcare practitioners to provide appropriate advice for a patient with nocturia. It undertook a series of systematic reviews (SRs) to scrutinise the current evidence base for nocturia mechanisms, assessment, and treatment in key medical areas. The protocol of the SRs was registered on PROSPERO (CRD42019157821). A series of expert consensus meetings were then undertaken to develop guidance suitable for settings where specialist knowledge is not directly available for the condition under consideration.

The current paper is a brief synthesis of the PLANET guidance on medical causes of nocturia, intended for advising urologists. It aims to offer a practical guide to key points looking at initial evaluation (Table 1) and supplementary evaluations (Table 2), the latter following on once initial testing results have been received and interpreted. For a detailed description of the evidence used and consensus statements, readers are referred to the relevant documents [3–7].

2. Methods

Nominal group technique (NGT) is a semiquantitative structured group interview process for developing consensus [8,9]. It was used to consider the relationship between medical conditions and nocturia for clinical management in a primary care setting. The NGT panels included specialists in nephrology, cardiology, endocrinology, sleep medicine, neurology, primary care, care of older people, and urology, along with public involvement. Participants received the studies identified in the SRs in advance of the NGTs. Both face-to-face and online meetings were held in a standardised format. Nominal groups were conducted until concept saturation was reached.

3. Recommendations

3.1. Establishing the impact of nocturia

The International Continence Society–standardised terminology should be used, which defines nocturia as the number of times urine is passed during the main sleep period. Having woken to pass urine for the first time, each urination must be followed by sleep or the intention to sleep [10]. This definition does not require "reason for waking" to be determined for nocturia to be diagnosed.

In the context of considering potential medical causes, the symptom of nocturnal polyuria (defined as passing large volumes of urine during the main sleep period [10]) is potentially important.

It is imperative to determine the degree to which function is impaired and the negative impact on quality of life, to make decisions about thresholds for treatment.

3.2. Review of medical history and medications

A review of the past medical history should consider potentially relevant "SCREeN" conditions already diagnosed in the patient:

1. Sleep medicine:
   (a) Insomnia.
   (b) Restless legs syndrome (RLS) and periodic limb movements of sleep (PLMS).
   (c) Parasomnias.
   (d) Obstructive sleep apnoea (OSA); this can be seen in isolation, or with respiratory, cardiovascular, endocrine, or neurological diseases [11].
2. Cardiovascular:
   (a) Hypertension.
   (b) Congestive heart failure (CHF).
3. Renal:
   (a) CKD.
4. Endocrine:
   (a) DM.
   (b) Overactive thyroid or profoundly underactive thyroid.
   (c) Pregnancy/menopause.
   (d) Diabetes insipidus.
   (e) Testosterone deficiency.
5. Neurology:
   (a) Most neurological diseases are potentially relevant.

Xerostomia ("dry mouth") may prompt increased fluid intake. Hence, autoimmune diseases identified in the past

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Table 1 – Initial evaluation

1. Establishing the impact of nocturia
   (a) Nocturia severity and overnight volume of urine
   (b) Impaired function the following day. Quality of life
2. Review of PMH and medications
   (a) Identify SCREeN conditions diagnosed previously:
   - Sleep medicine: OSA, insomnia, RLS/PLMS, parasomnias
   - Cardiovascular: hypertension, CHF
   - Renal: CKD
   - Endocrine
   - Neurology

   (b) Identify medical causes of xerostomia: autoimmune diseases affecting salivary glands, diabetes mellitus, CKD [12]
   (c) Review of medications: diuretics, calcium channel blockers, lithium, NSAIDs, and drug causes of xerostomia
3. Screening questions for identifying possible SCREeN conditions that have not been diagnosed previously
   (a) Do you have problems sleeping aside from needing to get up to urinate? (Sleep)
   (b) Have you been told that you gasp or stop breathing at night? (Sleep)
   (c) Do you wake up without feeling refreshed? Do you fall asleep in the day? (Sleep)
   (d) Do you experience ankle swelling? (Cardiac, Renal)
   (e) Do you get short of breath on walking for a certain distance? (Cardiac, Renal)
   (f) Do you get lightheaded on standing? (Cardiac, Neurological)
   (g) (Females of relevant age) Have you noticed changes in your periods? (Endocrine)
   (h) Have you been feeling excessively thirsty? (Endocrine)
   (i) Do you have any problems controlling your legs? Do you experience slowness of movement? Have you noticed a tremor in your hands? (Neurological)
4. Gross examination
   (a) Reduced salivation, scleroderma
   (b) Peripheral oedema
   (c) Lower limb weakness, abnormalities of gait or speech, tremor
5. Baseline investigations
   (a) 72-h bladder diary
   (b) Blood tests: electrolytes/renal function, thyroid function, calcium, HbA1c
   (c) Urine dipstick: ACR, blood (protein)
   (d) Blood pressure assessment
   (e) Pregnancy test (where applicable)

ACR = urine albumin:creatinine ratio; CHF = congestive heart failure; CKD = chronic kidney disease; NSAID = nonsteroidal anti-inflammatory drug; OSA = obstructive sleep apnoea; PLMS = periodic limb movements of sleep; PMH = past medical history; RLS = restless legs syndrome; SCREeN = Sleep medicine, Cardiovascular, Renal, Endocrine, and Neurology.

Table 2 – Additional questions where an underlying sleep disorder is suggested by initial screening

1. Insomnia
   "Do you have difficulty falling or staying asleep?"
   "How well do you function during the day?"
2. OSA
   "Do you snore and sometimes wake up choking?"
   "Does your partner say that you stop breathing?"
   "Do you often wake with a headache?"
3. RLS/PLMS
   "What does it feel like?"
   "Does it vary over the day and is it worse later in the day/evening?"
   "Is it relieved by movement?"
   "Does it come back again a few minutes after you sit or lie back down?"
   "Does your bed partner complain that you have twitchy legs or make kicking movements in your sleep?"
4. Parasomnias
   "Are you aware of, or have you been told about, any odd events at night such as walking around the home, screaming, eating, or engaging in sexual activity?"
   "At what age did you first experience the events?"
   "Do you recall the events?"
   "If woken from an episode do you recall dreaming?"
   "Are your eyes open during the episodes?"
   "What time of night do they occur?"
   "Do you stay in bed or get out of bed?"
   "Have you hurt yourself or someone else?"
   "Do you have nightmares, meaning terrifying awful dreams rather than just anxious unpleasant dreams?"

OSA = obstructive sleep apnoea; PLMS = periodic limb movements of sleep; RLS = restless legs syndrome.

medical history should be noted, due to potential effects on the salivary glands [12].

Fig. 1 lists a selection of medical diagnoses implicated in causing nocturia.

Relevant medications include diuretics, calcium channel blockers, lithium, and prolonged use of nonsteroidal anti-inflammatory drugs. Drugs that can cause xerostomia include anxiolytics, antidepressants (particularly tricyclics), antimuscarinics, antihistamines, decongestants, antiparkinsonians, and some pain medicines or antipsychotics. Alcohol and caffeine are also important because of a diuretic effect. Xerostomia is common in polypharmacy [13].

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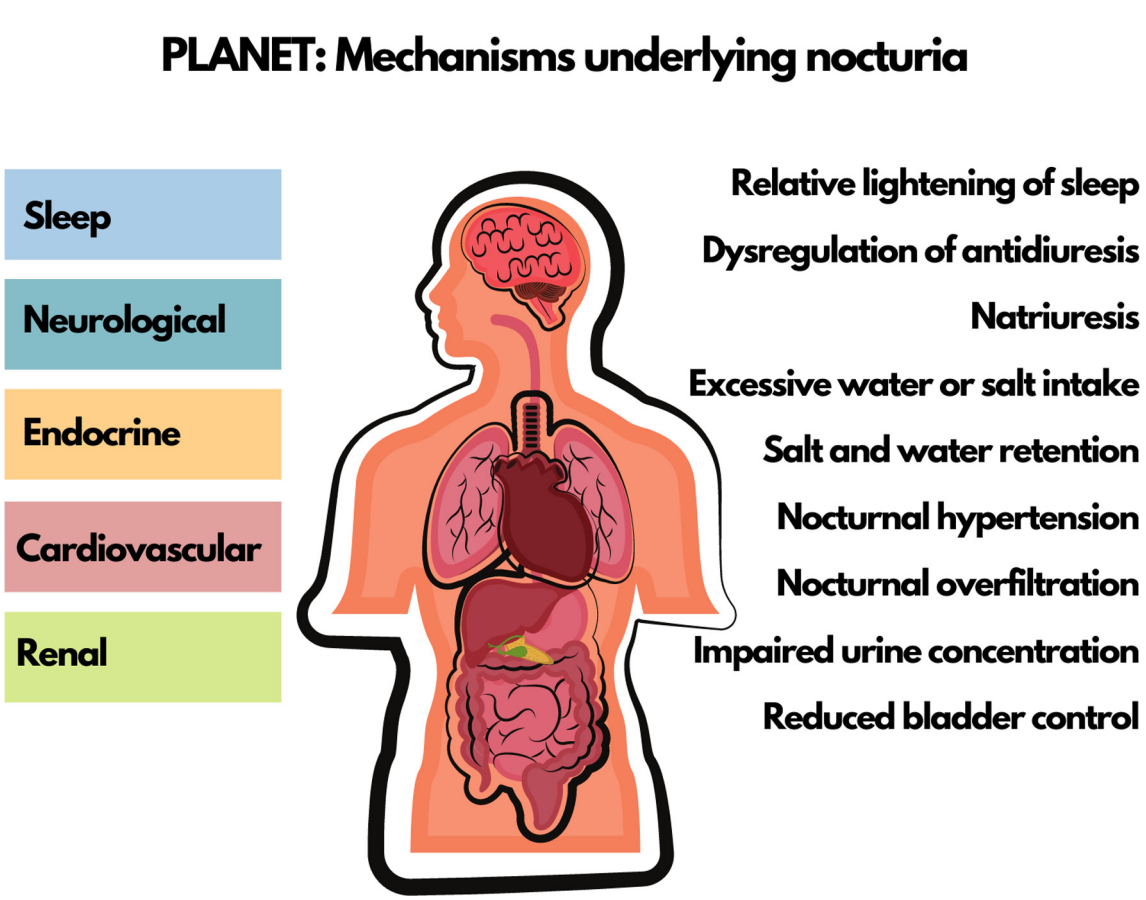

Fig. 1 – Mechanisms by which medical conditions can cause nocturia. PLANET = PLanning Appropriate Nocturia Evaluation and Treatment.

3.3. *Screening questions*

A list of questions is included in Table 1 and Fig. 2 to enable a practical approach to identifying possible presence of a SCREeN condition.

All the screening questions should be asked for every patient:

1. To help identify whether an undiagnosed SCREeN condition is present.
2. To indicate whether a SCREeN condition present in the past medical history needs therapeutic reassessment.

Table 2 includes further questions if an underlying sleep disorder is suggested by initial screening.

Specific consideration of a possible undiagnosed neurological disease is needed if the patient reports "suspicious" symptoms (eg, numbness, weakness, speech disturbance, gait disturbance, memory loss/cognitive impairment, and autonomic symptoms) or unusual aspects (eg, enuresis without chronic retention) [14].

3.4. *Examination*

A general examination is appropriate, but specific features for evaluating nocturia are not extensive:

1. Reduced salivation (xerostomia).
2. Peripheral oedema (noting that fluid retention can sometimes be present without manifest oedema).
3. Neurological dysfunction may be apparent from lower limb weakness, abnormal gait, speech, or tremor.

Carefully conducted measurement of blood pressure (BP) [15], if not included in the referral letter, is required.

3.5. *Initial investigations*

1. Bladder diary:
   (a) Nocturnal polyuria is defined as >20% (in younger age groups) and >33% (in older people) of daily urine volume being passed during the main sleep period [10].
   (b) Twenty-four–hour polyuria is defined as daily output of >40 ml/kg/24 h.
   (c) The International Consultation on Incontinence Questionnaires (ICIQ) bladder diary is suitable, as it can be used to identify nocturnal frequency, nocturnal polyuria index, and whether the patient experiences urinary urgency overnight [16,17].
   (d) The patient may need advice and support in completing the diary if they have any capacity limitations, such as impaired mobility in neurological disease.
2. Blood tests: electrolytes/renal function, thyroid function, calcium, and HbA1c:
   (a) These are aimed at identifying renal or endocrine disease.
3. Dipstick testing for haematuria and urine albumin:creatinine ratio; also proteinuria, though the test is only 80% sensitive [18]:
   (a) These are potential indicators of CKD.

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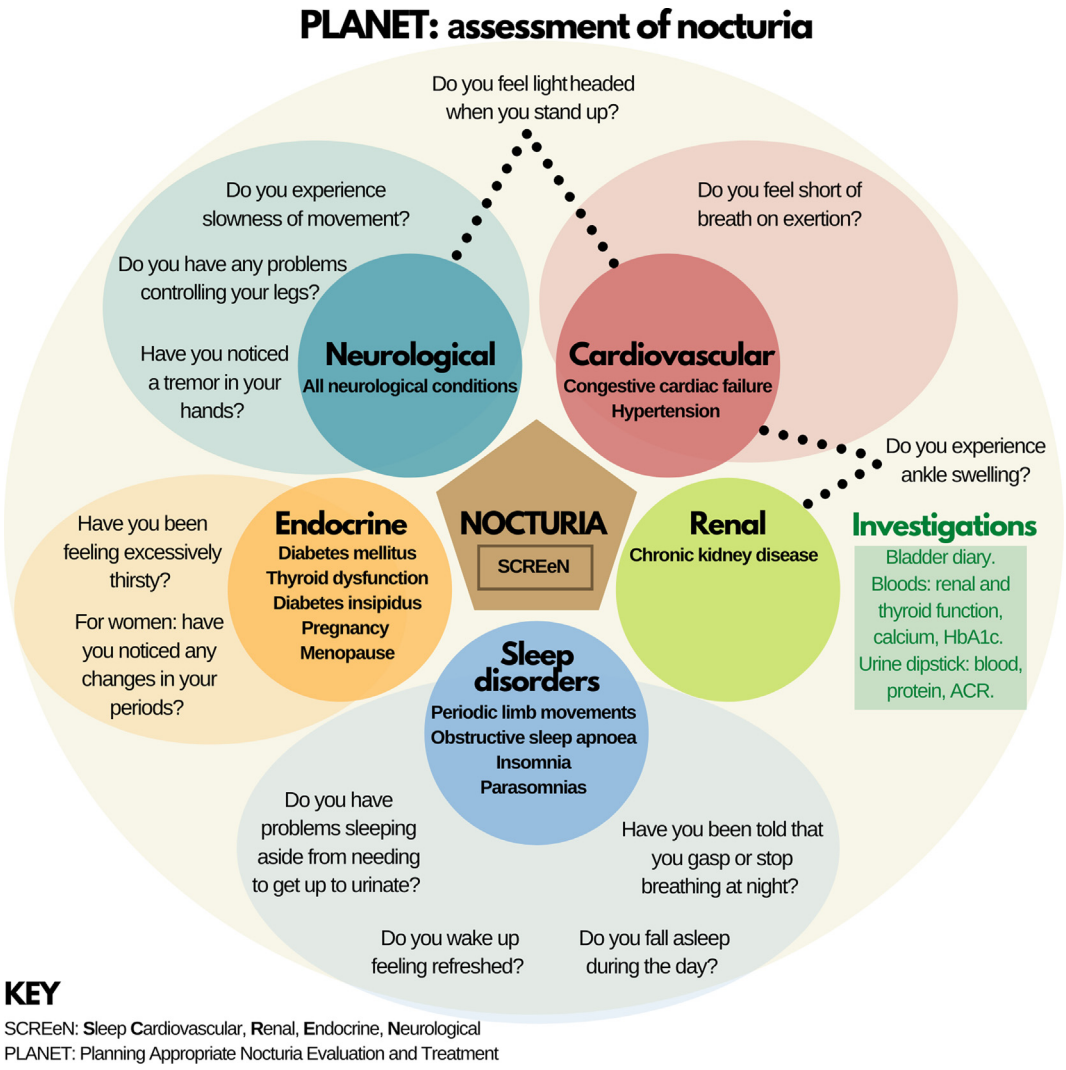

Fig. 2 – Medical conditions that can cause nocturia, with screening questions and initial investigations. ACR = urine albumin:creatinine ratio; PLANET = PLanning Appropriate Nocturia Evaluation and Treatment; SCREeN = Sleep medicine, Cardiovascular, Renal, Endocrine, and Neurology.

4. Clinical review and supplementary evaluations

The full checklist of conditions should be covered for each patient, to ensure that all possible causes are considered, since nocturia is commonly multifactorial.

The results of the initial investigations are likely to require a review at a follow-up appointment. Positive findings may necessitate supplementary evaluation before confirmed or suspected diagnosis can appropriately be made.

Some SCREeN diagnoses can be made in the primary care or urology setting (eg, DM or CKD). Some conditions may only be suspected, due to the necessity for the input of the relevant speciality for confirmatory diagnostic tests (eg, OSA). Hence, there may be diagnostic uncertainty.

Supplementary evaluations for medical causes are generally not suited to the urology clinic. In most cases, they are undertaken and coordinated by primary care physicians.

A link between a medical condition and nocturia should not be assumed in individual patients. Establishing a clinical link needs justification, such as successful treatment of the condition leading to clear-cut and simultaneous reduction in nocturia.

Table 3 sets out supplementary tests that might be considered for awareness of urologists. However, actual indications and test procedures followed are determined by local guidelines for testing, primary therapy, and potential specialist referral.

5. Treatment

It is appropriate to discuss the treatment strategy and expectations with the patient. This needs to cover both the medical condition and the nocturia symptom. Unfortunately, there can be a therapeutic conflict between these two considerations.

5.1. Treatment of the condition

1. Treatment focusses on established specialist priorities, relating to the condition and its prognosis.
2. Therapy of some medical conditions may potentially exacerbate nocturia:
   (a) As a consequence of therapeutic mechanism (eg, diuretics causing water loss).

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Table 3 – Supplementary evaluations following interpretation of initial testing results

Suspected sleep disorders
1. In-depth questions or questionnaires for RLS or OSA (eg, STOP-BANG [32])
2. Referral for overnight oximetry (usually to respiratory or ENT sleep clinic)
3. Ferritin level for RLS; supplementation if below 75 ng/ml associated with improved symptoms
4. If RBD is suspected, referral should be made to a sleep clinic (to reach diagnosis) and then to neurology if confirmed
5. Other suspected sleep disorders may be referred to a sleep clinic, where substantially impaired daytime function persists despite conservative treatment
Suspected cardiovascular disease
If it is suspected that heart failure may be contributing to nocturia, investigations should include:
1. Electrocardiogram
2. Brain natriuretic peptide; echocardiogram if positive
Known renal disease
1. Renal ultrasound (as per local guidelines for newly diagnosed chronic kidney disease)
2. Urine ACR
Suspected endocrine disorder
1. Where hypercalcaemia is detected; parathyroid hormone and endocrinology referral. Additionally, consider whether malignancy may be the cause and investigate accordingly
2. Morning urine osmolarity test after overnight fluid avoidance; concentrations above 600 mosm/l rule out diabetes insipidus. Indicated for patients urinating >2.5 l per 24 h despite attempts to reduce fluid intake
Known or suspected neurological disease
1. Lying/standing blood pressure—taken within 1st minute and at 3 min [34]; fall of 20 systolic or 10 diastolic is diagnostic for orthostatic hypotension and is suggestive of autonomic failure
2. Ability to undertake activities of daily living and review of home or living environment
3. Neurological disease may be suspected if there is new-onset severe LUTS (excluding infection), unusual aspects (eg, enuresis without chronic retention), or "suspicious" symptoms (eg, numbness, weakness, speech disturbance, gait disturbance, memory loss/cognitive impairment, and autonomic symptoms). These need direct referral to neurology [14]

ACR = urine albumin:creatinine ratio; ENT = ear, nose, and throat; LUTS = lower urinary tract symptoms; OSA = obstructive sleep apnoea; RBD = rapid eye movement sleep behaviour disorder; RLS = restless legs syndrome.

(b) Owing to secondary effects.
(c) If the condition is treated inadequately (eg, poor glycaemic control in diabetes).
(d) If there is a secondary effect on renal concentrating mechanism (eg, lithium).

3. Timing of medication doses, for example, diuretics, diabetes medications, and antiparkinsonian drugs, may need a review. The review should consider anticipated duration of drug effect, bearing the patient's usual bedtime in mind.

As an initial approach to the management of the SCREeN conditions in primary care, the following are recommended:

1. Sleep medicine. *Insomnia*: information/cognitive behavioural therapy. *OSA*: advice/support for weight loss. *RLS/PLMS*: investigate to identify a cause of iron deficiency and prescribe iron supplements (if low ferritin); reduce alcohol/-caffeine/nicotine, consider discontinuing antidepressant medication; dopamine agonists (risk of "augmentation" paradoxical worsening and impulse control disorders); pregabalin or codeine in low dose given at night only (risk of dependency). *Parasomnia*: advice on avoiding triggers, consider safety aspects for patient/bed partner.
2. Cardiovascular. Minimise salt intake, control fluid intake (1–2 l/d). *CHF*: manage according to local or national guidelines; adjust medication. *Hypertension*: improve BP control (target for clinic BP 140/90 mmHg for people under 80 yr or 150/90 for those over 80 yr of age [15]).
3. Renal. *CKD*: minimise salt intake; improve BP control.
4. Endocrine. Treat underlying endocrine dysfunction.
5. Neurology. Pelvic floor muscle training. Risk mitigation. Assess bowel function/manage constipation. Treat symptoms that affect ability to get to the toilet (eg, spasticity or severity of "off" state experienced overnight in Parkinson's disease).
6. Xerostomia. Consider whether medications can be adjusted (anxiolytics, antidepressants, antimuscarinics, antihistamines, decongestants, antiparkinsonians, pain medicines, or antipsychotics) or polypharmacy reduced. Consider options such as oxygenated glycerol triester saliva substitute spray or chewing gum to ameliorate symptoms, although evidence is weak [19].

Nocturia may improve with treatment of some of the SCREeN medical conditions, with the following provisos:

1. The condition is the direct and principal cause of the nocturia in that patient.
2. There is effective treatment available for the condition.
3. The patient is able to be concordant with treatment.
4. That frailty and life expectancy warrant a trial of treatment with the associated risks.

Persistence of nocturia could reflect insufficient response to treatment, nonconcordance with treatment, worsening of the condition, or multifactorial nocturia.

5.2. *Treatment of nocturia*

If nocturia persists, options to ameliorate the problem may be limited. Where nocturia is caused by an optimally controlled medical condition, urology referral is unlikely to identify any new therapeutic option.

The following should be discussed:

1. Behavioural advice:
   (a) Advice on sleep hygiene, for example, avoidance of detrimental behaviours and stimulants.
   (b) Discussion on whether adjusting disruptive sleep patterns is possible (eg, night shift working routines).
2. Advice regarding fluid intake is largely dictated by the circumstances of the individual case:

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(a) Many patients find that a guideline on fluid intake volume is helpful. The cardiovascular advice to control fluid intake to 1–2 l/d is suitable for many patients but should be considered on an individual basis.
(b) Thirst generally indicates need to catch up with fluid intake.
(c) Restricting fluid intake could worsen orthostatic hypotension.

3. Safety considerations: Patients must avoid situations that could be dangerous when excessively fatigued, for example, driving when sleepy. The environment at home may have risks that are exacerbated when someone is drowsy and disorientated by recent waking, for example, stairs.

5.3. *Considerations in older or frail patients*

With an ageing population throughout the world, associated with increasing medical complexity and comorbidity, it was deemed appropriate that special consideration should be given to the management of older patients with nocturia. Age itself should not specifically determine the nature or extent of investigation or management, though it affects the onset and prevalence of specific conditions. Older individuals are more likely to have a greater interaction between different dysfunctional systems, potentially complicating or frustrating the management of their nocturia. They are also more likely to be taking a large number of medications, which can increase the risk of nocturia. Hence, treatment should be individualised for each patient.

Intervention should be offered, particularly where nocturia is bothersome or could have a potential adverse impact. Assessment is necessary to explore the possibility of a reversible cause, but for some, the situation may not be remediable. Appropriate assessment can help the patient feel that their problems have been taken seriously.

Where treatment does not reduce nocturia, risk mitigation can help prevent adverse outcomes. Falls and consequent fractures can happen due to navigating the environment at night to visit the toilet. This risk may be reduced by consideration of the home environment, and practical advice on the use of commodes or the collection of urine in a handheld container. Fracture risk assessment tools (eg, FRAX; https://www.sheffield.ac.uk/FRAX/) evaluate the impact of multiple clinical factors to estimate fracture risk over a defined time interval [20]. It is important to consider prospective assessment of fracture risk in order to mitigate some of the downstream risks; collaboration with the primary care physician or geriatrician can be helpful.

Management of frail patients with limited life expectancy should be pragmatic, with consideration given to their cognition and capacity to make decisions. Often, the primary care doctor will have a good gauge of this situation.

Older people can be prone to side effects of medications, particularly those affecting the cholinergic system (which can affect cognition and walking). If a new prescription is offered, advice on discontinuing it in the event of side effects should be provided.

The use of indwelling catheters for treating nocturia was not supported by the consensus panel. Healthcare professionals and the patient should discuss the risks when making a decision to use a catheter, including catheter blockage and urosepsis. In severe cases of nocturia in neurological disease, an indwelling urinary catheter (potentially overnight only) might be considered where the risks of injury when toileting at night outweigh the potential harms of indwelling catheterisation.

6. Discussion

The urological causes of nocturia have been covered by guideline statements from relevant organisations [21,22]. The current guidance is complementary and reflects a pragmatic application of the conclusions of the five NGT consensus papers related to sleep medicine, cardiovascular medicine, endocrinology, nephrology, and neurology. Each of these papers incorporated an SR, though the evidence base was generally found to be limited and selective in each area. Thus, expert opinion underpins a substantial proportion of the recommendations.

The impact of the conditions can be extremely varied; for example, in sleep-disordered breathing (including OSA), some people experience little subjective daytime dysfunction. Indeed, going to pass urine may be part of a routine for getting back to sleep. Hence, the key driver for intervention is the impact on the patient's everyday life, determined by issues such as fatigue, inability to concentrate mentally, and negative effects on activities of daily living. The clinical course of the conditions is also varied. A chronic insidious course is common, and may allow disease to become established and potentially to progress. A relatively abrupt change in nocturia severity may be important, perhaps indicating onset (eg, diabetes insipidus) or progression.

The lists of assessments and therapies aim to be practical. It was not felt to be appropriate to provide an exhaustive description of the entire field, since the recommendations are intended for use in urology clinics, where expertise and clinical pathways are defined by the main clinical focus of the speciality. Completion of a bladder diary is the key, as it helps evaluate night-time frequency [23,24] and nocturnal polyuria [25,26]. The ICIQ bladder diary is suitable, as it is validated and includes a sensation scale used to identify the level of urgency for each void [27]. The sensation scale helps ascertain whether the patient experiences urinary urgency overnight [16]. In urology, administration and interpretation of a bladder diary are commonplace, along with the familiarity of the importance of standardised terminology [28], but this is often not the case in other specialities. Hence, this is an expectation of nocturia assessment in a urology clinic, even if it actually suggests that a medical condition is causative.

It is envisaged that the guidance can be adapted to reflect actual circumstances locally. Partnership with primary care providers is likely to be needed in many aspects, since common conditions such as DM, CHF, and hypertension are so important in nocturia and predominantly managed in a primary care setting. Measurement of BP is relevant in potential cardiovascular, renal, or endocrine disease. BP may be documented in the patient's referral letter, where recent primary care contacts are included (or many patients monitor their BP at home and will be aware of home readings). If recent readings are not available, it was felt suitable to include a one-off carefully conducted BP measurement in urology clinic settings, since a normal reading would direct further evaluation towards other possible mechanisms. An elevated BP would potentially need formal evaluation and

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appropriate therapy in primary care according to local guidance. Subsequent care related to the nocturia would be determined according to whether the nocturia improved/resolved.

Linking a condition to nocturia may be difficult to justify for some situations. Notably, well-treated DM was considered rather unlikely to be a key driver of nocturia in the expert consensus. On the contrary, medical conditions can be very influential for nocturia, and they can present a challenge for reducing nocturia, which may be insuperable with currently available interventions. This could be the case if no treatment is available or if the reduction in nocturia would be harmful in terms of the medical situation. Accordingly, it is important to discuss with the patient the priority given to overall health and the limitations of treatment, so they do not develop unrealistic expectations of nocturia improvement. The possible conflict between managing the medical condition and the nocturia symptom can be illustrated by considering the pressure changes of recumbency in blood vessels and the kidneys at bedtime, which can increase the likelihood of diuresis and natriuresis, and hence nocturia; since balance of water and salt is a clinical priority, prevention of diuresis or natriuresis to reduce nocturia may increase the risk of adverse effects of the underlying condition. On grounds of safety, therefore, the medical condition generally is prioritised over nocturia, meaning that the latter may well persist despite treatment.

Nocturia should improve with the treatment of the medical condition if the condition is the principal cause of nocturia in that patient, there is effective treatment, and compliance is good. For example, OSA is clearly recognised to cause nocturia and continuous positive airway pressure (CPAP) can reduce nocturia substantially. Unfortunately, many people do not tolerate the CPAP therapy well and so may not use the treatment reliably. This raises an issue that referral letters may mention CPAP based on the provision of equipment for use at home, but this does not necessarily mean that the patient is using it.

Medication adjustment is an important aspect of the recommendations. Clearly, this must be undertaken bearing in mind the condition for which the medication was prescribed, such that dialogue with the relevant prescriber is likely to be necessary. Fluid advice also needs to consider the overall needs of a patient, and recommendations to reduce intake may conflict with other conditions needing high fluid intake (eg, history of renal stones or conditions causing fluid loss). People who consciously drink large quantities of water to maintain a healthy lifestyle, referred to as dipsogenic polydipsia (compulsive water drinking), perceive that it improves or maintains good health. Recommendations to control the water intake can pose a compliance problem, particularly if there is a psychogenic aspect to polydipsia [29]. Potentially high volumes of beer, given its low solute content, can cause dilutional hyponatraemia and reduced clearance of excess fluid from the body, referred to as beer potomania [30]. Dealing with this can represent a further challenge in terms of compliance.

The evidence base identified by the SRs was restricted and selective. There were methodological limitations, relating to both the medical conditions and the associated nocturia. Common issues included incomplete reporting of baseline condition or progression during the study, failure to describe confounding variables, and use of subjective measures. Hence, there is considerable uncertainty relating to assessment and therapy, and a strong need for more information to guide future recommendations.

A short-term course of diuretic for subclinical salt and water retention is sometimes tried for nocturia patients [31]. However, the NGT consensus did not support this as a routine option in urology clinic, since ascertaining the presence of subclinical oedema is not standard urological assessment, an overview of the patient's full health picture may be lacking, and access to early follow-up is not reliable. Likewise, compression stockings were not recommended by the cardiovascular NGT, as cardiologists would generally advise these only for peripheral oedema if it was noncardiac in origin. There is moderately robust evidence for medical compression stockings in patients with venous symptoms for prevention and treatment of venous oedema [32]. These have been studied for the treatment of nocturia due to oedema in spinal cord injury [33]. Unfortunately, compression stockings can be difficult to fit and uncomfortable, and can lead to excessive warmth. Elevation of the legs in the evening is usually recommended for dependent oedema, and can be considered in patients with heart failure and peripheral oedema. However, there is no clear indication that this will consistently achieve useful reduction in nocturia.

7. Conclusions

The initial assessment and therapy of nocturia need to consider the possibility of one or more medical conditions from disease areas that can affect salt and water handling or sleep quality. Some key indicators for these can be identified in urology clinics and may require subsequent partnership working with the primary care provider. Therapy of the medical condition in some circumstances brings symptom relief of nocturia. However, in many cases there is a conflict between the two, in which case the medical condition generally takes priority on safety grounds.

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Study concept and design: Drake, Dawson, Rees, Henderson.
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